NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the safety of PDR001, LCL161, and CJM112 in people with multiple myeloma

Protocol number: CPDR001X2106

Thank you!

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. Thank you for taking part in this trial for the drugs PDR001, also known as spartalizumab, CJM112, and LCL161. You helped researchers learn more about how these trial drugs work in people with multiple myeloma.

As a clinical trial participant, you belong to a large community of people around the world. Your invaluable contribution to medicine and healthcare is greatly appreciated.

This summary only shows the results of a single 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.

How long was this trial?

The trial started in December 2017 and ended in March 2020. It was designed so that each participant could take part until their cancer got worse, they had a severe medical problem, or they decided to leave the trial. The length of time the participants took their trial treatments ranged from about 3 to 28 weeks.

Why did this trial end early?

The researchers did not complete this trial as planned. The sponsor decided to end this trial early because they were unable to recruit enough people with refractory or relapsed multiple myeloma who could be in the trial. The decision to stop was not related to safety.

When the 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.

Why was the research needed?

Researchers are looking for a better way to treat **refractory or relapsed multiple myeloma (RRMM)**. **Multiple myeloma** is a blood cancer that affects a type of immune system cell called a **plasma cell**. Plasma cells are white blood cells that help the body fight infection. Multiple myeloma that is not well treated by approved drugs is called either:

- **Refractory** if it was never well treated, or
- **Relapsed** if it had been well treated at one time, but isn't now

Researchers think certain trial drugs could help the immune system fight multiple myeloma. This trial looked at 3 trial drugs: **CJM112**, **PDR001**, and **LCL161**.

Trial purpose

The main purpose of this trial was to learn the highest doses of the trial drugs and combinations of the trial drugs that can be safely given to people with RRMM.

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

- What is the highest dose of the trial drugs that participants could receive without too much risk of serious harm?
- What medical problems did the participants have during the trial?

Trial drugs

The drugs given in this trial were:

CJM112, given as an intravenous (IV) infusion, which is through a needle in a vein. It had been previously tested in certain types of diseases that involve the immune system, such as psoriasis and asthma. It is designed to help the immune system by blocking a protein called IL-17 that may lead to disease.

PDR001, given as an IV infusion. It had been previously tested in many types of cancer, such as colorectal and blood cancers. It is designed to help the immune system fight cancer by blocking a protein called PD-1 that helps tumors grow.

LCL161, taken as a tablet by mouth. It had been previously tested in certain types of cancer, such as breast and ovarian cancer. It is designed to help kill cancer cells.

Who was in this trial?

26 participants were in this trial – 16 men and 10 women. The participants could take part in this trial if they had RRMM that was not well treated by at least 2 treatments. They also:

- Were able to perform daily tasks and take care of themselves without much help
- Were not taking certain medicines that weaken the immune system, such as certain steroids
- Did not have certain other diseases, such as other types of cancer

Participants' ages ranged from 55 to 82 years. Most participants identified themselves as Caucasian (White) and some did not report their race.

Participants took part at 8 trial sites in these countries:

- Germany
- Italy
- Spain
- 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.

What happened during this trial?

During screening

Up to 4 weeks before taking any trial drugs, trial doctors checked participants' health and RRMM to make sure they could be in this clinical trial. 26 participants took part in this trial.

During treatment

The participants were assigned to 1 of 3 treatment groups:

- **CJM112** alone as 50 or 100 mg, also called milligrams
- **PDR001**, as 400 mg, **and CJM112**, as 50 or 100 mg
- **PDR001**, as 400 mg, **and LCL161**, as 300 or 600 mg

Participants received PDR001 and CJM112 once every 4 weeks through an IV infusion. Participants took LCL161 by mouth as 1 or 2 tablets once a week.

To lower the chance of medical problems, participants received the low dose first. The clinical trial team checked each participant's health to decide if the participant could receive the high dose.

