NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of PDR001 given with other drugs in people with certain types of melanoma

Thank you!

Thank you to the participants who took part in the clinical trial for certain types of melanoma. Every participant helped the researchers learn more about the trial drug **PDR001**, also called spartalizumab, given with other drugs.

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: CPDR001J2201

Novartis drug studied: 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 findings.

What was the main purpose of this trial?

Researchers are looking for new ways to treat certain types of melanoma that got worse after previous treatment. The purpose of this trial was to learn how well **PDR001** works when given with other drugs in people with unresectable or metastatic melanoma.

Unresectable or metastatic melanoma is a skin cancer that cannot be removed by surgery or has spread to other parts of the body. Available treatments do not always work or stop working to treat these types of melanoma.

PDR001, also called spartalizumab (pronounced as spar-ta-liz-ue-mab), is an immunotherapy drug. It blocks a specific protein in the immune system that can stop the immune system from killing cancer cells.

In this trial, participants were in treatment groups in which they received PDR001 with one of these other drugs:

- **LAG525**, also known as ieramilimab (pronounced as ee-er-uh-mil-i-mab), which is an immunotherapy
- **INC280**, also known as capmatinib (pronounced as cap-ma-tin-nib), which is a targeted therapy
- **ACZ885**, also known as canakinumab (pronounced as kan-a-kin-ue-mab), which is an immunotherapy
- **LEE011**, also known as ribociclib (pronounced as rye-boe-sye-klib), which is a targeted therapy

Immunotherapy is a cancer treatment that uses the body's own immune system to find and fight cancer.

Targeted therapy is a cancer treatment that targets (works on) proteins that control how cancer cells grow, copy, and spread.

The trial purpose was to answer these main questions:

- How many participants in each treatment group had their tumors shrink or disappear?
- What adverse events did the 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 September 2018 and ended in December 2022.

This trial was designed to have 2 Parts:

- **Part 1:** Most participants had an equal chance of receiving PDR001 with one of these other drugs: LAG525, INC280, ACZ885, or LEE011. In June 2020, researchers added another group of participants who received PDR001 and LAG525. Participants were assigned to this group if their cancer had a certain result on genetic tests.
- **Part 2:** Researchers planned to assign treatment combinations that worked in Part 1 to more participants. However, data from Part 1 showed that none of the treatment combinations had enough of an effect on participants' cancer. Because of this, Part 2 did not start.

Who was in this trial?

196 participants with unresectable or metastatic melanoma were in this trial. Participants' ages ranged from 21 to 83 years.

195 participants received treatment in this trial. 1 participant decided to leave the trial before starting treatment.

