NOVARTIS

Clinical trial results summary

A clinical trial to learn about the safety of PDR001 with regorafenib in people with metastatic colorectal cancer

Protocol number: CPDR001I2102

Our thanks to the participants!

Novartis, the sponsor of this clinical trial, would like to thank the participants who took part in this trial for the drug PDR001, also known as spartalizumab. They helped researchers learn more about how PDR001, which is an immunotherapy, works in people with metastatic colorectal cancer.

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

Important note: 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.

Why was this research needed?

Researchers are looking for a better way to treat metastatic colorectal cancer, which is cancer that started in the colon or rectum and spread to other parts of the body. The usual treatment for metastatic colorectal cancer involves a combination of surgery, chemotherapy, and radiation therapy. However, people often do not survive long with metastatic colorectal cancer.

Immunotherapy is a newer kind of cancer treatment that uses the body's own immune system to help detect and fight cancer. Immunotherapy often has fewer side effects than other cancer treatments and can prevent cancers from coming back. However, it only works for certain types of colorectal cancers. Immunotherapy often doesn't work for the most common type of colorectal cancer, called **MicroSatellite Stable (MSS) colorectal cancer**.

PDR001, also known as spartalizumab, is an immunotherapy that has been tested in other types of cancer. Researchers want to learn more about PDR001 and if it could help people with metastatic MSS colorectal cancer. To do this, they designed this clinical trial to learn about the safety of PDR001 when taken with regorafenib.

Trial drugs

The drugs given in this trial were:

- **PDR001**, also known as spartalizumab (pronounced spar-ta-LIZ-uh-mab): a trial drug immunotherapy designed to help the body's immune system to control and stop cancer growth
- **Regorafenib** (pronounced re-goe-RAF-e-nib): a chemotherapy medicine that is already approved to treat metastatic colorectal cancer

Trial purpose

The main purpose of this trial was to learn about the safety of the immunotherapy, PDR001, taken together with regorafenib, a chemotherapy approved to treat metastatic colorectal cancer. The main question the researchers wanted to answer in this trial was:

> What is the highest dose of PDR001 with regorafenib that participants could receive without too much risk of harm?

Researchers also checked participants' health and kept track of any medical problems throughout the trial.

How long was this trial?

This trial started in June 2017 and ended in May 2019. The time each participant got treatment in the trial ranged from 2 to 17 months.

The researchers did not complete this trial as planned. The researchers planned a higher dose of PDR001 with regorafenib. But, after reviewing the safety results from the first dose, the researchers decided to end the trial early because they found that participants had too much risk of harm from the doses given in this trial.

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

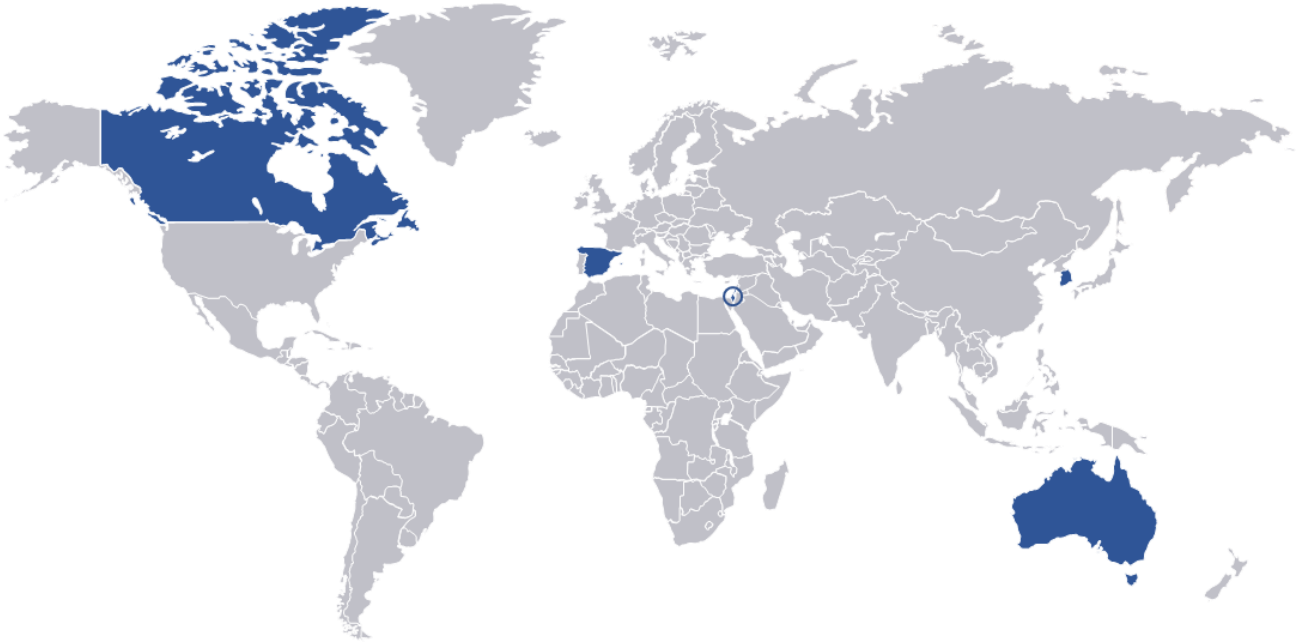
Who was in this trial?

