NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the safety of LHC165 given alone or with PDR001 in people with certain types of advanced cancer

Clinical trial protocol number: CLHC165X2101

Thank you!

Thank you to the participants who took part in the clinical trial for the drugs **LHC165** and **PDR001**.

All the participants helped the researchers learn more about LHC165 given alone or with PDR001 in people with certain types of **advanced cancer**. Novartis sponsored this clinical trial and believes it is important to share what was learned from the results of this trial.

Clinical trial participants belong to a large community of people around the world. Their invaluable contribution to medicine and healthcare is greatly appreciated.

? **If you or your loved one was a participant and you have 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.

Why was the research needed?

Researchers are looking for better ways 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

LHC165 is a trial drug designed to activate (turn on) certain cells in the immune system that attack cancer cells. It is injected directly into the tumor.

PDR001, also known as spartalizumab, is a trial drug designed to help the immune system fight cancer by blocking a certain protein that allows cancer to grow.

Trial purpose

The main purpose of this trial was to learn more about the safety of different doses of LHC165 given alone or with PDR001 in people with certain types of advanced cancer.

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

- What was the highest dose of LHC165 that was safe for participants to receive alone or with PDR001?
- What medical problems did the participants have during the trial?

How long was this trial?

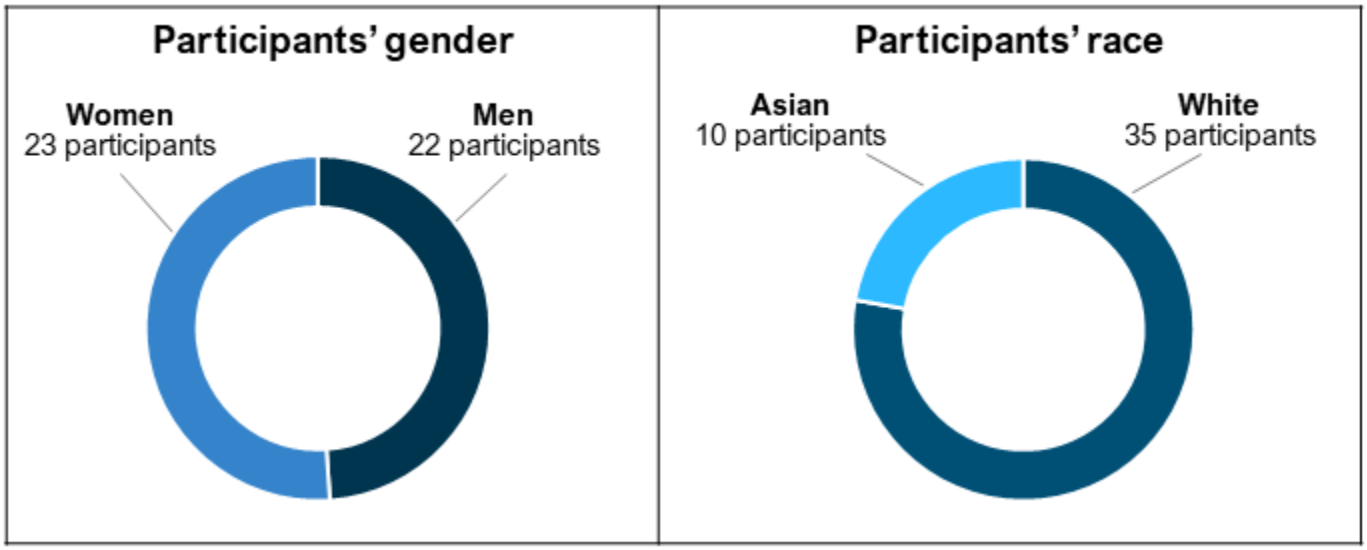
This trial was designed so that each participant could take part for up to about 4 years. The trial started in January 2018 and ended in June 2022.

The sponsor decided to end enrollment early due to difficulty finding participants to join the trial. The decision to stop early was not due to safety concerns. Participants who received PDR001 during this trial had the option to join another trial (CPDR001X2X01B) to continue receiving PDR001. Participants who received LHC165 alone did not have the option to join another trial to continue receiving it.

When this trial ended, the researchers collected information on the trial treatments and created a report of the trial results. This summary is based on that report.

Who was in this trial?

