NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of PDR001 and LAG525 in people with advanced cancer

Protocol number: CPDR001XUS01

Thank you!

Novartis sponsored this trial and believes it is important to share the results of the trial with you and the public. Thank you for taking part in this trial for the drugs **PDR001, also known as spartalizumab, and LAG525**. You helped researchers learn more about how PDR001 and LAG525 work in **people with advanced cancer**, which is unlikely to be cured or controlled with treatment.

This summary only shows the results of one clinical trial. Other clinical trials may have different findings. Researchers and health authorities look at the results of many clinical trials to understand which drugs work and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

Why was the research needed?

Researchers are looking for a better way to treat advanced and metastatic cancer that relapsed or is refractory:

- **Advanced** describes cancer that is unlikely to be cured or controlled with treatment
- **Metastatic** means cancer has spread to other parts of the body
- **Relapsed** means cancer came back after treatment
- **Refractory** means approved treatments didn't work to shrink or stop cancer growth

Researchers think certain trial drugs could help the immune system fight these types of cancers. This trial looked at a combination of 2 trial drugs, which could help the immune system kill cancer cells by blocking 2 different proteins.

Trial drugs

The drugs given in this trial were:

PDR001, which is a trial drug designed to help the immune system fight cancer by blocking a protein called PD-1, which can prevent the immune system from killing cancer cells. It was given as an intravenous (IV) infusion, which is through a needle in a vein.

LAG525, which is a trial drug designed to be like PDR001, but it blocks a protein called LAG-3, which can prevent the immune system from killing cancer cells. It was given as an IV infusion.

Trial purpose

The main purpose of this trial was to learn about the effects and safety of PDR001 combined with LAG525 for people with certain types of cancer.

The main questions the researchers wanted to answer in this trial were:

- What percent of participants had tumors that shrank or stopped growing after treatment with PDR001 and LAG525?
- What medical problems did the participants have during the trial?

How long was this trial?

This trial started in January 2018 and ended in September 2020. It was designed so that each participant could take part for about 2.5 years, or until their cancer got worse, they had a severe medical problem, or they decided to leave the trial.

The trial was designed to recruit more participants if early results suggested that PDR001 combined with LAG525 may be worth studying as a possible treatment for a certain type of cancer. After the first group of participants joined the trial, the sponsor decided not to recruit more participants for any type of cancer. During this trial, more treatments that help the immune system fight the types of cancer in this trial became available for patients to use. Because the participants in this trial could not have received these other types of treatment before starting this trial, recruitment became more difficult. This led to the sponsor's decision to not recruit more participants. The decision to end recruitment was not related to safety.

Because of the limited number of participants with each type of cancer, there was not enough data for the researchers to be sure the results were meaningful.

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

Who was in this trial?

76 participants were in this trial – 45 men and 31 women. Participants' ages ranged from 25 to 86 years. Their average age was 65 years.

The participants could take part in this trial if they had 1 of 7 cancers that the researchers thought PDR001 combined with LAG525 might shrink or stop growth. These included:

Type of cancer (number participants) Medical term for the cancer type	**Part of the body where it first formed**
Neuroendocrine cancer (7 participants) Advanced well-differentiated neuroendocrine tumors	Neuroendocrine cells, which receive messages from the nervous system (nerves) and also make hormones. They are mainly found in the small intestine, pancreas, and lungs.
Prostate cancer (11 participants) Castrate resistant prostate adenocarcinoma	Prostate (the organ in men that makes a fluid that mixes with sperm to make semen)
B-cell lymphoma (9 participants) Diffuse large B-cell lymphoma (DLBCL)	White blood cells called lymphocytes
Gastric/esophageal cancer (13 participants) Gastric/esophageal adenocarcinoma	Stomach or esophagus (the tube that connects the mouth to the stomach)
Ovarian cancer (10 participants) Ovarian adenocarcinoma	Ovaries (the pair of organs in women where eggs are made)
Lung cancer (16 participants) Small cell lung cancer (SCLC)	Lungs
Soft tissue cancer (10 participants) Soft tissue sarcoma	Soft body tissues, such as muscle, fat, or blood vessels

The participants could not have received certain treatments that help the immune system fight cancer before joining this trial. Participants took part at 20 trial sites in the United States.

What kind of trial was this?

