NOVARTIS

Clinical Trial Results Summary

A trial to learn more about the safety of receiving MIW815 (ADU-S100) together with PDR001 in participants with advanced or metastatic solid tumors or lymphomas

Trial Number: CMIW815X2102J

Thank you

Thank you to the participants who took part in the clinical trial for the trial treatment MIW815, also called ADU-S100, given together with PDR001, also known as spartalizumab. All of the participants helped the researchers learn about the safety of this treatment combination and how it works in advanced cancer.

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.

If you participated in the trial and have questions about the results, please speak with the trial doctor or staff at your trial site.

You can find more information about this trial on the websites listed on the last page of this summary.

Overview of this trial

What was the purpose of this trial?

The researchers studied the safety of receiving a trial treatment called MIW815 with another trial treatment called PDR001.

The researchers also studied how MIW815 affected the participants' cancer and immune response against their tumors.

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

- What were the highest doses of MIW815 and PDR001 that were safe for participants to receive?
- What medical problems happened during this trial?

Keeping track of the participants' medical problems helped the researchers learn about the safety of MIW815 when received with PDR001.

Other questions the researchers wanted to answer were:

- Did the participants' tumor size increase, stay the same, or shrink during the trial?
- Did the participants' immune response against their tumors change during the trial?

Who was in this trial?

There were 106 men and women who had advanced or metastatic solid tumors or lymphomas that participated in this clinical trial.

What treatments did the participants receive?

The participants in this trial received both MIW815 and PDR001. MIW815 is also called ADU-S100, and PDR001 is also called spartalizumab. In this summary, these treatments are referred to as MIW815 and PDR001.

What were the main results of this trial?

Overall, the researchers learned that:

- 103 out of 106 participants had medical problems during this trial. This was 97.2% of the participants.
- Some of these medical problems were serious.
- Some of the participants left the trial due to medical problems.

The sponsor decided to end the trial early. This was because the results from the first part of the trial did not show that the participants' tumors were shrinking. The decision to stop the trial was not related to safety.

More details about the results of this trial are included later in this summary.

What was the purpose of the trial?

The purpose of this trial was to test the combination of MIW815 with PDR001 as a possible treatment for participants with advanced or metastatic solid tumors or lymphomas.

What are advanced or metastatic solid tumors or lymphomas?

- Cancer is a disease that happens when the body cannot control the growth of cells. These extra cells can come together to form tumors. Tumors can start in any part of the body.
- “Metastatic” or “advanced” means that the cancer has spread to other parts of the body to form new tumors. This can make the cancer more difficult to treat.
- Lymphoma is a type of cancer in the “lymphatic system”. The lymphatic system is a group of channels and glands in the body that helps the body to fight infection and remove extra fluid.

How do researchers think the trial treatment combination can help?

- The trial treatment PDR001 blocks a specific protein in the body called PD-1. When PDR001 stops PD-1 from working, the body’s immune system may be able to fight tumor cells more effectively. Other trials have been done to learn more about how treatments that block PD-1, like PDR001, work in patients with cancer. However, these types of treatments do not work for all patients, or for all types of cancer.
- The trial treatment MIW815 was designed to activate the body’s immune response to fight the tumor cells. Researchers think MIW815 may also help PDR001 to work better.

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

- What were the highest doses of MIW815 and PDR001 that were safe for participants to receive?
- What medical problems happened during this trial?

Other questions the researchers wanted to answer were:

- Did the participants' tumor size increase, stay the same, or shrink during the trial?
- Did the participants' immune response against their tumors change during the trial?