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

Gender

120 Men	76 Women

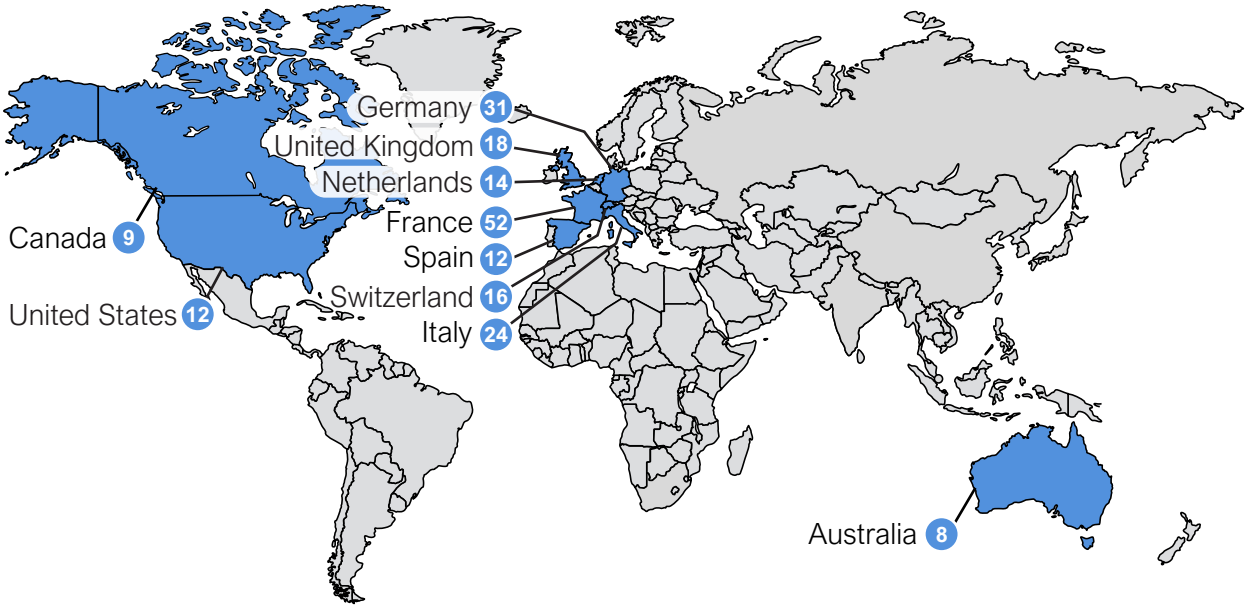
Race

2 Asian	187 White	7 Unknown

The participants could take part in this trial if they:

- Had previously received treatment for their melanoma
- Didn't have any other cancers, other than unresectable or metastatic melanoma

196 participants took part in 10 countries. 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:

PDR001, 400 milligrams (mg), given through a needle into a vein as an intravenous (IV) infusion once a month with one of the drugs below:

- **LAG525**, 600 mg, given as an IV infusion once a month
- **INC280**, 400 mg, taken by mouth as tablets twice a day
- **ACZ885**, 300 mg, given as injections under the skin (subcutaneous) once a month
- **LEE011**, 600 mg, taken by mouth as tablets once a day for 3 weeks every month

Each participant received their treatment for as long as the researchers thought the participant was benefiting from the treatment.

In this trial, the participants and clinical trial team knew what treatment each participant took.

What happened during this trial?

Before treatment — 1 month

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

During treatment — Up to 4 years

195 participants received treatment in one of these groups:

Group 1:	**PDR001** + **LAG525**	45 participants
Group 2:	**PDR001** + **INC280**	43 participants
Group 3:	**PDR001** + **ACZ885**	42 participants
Group 4:	**PDR001** + **LEE011**	44 participants
Group 1A:	**PDR001** + **LAG525**	21 participants

Researchers randomly assigned participants to Groups 1 through 4 using a computer.

After participants in Groups 1 through 4 had received treatment, researchers added Group 1A because a planned, early data analysis suggested that PDR001 with LAG525 may be more likely to shrink tumors if the cancer had a certain result on genetic tests.

To confirm this, researchers added more participants who had certain genetic test results and assigned them to Group 1A. Trial doctors checked the participants' melanoma and general health throughout the trial.

After treatment — 5 months after treatment or until the trial ended

Participants returned to their trial site about once a month for up to 5 months after receiving their last dose of treatment for trial doctors to check their health and melanoma. Trial staff also contacted participants by phone every 3 months until the end of the trial.

What were the main results of this trial?

How many participants in each treatment group had their tumors shrink or disappear?

Less than 15% of participants in each group had their tumors shrink or disappear after treatment.

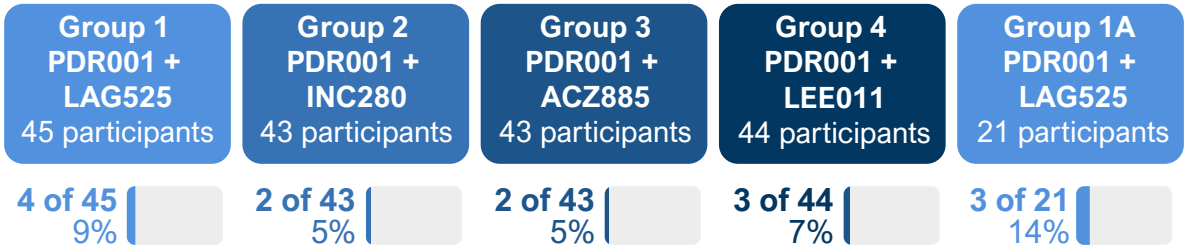
To learn this, researchers looked at the participants' physical exams and imaging tests to measure the change in the size of their tumors.

Before the trial started, the researchers decided that they would conclude a treatment combination did not have enough of an effect if:

- **15% or less** of participants in Groups 1, 2, 3, and 4 had their tumors shrink or disappear after up to 4 years of treatment
- **20% or less** of participants in Group 1A had their tumors shrink or disappear after up to 1 and a half years of treatment

In each treatment group, less than 15% of participants had their tumors shrink or disappear.

Participants who had their tumors shrink or disappear



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 treatment** (from first dose of treatment to 30 days after the last dose)
- **During safety follow-up** (31 to 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 had adverse events. Almost half had adverse events that were considered serious. About a third of the participants died during this trial, mostly due to melanoma. The researchers concluded the safety results for the treatments in this trial were similar to other trials for these treatments.