10 men began this clinical trial. The participants could take part in this trial if they had:

- Metastatic MSS colorectal cancer
- Previously received 2 different cancer treatments that did not work. One of these treatments must have been an immunotherapy and the other could've been radiation or chemotherapy.

Participants' ages ranged from 42 to 77 years old. They were 62 years old on average. They identified their race (ethnicity) as Caucasian (White), Asian (East Asian), and Other (Hispanic/Latino).

Participants took part at 6 trial sites in Australia, Canada, Israel, the Republic of Korea, and Spain.



What kind of trial was this?

This was an open-label trial, which means that the participants and clinical trial team knew what treatment the participants got. All participants got the same treatment in this trial.

What happened during this trial?

During screening
Trial doctors checked participants' tumors and health to make sure they could be in this clinical trial. They also took blood samples.

During treatment
Researchers assigned the same treatment and dose to all participants:

- 400 mg (milligrams) **PDR001**, given through a vein as an intravenous (IV) infusion, and
- 120 mg **regorafenib**, as pills

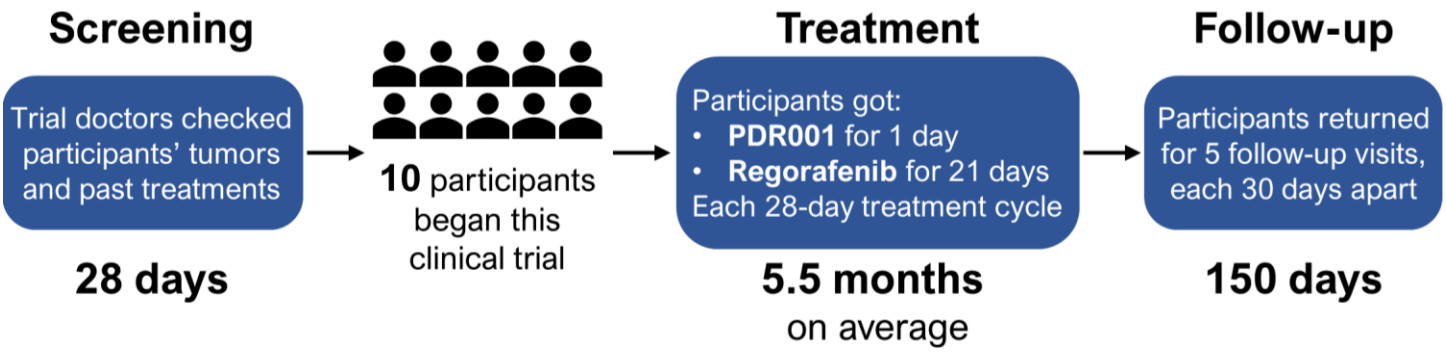
Trial doctors gave participants PDR001 on the first day of a 28-day treatment cycle. Participants also got regorafenib, as pills, to take each day for the first 21 days of the cycle. Trial doctors could change the dose of regorafenib based on a participant's health.