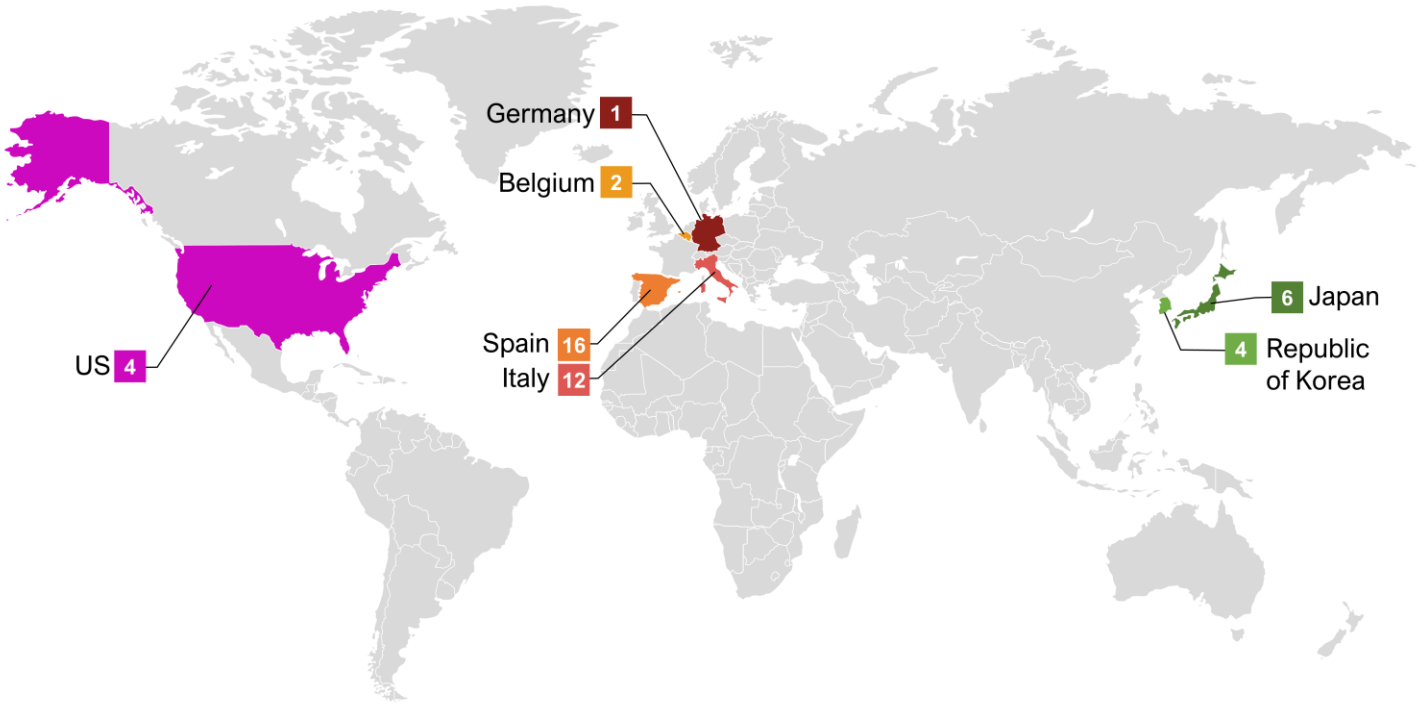
45 participants received treatment in this trial. Participants' ages ranged from 26 to 82 years. Their average age was 56 years.



The participants could take part in this trial if they:

- Had certain types of metastatic or advanced cancer with a **solid tumor** (a group of cells that is not in liquid such as blood), including:
  - Skin cancer (cutaneous melanoma)
  - Head and neck cancer (head and neck squamous cell carcinoma)
- Had relapsed or refractory cancer
- Had not received certain other cancer treatments

Participants took part at 9 trial sites in 7 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:

LHC165 given as an injection directly into the tumor (intratumoral injection). Participants received LHC165 every 2 weeks for up to 8 doses. After participants received their first 4 doses, they had a pause for 8 weeks before receiving the rest of their doses.

PDR001, 400 milligrams (mg), given through a needle in a vein as an intravenous (IV) infusion every 4 weeks. Some participants received PDR001 until they left the trial or the trial ended.

In this trial, the participants and clinical trial team knew what treatment each participant received. In this trial, all participants received LHC165, either alone or with PDR001.

What happened during this trial?

This trial was designed to have 2 parts:

- **Part 1** looked at the safety of increasing doses of LHC165 given alone or with PDR001 in small groups of participants to chooses doses for Part 2
- **Part 2** was not completed, but was designed to look at the safety and effects of the chosen doses of LHC165 given alone or with PDR001 in a larger group of participants

Before treatment

Before treatment

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

45 participants took part in this trial. Then, the sponsor stopped enrollment early.

Up to 4 years

During treatment

Participants were in 1 of 8 treatment groups based on when they joined the trial.

In Part 1, participants in Group 1 started treatment first and received the lowest dose of **LHC165 alone.** If there were no safety concerns after participants completed 4 weeks of treatment, the next group started treatment with a higher dose. This continued with each group receiving higher doses of LHC165 alone or with PDR001, until researchers found the highest dose that was safe for participants to receive.