This was an open-label trial, which means that the participants and clinical trial team knew what treatment each participant received. In this trial, all participants received PDR001 and LAG525.

What happened during this trial?

Up to **3 weeks** before treatment

During screening

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

76 participants took part in this trial.

About **2 years**

During treatment

Each participant received a separate infusion for each of these drugs:

- **PDR001**, one infusion, every 3 weeks for about 30 minutes
- **LAG525**, one infusion, every 3 weeks for about 30 minutes

The participants received the infusions on the same day, with a break in between infusions. The length of time the participants received their trial treatments ranged from about 3 weeks to 2 years.

Each participant could continue to receive the trial drugs until their cancer got worse, they had a serious medical problem, or they decided to leave the trial. 4 participants completed the full 2 years of treatment. The most common reason participants did not complete the full 2 years of treatment was because their cancer got worse.

Researchers checked the participants' cancer and general health throughout the trial.

About **5 months** after treatment

During post-treatment follow-up

Participants returned to their trial site or spoke to trial staff on the phone about once a month after receiving their last dose of treatment.

What were the main results of this trial?

This is a summary of the overall results for all participants. It does not show the results of each individual participant. Results of individual participants could be different from the results of the total group of participants. More details on the results can be found on the websites listed at the end of this summary.

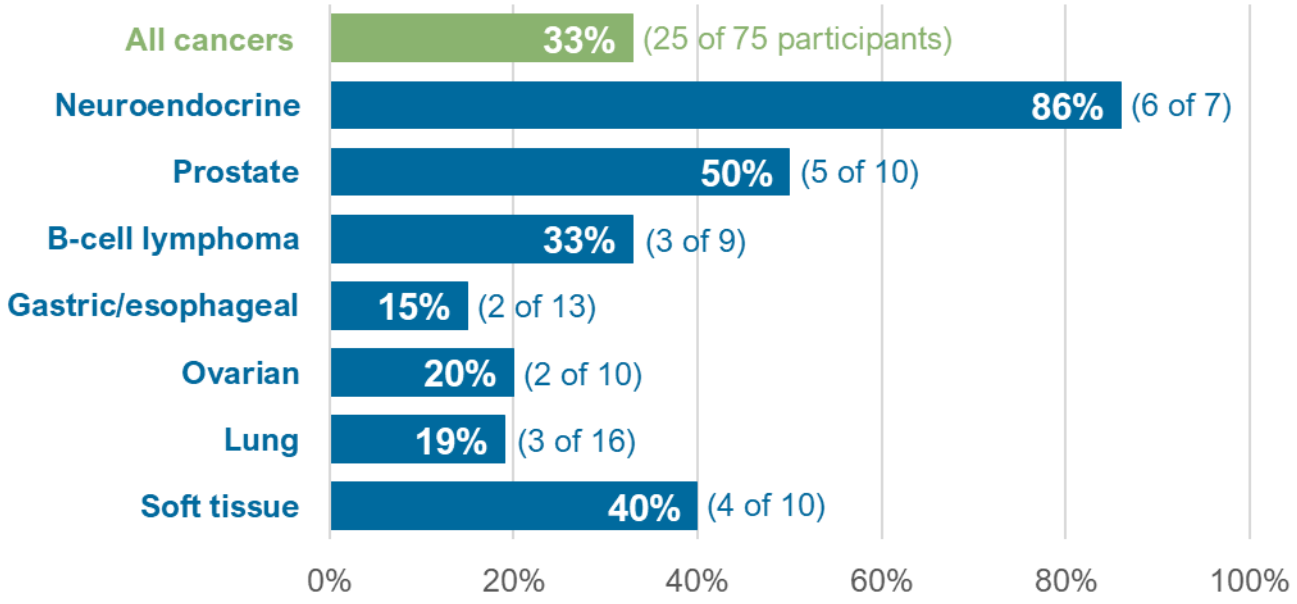
What percent of participants had tumors that shrank or stopped growing after treatment with PDR001 and LAG525?

During certain visits to the trial site, trial staff used imaging scans to measure the size of participants' tumors. They used this information to calculate the **Clinical Benefit Rate (CBR)**. The CBR is the percent of participants whose tumors shrank or stopped growing after receiving the trial treatment.

In the first 24 weeks after starting treatment, about 33% of the participants (25 out of 75 participants) had tumors that shrank or stopped growing. The researchers also looked at the average CBR for each of the 7 types of cancer.