A participant could start another treatment cycle if they wanted to continue and the trial doctor agreed it could help. A participant could continue for as many cycles as needed, until they left the trial or the sponsor ended the trial. On average, participants got treatment for about 5.5 months.

Trial doctors checked participants' health throughout the trial.

During follow-up
After their last dose, participants returned to their trial site for 5 visits, each 30 days apart.

How researchers designed this trial:



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 PDR001 with regorafenib that participants could get without too much risk of harm?

Researchers found that participants had too much risk of harm from the doses of PDR001 with regorafenib given in this trial.

To find this out, trial doctors kept track of certain medical problems that happened during the first 2 treatment cycles, which was a total of 56 days (8 weeks). Before this trial started, the researchers decided which medical problems had too much risk of harm based on their type, severity, and timing. If participants had these medical problems during treatment, it meant the dose's risk of harm may have been too high.

Because 1 participant didn't take enough regorafenib, these results are for 9 of the 10 participants in this trial.

Of the 9 participants, 1 participant had medical problems that had too much risk of harm. These were:

- Ongoing period of confusion
- High bilirubin level, which can be a sign of liver problems

Participants with medical problems that had too much risk of harm

Based on these results, the trial was ended early.

What other medical problems did participants have?

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.

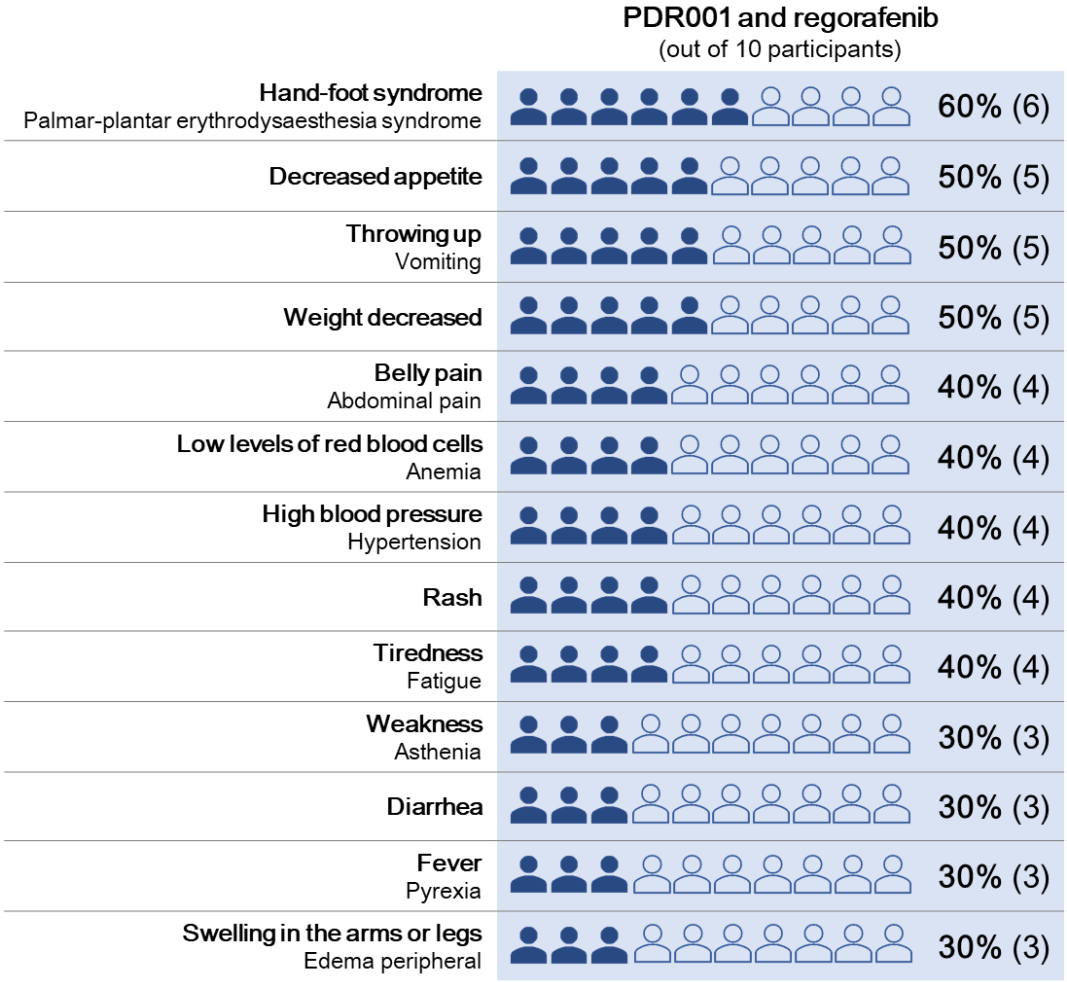
A lot of research is needed to know whether a drug causes an adverse event. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug. So, when new drugs are being studied, researchers keep track of all adverse events the participants have.