How many participants had adverse events?

During treatment and up to 30 days after last dose

	Group 1 PDR001 + LAG525 45 participants	Group 2 PDR001 + INC280 43 participants	Group 3 PDR001 + ACZ885 42 participants	Group 4 PDR001 + LEE011 44 participants	Group 1A PDR001 + LAG525 21 participants
Had at least 1 **serious adverse event**	21 of 45	21 of 43	12 of 42	22 of 44	7 of 21
Had at least 1 **other adverse event**	40 of 45	42 of 43	32 of 42	44 of 44	18 of 21
Left the trial due to an adverse event	3 of 45	3 of 43	5 of 42	11 of 44	1 of 21
Died during treatment	5 of 45	3 of 43	3 of 42	3 of 44	1 of 21

During safety follow-up, 31 to 150 days after last dose

	Group 1 PDR001 + LAG525 45 participants	Group 2 PDR001 + INC280 43 participants	Group 3 PDR001 + ACZ885 42 participants	Group 4 PDR001 + LEE011 44 participants	Group 1A PDR001 + LAG525 21 participants
Had at least 1 **serious adverse event**	5 of 45	0 of 43	4 of 42	8 of 44	2 of 21
Had at least 1 **other adverse event**	5 of 45	6 of 43	5 of 42	10 of 44	2 of 21
Died during the safety follow-up	14 of 45	11 of 43	15 of 42	11 of 44	4 of 21

What serious adverse events did the participants have?

During treatment and up to 30 days after last dose

83 participants had serious adverse events during treatment, and 15 of these participants died. Most of the deaths were related to melanoma.

The table below shows the most common serious adverse events that happened in 2 or more participants in any group.

	Group 1 PDR001 + LAG525 45 participants	Group 2 PDR001 + INC280 43 participants	Group 3 PDR001 + ACZ885 42 participants	Group 4 PDR001 + LEE011 44 participants	Group 1A PDR001 + LAG525 21 participants
Pain around the area of the tumor Tumor pain	1 of 45 2%	1 of 43 2%	2 of 42 5%	1 of 44 2%	0 of 21 0%
Belly pain Abdominal pain	0 of 45 0%	2 of 43 5%	1 of 42 2%	1 of 44 2%	0 of 21 0%
Feeling sick to the stomach Nausea	2 of 45 4%	1 of 43 2%	1 of 42 2%	0 of 44 0%	0 of 21 0%
Pain in the arms or legs Pain in extremity	1 of 45 2%	0 of 43 0%	1 of 42 2%	2 of 44 5%	0 of 21 0%
Bleeding in a tumor Tumor hemorrhage	2 of 45 4%	0 of 43 0%	0 of 42 0%	0 of 44 0%	0 of 21 0%
Broken bone Pathological fracture	0 of 45 0%	0 of 43 0%	0 of 42 0%	0 of 44 0%	2 of 21 10%
Fever Pyrexia	0 of 45 0%	0 of 43 0%	0 of 42 0%	2 of 44 5%	0 of 21 0%
Liver disease from an immune system disorder Immune-mediated hepatitis	0 of 45 0%	0 of 43 0%	0 of 42 0%	2 of 44 5%	0 of 21 0%
Unusual physical condition General physical condition abnormal	2 of 45 4%	0 of 43 0%	0 of 42 0%	0 of 44 0%	0 of 21 0%

During safety follow-up, 31 to 150 days after last dose

19 participants had serious adverse events during the safety follow-up, and 58 participants died.

The table below shows the most common serious adverse events that happened in 2 or more participants in any group:

	Group 1 PDR001 + LAG525 45 participants	Group 2 PDR001 + INC280 43 participants	Group 3 PDR001 + ACZ885 42 participants	Group 4 PDR001 + LEE011 44 participants	Group 1A PDR001 + LAG525 21 participants
Lung infection Pneumonia	2 of 45 4%	0 of 43 0%	0 of 42 0%	0 of 44 0%	0 of 21 0%
Fever Pyrexia	0 of 45 0%	0 of 43 0%	0 of 42 0%	2 of 44 5%	0 of 21 0%

What other adverse events did the participants have?

During treatment and up to 30 days after last dose

176 participants had other adverse events during treatment.

The table below shows the most common other adverse events that happened in 15 or more participants in any group.