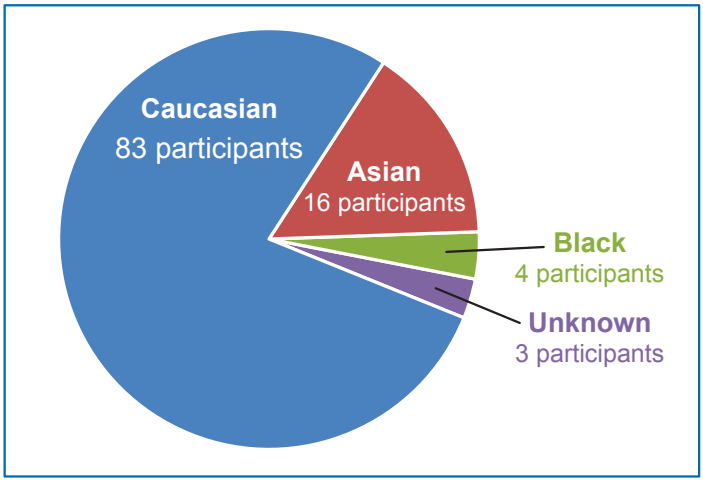
Who was in this trial?

To answer the questions in this trial, the researchers asked for the help of men and women who had advanced or metastatic solid tumors or lymphomas.

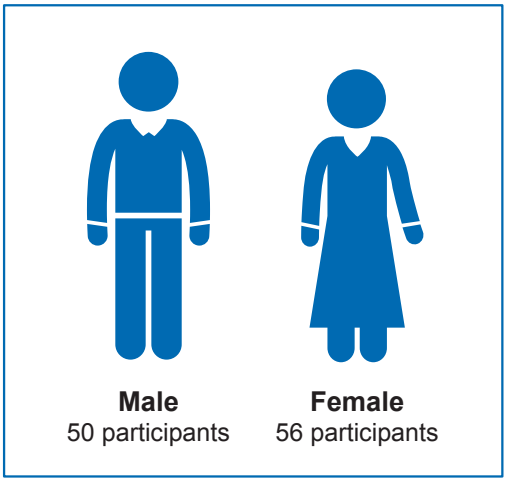
Everyone in this trial was 27 to 93 years old when they joined the trial.

The charts below show the race and gender of the participants in this trial.

Participants' race
(out of 106 participants)