In Part 2, more participants joined Group 8 to confirm the highest dose of LHC165 was safe.

		Dose of LHC165	Dose of PDR001
Group 1	4 participants	100 µg LHC165	None
Group 2	4 participants	200 µg LHC165	None
Group 3	9 participants	400 µg LHC165	None
Group 4	4 participants	600 µg LHC165	None
Group 5	3 participants	100 µg LHC165	400 mg PDR001
Group 6	4 participants	200 µg LHC165	400 mg PDR001
Group 7	8 participants	400 µg LHC165	400 mg PDR001
Group 8	9 participants	600 µg LHC165	400 mg PDR001

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

Up to 5 months

After treatment

Participants who received **LHC165 alone** returned to the trial site 1 month after their last dose for a follow-up visit.

Participants who received **LHC165** with **PDR001** returned to the trial site 1, 3, and 5 months after their last dose of trial treatment for a follow-up visit.

Some participants also visited the trial site every 2 to 3 months for researchers to check their tumors.

What was the main result of this trial?

What was the highest dose of LHC165 that was safe for participants to receive alone or with PDR001?

The researchers concluded that **600 µg LHC165** was the highest dose that was safe for participants to receive alone or with 400 mg PDR001.

To learn this, researchers looked at the participants' physical exams, imaging tests, and blood tests, and kept track of participants who had **dose limiting toxicities (DLTs)** up to 4 weeks after starting treatment with LHC165 alone or with PDR001.

Before this trial started, the researchers decided which medical problems were DLTs based on their type, severity, and timing. The participants assigned to higher dose levels of LHC165 received a higher overall total amount (dose intensity) of treatment.

A **dose limiting toxicity (DLT)** is a medical problem with risk of serious harm if the dose went up. DLTs are not related to cancer and the researchers think they could possibly be related to the trial treatment.

In **Group 7**, **400 µg LHC165** with **400 mg PDR001**, 1 of the 8 participants had a DLT. The DLT was inflammation of the pancreas (pancreatitis).

From these results, the researchers chose **600 µg LHC165** alone or with **400 mg PDR001** to use in Part 2.

Number of participants who had a DLT up to 4 weeks after starting treatment

	Group 1 4 participants	Group 2 4 participants	Group 3 9 participants	Group 4 4 participants	Group 5 3 participants	Group 6 4 participants	Group 7 8 participants	Group 8 9 participants
Dose of LHC165	100 µg	200 µg	400 µg	600 µg	100 µg	200 µg	400 µg	600 µg
Dose of PDR001	None	None	None	None	400 mg	400 mg	400 mg	400 mg
Participants who had DLTs	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**1** 13%	**0** 0%

What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called "**adverse events**".

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

This section is a summary of the adverse events that happened up to:

- 1 month after the last dose of trial treatment for participants who received **LHC165 alone**
- 5 months after the last dose of trial treatment for participants who received **LHC165** with **PDR001**

An **adverse event** is any 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 treatment.

The websites listed at the end of this summary have more information about the adverse events that happened in this trial.

How many participants had adverse events?

	Group 1 4 participants	Group 2 4 participants	Group 3 9 participants	Group 4 4 participants	Group 5 3 participants	Group 6 4 participants	Group 7 8 participants	Group 8 9 participants
Dose of LHC165	100 µg	200 µg	400 µg	600 µg	100 µg	200 µg	400 µg	600 µg
Dose of PDR001	None	None	None	None	400 mg	400 mg	400 mg	400 mg
Participants who had at least 1 adverse event	3 75%	3 75%	7 78%	4 100%	3 100%	4 100%	7 88%	9 100%
Participants who had at least 1 serious adverse event	1 25%	1 25%	1 11%	2 50%	0 0%	1 25%	3 38%	1 11%
Participants who left the trial due to an adverse event	1 25%	0 0%	0 0%	0 0%	0 0%	0 0%	1 13%	0 0%
Participants who paused their dose of LHC165 due to an adverse event	0 0%	0 0%	1 11%	0 0%	0 0%	1 25%	2 25%	1 11%
Participants who paused their dose of PDR001 due to an adverse event					0 0%	1 25%	1 13%	1 11%
Deaths due to any cause	0 0%	0 0%	2 22%	1 25%	0 0%	1 25%	0 0%	0 0%

What were the most common serious adverse events?

There were 4 deaths reported during this trial. The most common cause of death was cancer that got worse.

10 of 45 participants (22%) had serious adverse events.