This section is a summary of the adverse events that happened during and after treatment. These are listed in tables as non-serious adverse events and serious adverse events. The websites listed at the end of this summary have more information about the adverse events that happened in this trial.

What were the non-serious adverse events?

All participants had at least one non-serious adverse event. The most common non-serious adverse event was **hand-foot syndrome**, which is redness, swelling, and pain on the palms of hands or bottoms of feet. The following table shows the non-serious adverse events that happened in 3 or more participants. There were other adverse events, but these happened in fewer participants.

Most common non-serious adverse events

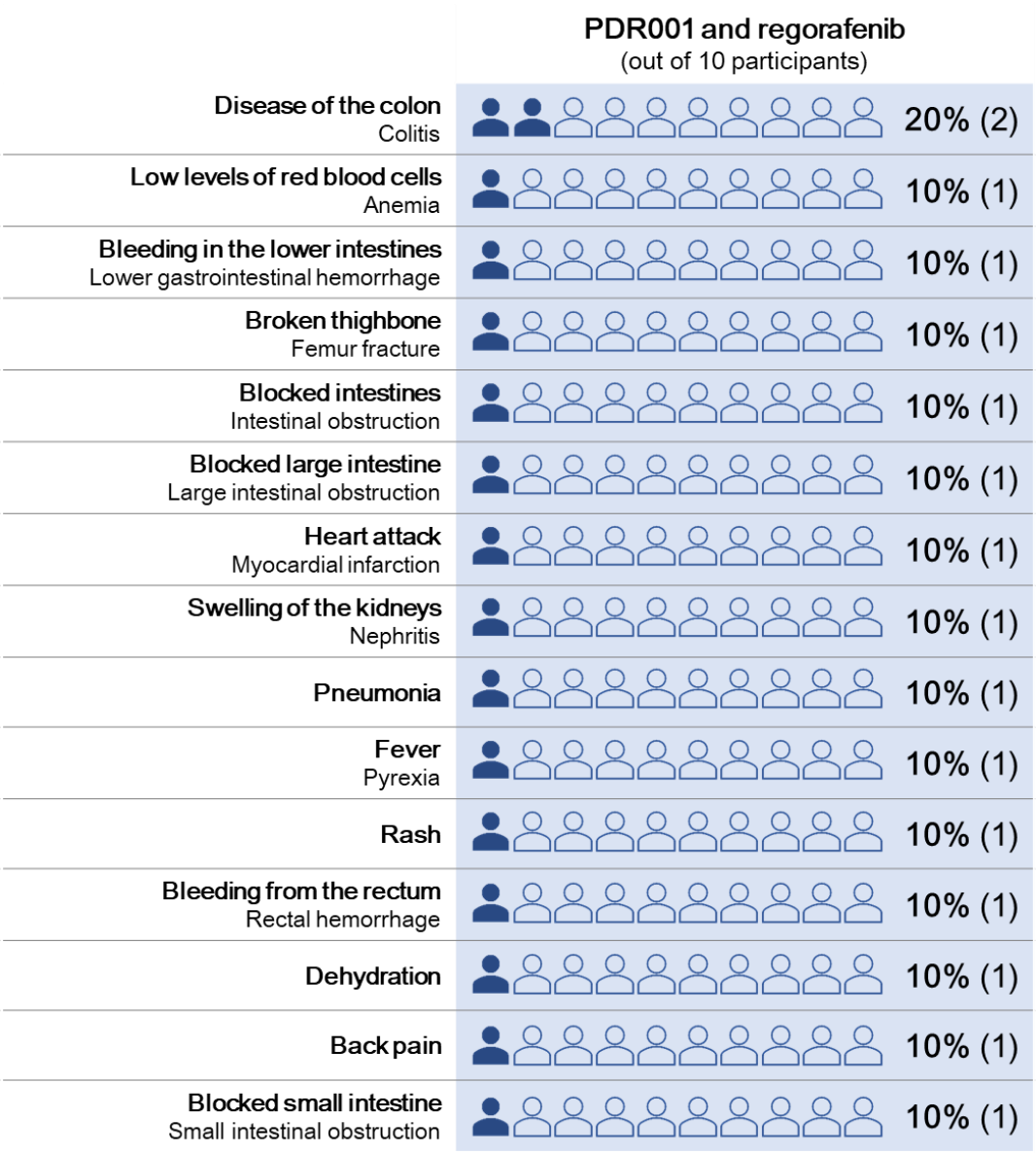


What were the serious adverse events?

A serious adverse event is when the adverse event is life-threatening, causes lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial drug. During this trial, 8 participants had at least one serious adverse event. All of the serious adverse events that happened 30 days or less after receiving the trial treatment are listed below.

One participant died during this clinical trial. This participant died because their colorectal cancer got worse, and they did not have any other serious adverse events.