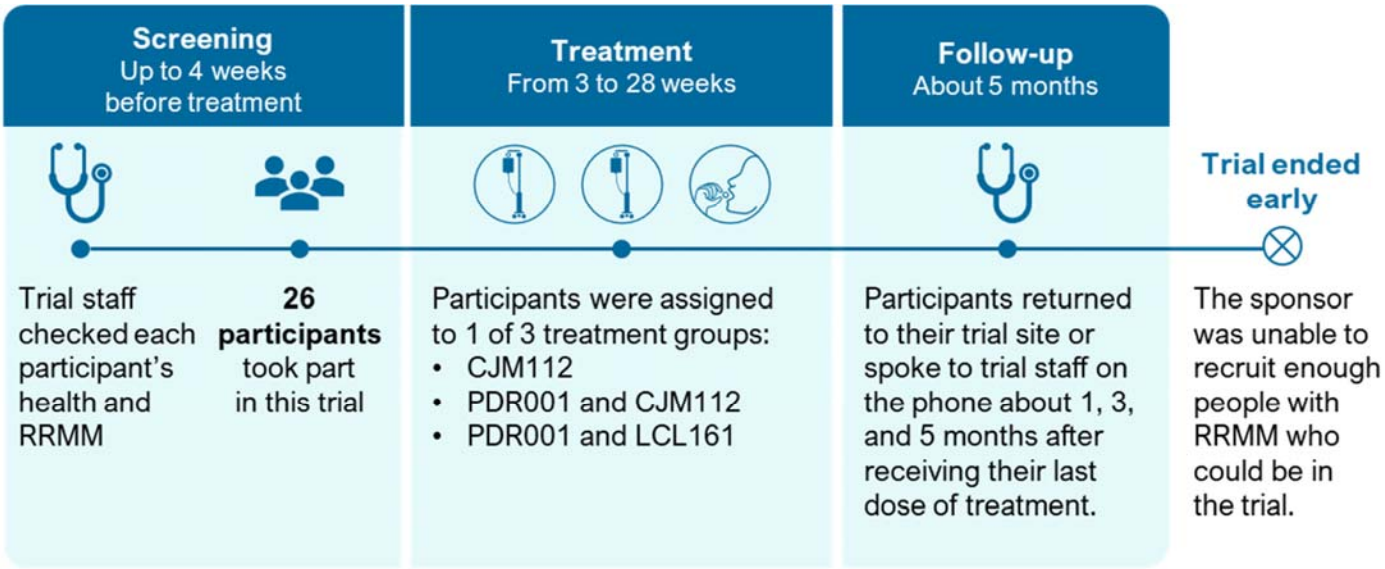
The length of time the participants took their trial treatments ranged from about 3 to 28 weeks. Each participant could continue to take the trial treatments until their cancer got worse, they had a serious medical problem, or they decided to leave the trial. Participants assigned CJM112 alone were allowed to switch to PDR001 and CJM112 if their RRMM got worse during the trial.

In addition to the trial drugs above, participants could receive certain other drugs for their cancer and symptoms. Trial staff checked the participants' RRMM and general health throughout the trial.

During follow-up

Participants returned to their trial site or spoke to trial staff on the phone about 1, 3, and 5 months after receiving their last dose of treatment.

How this trial was done:



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 is the highest dose of the trial drugs that participants could receive without too much risk of serious harm?

The clinical trial team learned that the doses and combinations of trial drugs used in this trial did not cause too much risk of serious harm for most participants. Most participants also did not need to lower their dose or stop their trial drugs because of medical problems.

However, the team was not able to learn the highest doses that could be safely given to participants because the trial ended early.

To learn about the risk of harm, trial doctors kept track of **dose limiting toxicities**, also called **DLTs**. DLTs are medical problems that had too much risk of serious harm if the dose level went up. Before this trial started, the researchers decided which medical problems were DLTs based on their type, severity, and when they happened. If participants had DLTs during treatment, it meant the dose's risk of harm may have been too high.

Of the 26 participants, 3 participants had DLTs: 1 participant in each treatment group.

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

What were the serious adverse events?

6 participants died during the trial:

- 4 deaths were from their cancer getting worse
- 2 deaths were from problems related to their cancer: life-threatening infection (sepsis) and the kidneys suddenly stopped working (acute kidney injury)

12 participants had serious adverse events. All serious adverse events that happened in all participants in each group are listed in the table on the next page.