Clinical Benefit Rate (CBR) in the first 24 weeks after starting treatment

The graph below shows the average percent of participants whose tumors shrank or stopped growing overall and for each type of cancer.



Note: This graph does not include one participant with prostate cancer whose tumor size was not measured at the start of the trial.

What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called "**adverse events**". An adverse event is an unwanted sign or symptom that participants have during a trial. An adverse event is considered "**serious**" when it is life-threatening, causes lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial drug.

A lot of research is needed to know whether a drug causes an adverse event. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug. So, when new drugs are being studied, researchers keep track of all adverse events the participants have.

This section is a summary of the adverse events that happened during treatment and follow-up. The websites listed at the end of this summary have more information about the adverse events that happened in this trial.

What were the most common serious adverse events?

31 participants had serious adverse events during treatment.

Serious adverse events that happened in at least **3 out of 76 participants** (4% of participants):

	PDR001 combined with LAG525
	Number out of 76 participants (percent %)
Lung infection that fills the lungs with fluid Pneumonia	**5 participants** (7%)
Lack of energy and strength Asthenia	**3 participants** (4%)

A total of 27 participants died during the trial – 9 died during treatment and 18 died during the post-treatment follow-up. The main reason these participants died was because their cancer got worse.

What were the most common non-serious adverse events?

74 participants had adverse events that were not considered serious during treatment.

Non-serious adverse events that happened in at least **20 out of 76 participants** (26% of participants):

	PDR001 combined with LAG525
	Number out of 76 participants (percent %)
Feeling tired Fatigue	**28 participants** (37%)
Feeling sick to the stomach Nausea	**26 participants** (34%)
Less hungry than usual Decreased appetite	**22 participants** (29%)
Throwing up Vomiting	**20 participants** (26%)
Trouble passing stool Constipation	**20 participants** (26%)

One participant reported feeling sick to the stomach during follow-up.

How has this trial helped?

The sponsor decided not to recruit more participants because it became difficult to recruit cancer patients who had not already received treatments designed to help the immune system fight cancer. This decision meant that the trial did not have enough participants with each cancer type to conclude if PDR001 combined with LAG525 worked to shrink or stop tumor growth.

The researchers found that:

- The participants had mostly mild side effects after receiving treatment
- About 33% of the participants' (25 out of 75 participants') tumors shrank or stopped growing for some amount of time

To see if Novartis has other clinical trials on PDR001 and LAG525, visit the websites on the next page and search for "PDR001", "spartalizumab", and "LAG525."

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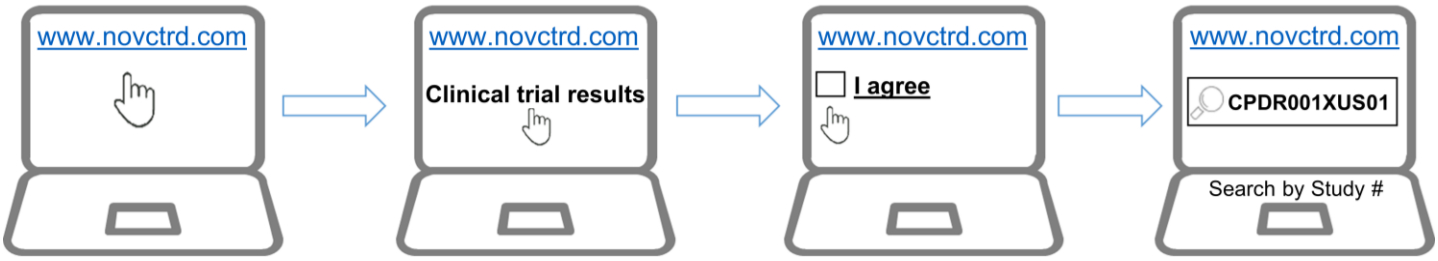
Where can I learn more about this trial?

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).



You can find more information about this trial on this website:

- www.clinicaltrials.gov. Use the NCT identifier **NCT03365791** in the search field.

Full clinical trial title: Modular phase 2 study to link combination immune-therapy to patients with advanced solid and hematologic malignancies. Module 9: PDR001 plus LAG525 for patients with advanced solid and hematologic malignancies.

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of participants around the world. You helped researchers answer important health questions and test new medical treatments.

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

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