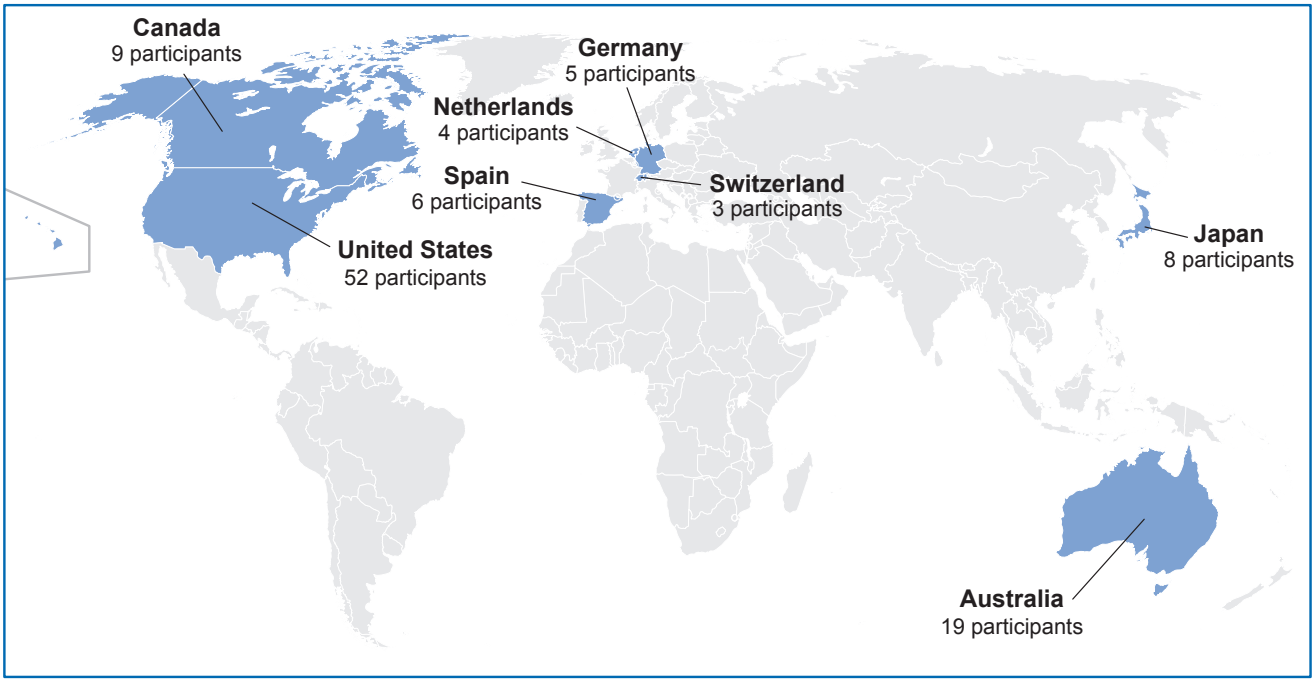


Participants' genders
(out of 106 participants)



This trial included participants in the following countries:

Participants' countries (out of 106 participants)



What treatments did the participants receive?

The participants in this trial received both MIW815 and PDR001. This was an "open-label" trial. This means each participant knew what they were receiving. The trial staff and sponsor staff also knew what each participant was receiving.

The participants in this trial were split into 2 groups, called Group A and Group B. The participants received the trial treatment in 28-day periods called "cycles".

The participants could take part in as many treatment cycles as they wanted, unless their cancer got worse. If their cancer got worse, or they experienced serious medical problems, the participants stopped the treatment cycles.

The doses of MIW815 were measured in micrograms, also called µg. The doses of PDR001 were measured in milligrams, also called mg.

This trial was a “dose escalation” trial. Researchers use dose escalation trials to learn about the safety of a specific dose before additional participants are given a higher dose. The first group of participants in the trial started with a low dose of 50 µg of MIW815 in their first treatment cycle. The next group of participants started with 100 µg of MIW815 in their first treatment cycle. MIW815 was given as an injection into the participants’ tumors.

Based on the participants’ medical problems, the researchers decided whether the next group of participants would receive a higher dose of MIW815. The maximum dose of MIW815 that was tested in this trial was 3,200 µg.

The dose of PDR001 did not change during the trial. All the participants received a dose of 400 mg of PDR001 by an injection through a needle into the vein, also called an IV infusion, on the first day of each treatment cycle.

The chart below shows the treatments that each group of participants received during the trial.

	Group A (67 participants)	Group B (39 participants)
	• MIW815 was given as an injection into the tumor • PDR001 was given as an injection through a needle into the vein, which is called an IV infusion	• MIW815 was given as an injection into the tumor • PDR001 was given as an injection through a needle into the vein, which is called an IV infusion
	• MIW815 on days 1, 8, and 15 of each cycle • PDR001 on day 1 of each cycle	• MIW815 on day 1 of each cycle • PDR001 on day 1 of each cycle
	• 7 participants received 50 µg of MIW815 and 400 mg of PDR001 • 10 participants received 100 µg of MIW815 and 400 mg of PDR001 • 13 participants received 200 µg of MIW815 and 400 mg of PDR001 • 9 participants received 400 µg of MIW815 and 400 mg of PDR001 • 9 participants received 800 µg of MIW815 and 400 mg of PDR001 • 8 participants received 1,600 µg of MIW815 and 400 mg of PDR001 • 11 participants received 3,200 µg of MIW815 and 400 mg of PDR001	• 5 participants received 50 µg of MIW815 and 400 mg of PDR001 • 5 participants received 100 µg of MIW815 and 400 mg of PDR001 • 6 participants received 200 µg of MIW815 and 400 mg of PDR001 • 7 participants received 400 µg of MIW815 and 400 mg of PDR001 • 4 participants received 800 µg of MIW815 and 400 mg of PDR001 • 7 participants received 1,600 µg of MIW815 and 400 mg of PDR001 • 5 participants received 3,200 µg of MIW815 and 400 mg of PDR001

What happened during this trial?