Participants with serious adverse events



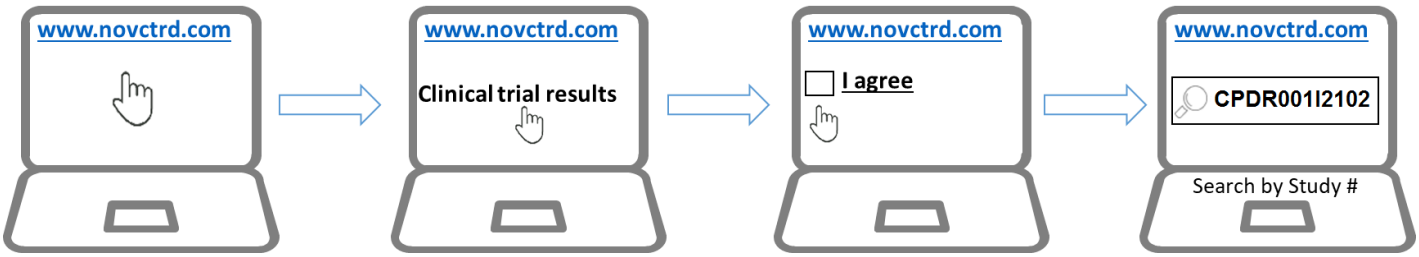
How has this trial helped?

This trial helped to learn about the safety of the trial drug PDR001, an immunotherapy, taken together with the approved chemotherapy regorafenib. Researchers learned that PDR001 with 120 mg regorafenib was not safe to treat participants with metastatic MSS colorectal cancer in this trial.

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.

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 on the Novartis Clinical Trial Results website (www.novctrd.com).



You can find more information about this trial on these websites:

- www.clinicaltrials.gov. Use the NCT identifier 03081494 in the search field.
- www.clinicaltrialsregister.eu. The EudraCT identifier is 2017-000466-30. This result was submitted to the EU as required but is not made public in the EU Clinical Register per the EU regulations.

Full clinical trial title: Phase Ib study of PDR001 in combination with regorafenib in adult patients with previously treated metastatic microsatellite stable (MSS) colorectal cancer

Thank you

We thank the participants for taking part in this trial. Clinical trial participants belong to a large community of people around the world. The participants 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