	Group 1 PDR001 + LAG525 45 participants	Group 2 PDR001 + INC280 43 participants	Group 3 PDR001 + ACZ885 42 participants	Group 4 PDR001 + LEE011 44 participants	Group 1A PDR001 + LAG525 21 participants
Feeling sick to the stomach Nausea	13 of 45 29%	18 of 43 42%	9 of 42 21%	15 of 44 34%	6 of 21 29%
A possible sign of liver damage Aspartate amino-transferase increase	1 of 45 2%	5 of 43 12%	3 of 42 7%	17 of 44 39%	1 of 21 5%
A possible sign of liver damage Alanine amino-transferase increase	1 of 45 2%	6 of 43 14%	2 of 42 5%	15 of 44 34%	1 of 21 5%
A low number of a type of white blood cells Neutropenia	3 of 45 7%	0 of 43 0%	1 of 42 2%	20 of 44 45%	0 of 21 0%

During safety follow-up, 31 to 150 days after last dose

28 participants had other adverse events during follow-up.

The table below shows the most common other adverse events that happened in 2 or more participants in any group.

	Group 1 PDR001 + LAG525 45 participants	Group 2 PDR001 + INC280 43 participants	Group 3 PDR001 + ACZ885 42 participants	Group 4 PDR001 + LEE011 44 participants	Group 1A PDR001 + LAG525 21 participants
Low levels of red blood cells Anemia	2 of 45 4%	1 of 43 2%	1 of 42 2%	0 of 44 0%	1 of 21 5%
Feeling weak or not having energy Asthenia	1 of 45 2%	1 of 43 2%	0 of 42 0%	2 of 44 5%	0 of 21 0%
Feeling sick to the stomach Nausea	0 of 45 0%	0 of 43 0%	1 of 42 2%	2 of 44 5%	0 of 21 0%
Feeling less hungry than usual Decreased appetite	0 of 45 0%	1 of 43 2%	0 of 42 0%	2 of 44 5%	0 of 21 0%
Pain in the arms or legs Pain in extremity	0 of 45 0%	2 of 43 5%	0 of 42 0%	1 of 44 2%	0 of 21 0%
Weight loss Weight decreased	0 of 45 0%	0 of 43 0%	1 of 42 2%	2 of 44 5%	0 of 21 0%
A possible sign of liver damage Alanine amino-transferase increased	0 of 45 0%	0 of 43 0%	1 of 42 2%	2 of 44 5%	0 of 21 0%
Fever Pyrexia	0 of 45 0%	0 of 43 0%	0 of 42 0%	2 of 44 5%	0 of 21 0%
A possible sign of certain health conditions Blood lactate dehydrogenase increased	2 of 45 4%	0 of 43 0%	0 of 42 0%	0 of 44 0%	0 of 21 0%
Pain	0 of 45 0%	0 of 43 0%	0 of 42 0%	2 of 44 5%	0 of 21 0%

What was learned from this trial?

Researchers learned more about the effects of PDR001 given with other trial drugs in people with unresectable or metastatic melanoma.

The researchers concluded that none of the treatment combinations could effectively shrink melanoma tumors in enough participants.

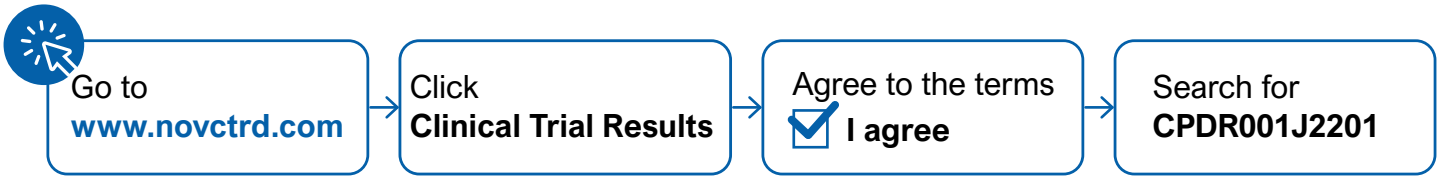
The researchers concluded the safety results for the treatments in this trial were similar to other trials for these treatments.

When this summary was written, there were no plans for future trials of PDR001 in people with certain types of melanoma.

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 **NCT03484923**
- clinicaltrialsregister.eu/ctr-search/search – search using the number **2018-000610-38**

Full clinical trial title: A randomized, open-label, phase II open platform study evaluating the efficacy and safety of novel spartalizumab (PDR001) combinations in previously treated unresectable or metastatic melanoma

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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