The table below shows the **most common categories of serious adverse events** that happened in 2 or more of all participants:

	Group 1 4 participants	Group 2 4 participants	Group 3 9 participants	Group 4 4 participants	Group 5 3 participants	Group 6 4 participants	Group 7 8 participants	Group 8 9 participants
Dose of LHC165	100 µg	200 µg	400 µg	600 µg	100 µg	200 µg	400 µg	600 µg
Dose of PDR001	None	None	None	None	400 mg	400 mg	400 mg	400 mg
Problems with the stomach and digestive tract Gastrointestinal disorders 3 participants								
Pain in the lower belly Abdominal pain lower	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**1** 11%
Something blocking movement in the intestines Intestinal obstruction	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**1** 25%	**0** 0%	**0** 0%
Inflammation in the pancreas Pancreatitis	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**1** 13%	**0** 0%
Problems in the blood or lymph nodes Blood and lymphatic system disorders 2 participants								
Low levels of red blood cells Anemia	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**1** 13%	**0** 0%
High levels of white blood cells Leukocytosis	**0** 0%	**1** 25%	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**0** 0%	**0** 0%

What were the most common other adverse events?

40 of 45 participants (89%) had other adverse events that were not considered serious.

The table below shows the **other adverse events** that happened in 6 or more of all participants:

	Group 1 4 participants	Group 2 4 participants	Group 3 9 participants	Group 4 4 participants	Group 5 3 participants	Group 6 4 participants	Group 7 8 participants	Group 8 9 participants
Dose of LHC165	100 µg	200 µg	400 µg	600 µg	100 µg	200 µg	400 µg	600 µg
Dose of PDR001	None	None	None	None	400 mg	400 mg	400 mg	400 mg
Fever Pyrexia	**0** 0%	**1** 25%	**5** 56%	**0** 0%	**0** 0%	**2** 50%	**5** 63%	**4** 44%
Low levels of red blood cells Anemia	**0** 0%	**1** 25%	**1** 11%	**3** 75%	**0** 0%	**1** 25%	**1** 13%	**4** 44%
Physical weakness or lack of energy Asthenia	**0** 0%	**1** 25%	**1** 11%	**3** 75%	**0** 0%	**1** 25%	**2** 25%	**0** 0%
Itching Pruritus	**0** 0%	**1** 25%	**0** 0%	**0** 0%	**0** 0%	**2** 50%	**1** 13%	**3** 33%
Feeling sick to the stomach Nausea	**0** 0%	**0** 0%	**0** 0%	**1** 25%	**1** 33%	**1** 25%	**1** 13%	**2** 22%
Throwing up Vomiting	**0** 0%	**0** 0%	**1** 11%	**1** 25%	**0** 0%	**1** 25%	**1** 13%	**2** 22%

How has this trial helped?

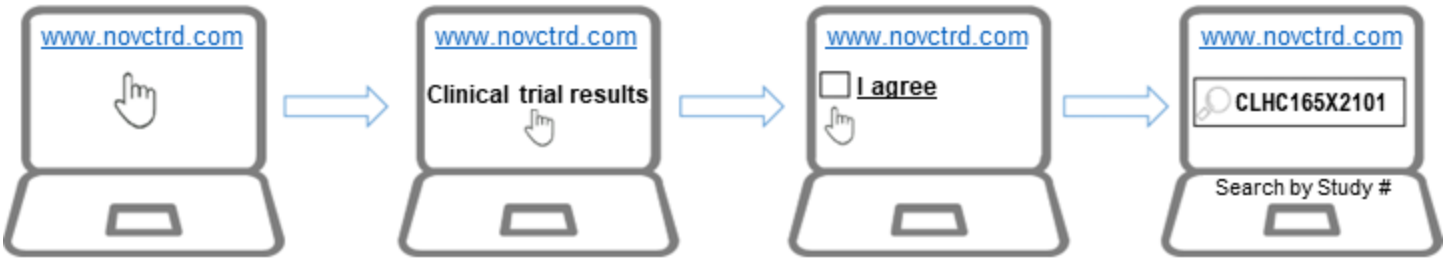
This trial helped learn about the safety of different doses of LHC165 given alone or with PDR001 in participants with advanced cancers. The researchers concluded that **600 µg LHC165** was the highest dose that was safe for participants to receive alone or with 400 mg PDR001.

Because enrollment ended early and there were too few participants, the researchers could not make any conclusions about the effects of LHC165 given alone or with PDR001 on shrinking cancer. The sponsor has no plans for other trials of LHC165 in people with advanced cancers.

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:



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

- www.clinicaltrials.gov. Use the NCT identifier **NCT03301896** in the search field.

Full clinical trial title: A Phase I/Ib, open-label, multi-center dose-escalation and dose-expansion study of the safety and tolerability of intra-tumorally administered LHC165 single agent and in combination with PDR001 in patients with advanced malignancies

Thank you

Thank you to all trial participants. Clinical trial participants belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and test new medical treatments for patients.

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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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www.novartisclinicaltrials.com