The trial started in September 2017 and ended in December 2020. Each participant could have stayed for the entire length of the trial. But participants left the trial if their cancer got worse, if they experienced serious medical problems, or if they decided they no longer wanted to be in the trial for any reason.

There were 2 parts planned for this trial. The sponsor decided to end the trial in December 2019, before the second part started. This was because the results from the first part of the trial did not show that the participants' tumors were shrinking. The decision to stop the trial was not related to safety. The researchers continued to monitor the participants until the trial ended in December 2020.

The chart below shows what happened during the trial.

Before the participants received treatment

The trial doctors checked the participants' health to make sure they could be in the trial. They also checked that the participants met all the requirements needed to be in the trial.

Within 21 days before treatment

While the participants received treatment

The participants:

- had blood and urine samples taken
- had tissue samples taken from their tumors
- had pictures taken to measure the size of their tumors
- had their overall health checked and answered questions about any medical problems they were having
- received their assigned treatments

Up to about 119 weeks

After the participants received treatment

- The participants visited their trial site or had a telephone call.
- The doctors asked them questions about any medical problems they were having and about the medications they were taking.
- If a participant visited their trial site, the doctors took more blood samples.

Up to 150 days after their last dose

What were the main results of this trial?

This is a summary of the overall results from this trial. The individual results of each participant might be different and are not in this summary.

The results from several trials are needed to decide which treatments are safest and work best. Other trials may provide new information or different results. Always talk to a doctor before making changes to your healthcare.

What were the highest doses of MIW815 and PDR001 that were safe for participants to receive?

In order to answer this question, the researchers wanted to find the "maximum tolerated dose", also called the MTD, of MIW815 in combination with PDR001. The "MTD" is the highest dose of a treatment that doesn't cause a certain number of "dose-limiting toxicities", also called DLTs.

A "DLT" is any medical problem that:

- is serious enough to keep the doctors from giving that dose to any other participants in that group.
- is serious enough to keep the doctors from increasing the trial treatment dose for participants in other groups.

In this trial, the researchers determined that a treatment dose would be the MTD if at least 33 participants (33% of the participants) had a DLT while receiving that treatment dose. The researchers studied the DLT results for 100 of the participants during the first treatment cycle.

Overall, the researchers could not determine the MTD of MIW815 in combination with PDR001. This was because none of the treatment doses caused at least 33% of the participants to have a DLT. Overall, there was 1 participant who had a DLT. This DLT happened in a participant in Group A who received 3,200 µg of MIW815 and 400 mg of PDR001.

What medical problems happened during this trial?

Medical problems that happen in clinical trials are called “adverse events”. An **adverse event** is any unwanted sign or symptom that participants have during a trial. An **adverse event** is 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 the treatments in the trial. A lot of research is needed to know whether a treatment causes an adverse event. Doctors keep track of all the adverse events that happen in trials, even if they do not think the adverse events might be related to the treatments.

This section is a summary of the adverse events that happened in at least 1 participant during this trial. Some of these adverse events were considered serious, and some were considered not serious.

- **97.2% of the participants had adverse events during this trial. This was 103 out of 106 participants.**
- **Some of the adverse events were serious.**
- **Some of the participants left the trial due to an adverse event.**

Summary of adverse events

	Group A (percentage and number of participants)	Group B (percentage and number of participants)
Participants who had adverse events	67 of 67 **100.0%**	36 of 39 **92.3%**
Participants who had serious adverse events	24 of 67 **35.8%**	13 of 39 **33.3%**
Participants who left the trial due to an adverse event	2 of 67 **3.0%**	1 of 39 **2.6%**

What were the most common serious adverse events?