	CJM112 alone	PDR001 and CJM112	PDR001 and LCL161
	Percent % (out of 6 participants)	**Percent %** (out of 11 participants)	**Percent %** (out of 9 participants)
Kidneys suddenly stopped working Acute kidney injury	**0%** (0)	**9%** (1)	**33%** (3)
Harmful blood levels of certain chemicals released when cancer cells quickly die Tumor lysis syndrome	**0%** (0)	**9%** (1)	**0%** (0)
General health got worse Condition aggravated	**17%** (1)	**0%** (0)	**0%** (0)
Inflammation in the lungs Pneumonitis	**0%** (0)	**9%** (1)	**0%** (0)
Infection in the nose, throat, airways, or lungs Respiratory tract infection	**17%** (1)	**0%** (0)	**0%** (0)
Kidneys stopped working Renal failure	**0%** (0)	**0%** (0)	**11%** (1)
Kidneys stopped working well Renal impairment	**0%** (0)	**9%** (1)	**0%** (0)
Life-threatening infection Sepsis	**17%** (1)	**0%** (0)	**0%** (0)
RRMM got worse Disease progression	**17%** (1)	**0%** (0)	**0%** (0)
Tumor pain	**0%** (0)	**9%** (1)	**0%** (0)
Infection in the nose, throat, or airways Upper respiratory tract infection	**17%** (1)	**0%** (0)	**0%** (0)

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 15% (4 out of 26) of all participants are listed in the table below.

	CJM112 alone	PDR001 and CJM112	PDR001 and LCL161
	Percent % (out of 6 participants)	**Percent %** (out of 11 participants)	**Percent %** (out of 9 participants)
Low level of red blood cells Anemia	**33%** (2)	**18%** (2)	**33%** (3)
Back pain	**17%** (1)	**27%** (3)	**11%** (1)
Feeling sick to the stomach Nausea	**0%** (0)	**18%** (2)	**22%** (2)
Lack of energy and strength Asthenia	**33%** (2)	**9%** (1)	**11%** (1)
Feeling tired Fatigue	**0%** (0)	**27%** (3)	**11%** (1)

What were the other results of this trial?

The clinical trial team used several measures to learn if the trial drugs had an effect on the participants' cancer. Because this trial ended early, the clinical trial team could not conclude if the trial drugs had a meaningful effect on the participants' cancer.

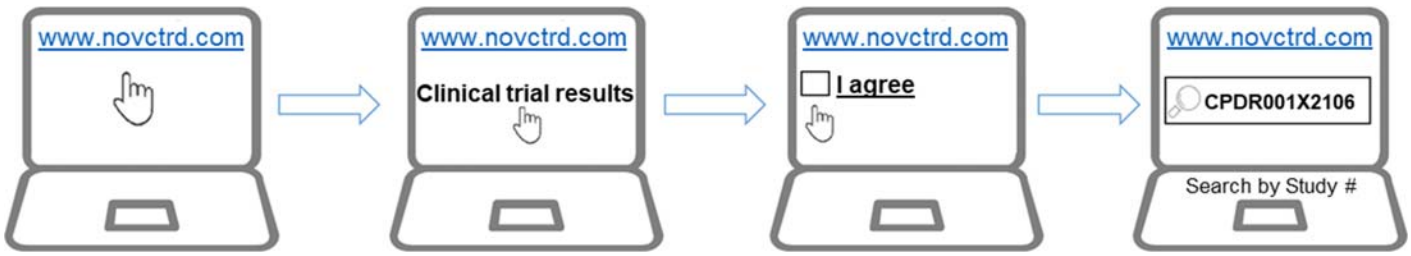
How has this trial helped?

This trial helped researchers learn about the doses and combinations of trial drugs that could be safe to use in people with RRMM. The clinical trial team concluded that the doses and combinations of trial drugs used in this trial did not cause too much risk of serious harm for most of the participants. However, they were not able to learn the highest doses that could be safely given to participants because the trial ended early.

Please remember, this summary only shows the results of one clinical trial. Other clinical trials may have different results. 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.

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 NCT03111992 in the search field.

Full clinical trial title: Phase I/Ib, multi-center, open-label, study of single agent CJM112, and PDR001 in combination with LCL161 or CJM112 in patients with relapsed and/or refractory multiple myeloma

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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www.novartisclinicaltrials.com