The serious adverse events below happened in at least 2 participants overall. There were other serious adverse events, but these happened in fewer participants.

Most common serious adverse events

Serious adverse event	Group A (percentage and number of participants)	Group B (percentage and number of participants)
Difficulty breathing	5 of 67 **7.5%**	0 of 39 **0.0%**
Diarrhea	1 of 67 **1.5%**	2 of 39 **5.1%**
Low levels of red blood cells	1 of 67 **1.5%**	2 of 39 **5.1%**
Feeling tired	2 of 67 **3.0%**	1 of 39 **2.6%**
Fever	2 of 67 **3.0%**	1 of 39 **2.6%**
Inflammation of the skin	1 of 67 **1.5%**	1 of 39 **2.6%**
High blood pressure	2 of 67 **3.0%**	0 of 39 **0.0%**
Pain in the abdomen	2 of 67 **3.0%**	0 of 39 **0.0%**
Pain in the back	2 of 67 **3.0%**	0 of 39 **0.0%**

There were participants who died due to serious adverse events during this trial.

- In Group A, 10.4% of participants died due to serious adverse events. This was 7 out of 67 participants.
- In Group B, 15.4% of participants died due to serious adverse events. This was 6 out of 39 participants.

What were the most common adverse events?

The adverse events below happened in at least 12% of the participants overall. There were other adverse events, but these happened in fewer participants.

Most common adverse events

Adverse event	Group A (percentage and number of participants)	Group B (percentage and number of participants)
Fever	21 of 67 **31.3%**	9 of 39 **23.1%**
Low levels of red blood cells	19 of 67 **28.4%**	10 of 39 **25.6%**
Diarrhea	11 of 67 **16.4%**	10 of 39 **25.6%**
Feeling tired	12 of 67 **17.9%**	7 of 39 **17.9%**
Pain where the treatment was injected or infused	17 of 67 **25.4%**	4 of 39 **10.3%**
Constipation	9 of 67 **13.4%**	8 of 39 **20.5%**
Difficulty breathing	13 of 67 **19.4%**	5 of 39 **12.8%**
Vomiting	9 of 67 **13.4%**	6 of 39 **15.4%**
Cough	10 of 67 **14.9%**	5 of 39 **12.8%**
Nausea	10 of 67 **14.9%**	3 of 39 **7.7%**

What other results were learned?

Did the participants' tumor size increase, stay the same, or shrink during the trial?

Overall, the researchers found that there was not a meaningful change in tumor size for every participant who received treatment. This was true for the participants in both Group A and Group B.

Did the participants' immune response against their tumors change during the trial?

Overall, the researchers found that there was not a meaningful change in every participant's immune response against their tumors after receiving treatment. This was true for the participants in both Group A and Group B.

What was learned from this trial?

The information described above helped the researchers learn that overall, there were no safety concerns about receiving the trial treatments MIW815 and PDR001 together in this trial. The researchers also learned that overall, receiving MIW815 and PDR001 together did not affect the tumor size of every participant, or the immune response against their tumors in a meaningful way in this trial.

The results presented here are for a single trial. This summary shows only the main results from this one trial. If you have any questions, please talk to the doctor or staff at your trial site.

Where can I learn more about this trial?

More information about the results of this trial can be found in the scientific results summary available on the Novartis Clinical Trial Results website, www.novctrd.com.

You can also find information about this trial on www.clinicaltrials.gov and www.clinicaltrialsregister.eu.

Full trial title: A Phase Ib, open label, multicenter study of the safety and efficacy of MIW815 (ADU-S100) administered by intratumoral injection with PDR001 to patients with advanced/metastatic solid tumors or lymphomas

Protocol number: CMIW815X2102J

ClinicalTrials.gov number: NCT03172936

EudraCT number: 2017-000707-25

Thank you

Clinical trial participants belong to a large community of participants around the world. They help researchers answer important health questions and study 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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