Clinical Trial Results Summary

Research Sponsor: Novartis
Drug Studied: KRP203
Trial Number: CKRP203A2105
Plain Language Title: A trial to learn about the safety of KRP203 in participants with blood cancer who need stem cell transplants

Thank you

Thank you to the participants who took part in the clinical trial for the drug KRP203. All of the participants helped the researchers learn more about how KRP203 works and how safe it is to take.

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. Novartis reviewed the results of the trial when it ended. An independent organization prepared this summary of the trial results for you.

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.

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

Overview of this trial

What was the purpose of this trial?

In this clinical trial, the researchers learned more about the safety of a drug called KRP203 in participants who received a stem cell transplant. The researchers also learned how much KRP203 got into the blood, and if it affected participants having graft versus host disease, also known as GvHD.

GvHD occurs in some people after they receive a stem cell transplant. In GvHD, the transplanted stem cells attack the body after the transplant.

What treatments did the participants take in this 2-part trial?

Part 1

Participants took KRP203 and cyclosporine A.

Part 2

Participants could take either:

- KRP203, cyclosporine A, and methotrexate
- KRP203, tacrolimus, and methotrexate

In both parts, treatments were given 10 days before the stem cell transplants. Participants continued to take their treatment up to 111 days.

Who took part in the trial?

23 men and women with blood cancer who had stem cell transplants.

What did the researchers want to learn?

- What medical problems did the participants have during the trial?
- How much and how quickly KRP203 got into the participants' blood?
- How many participants survived for at least 6 months after their last treatment without having GvHD?

Keeping track of the participants' medical problems helped the researchers learn about the safety of KRP203. This was the main focus of this trial.

What were the main results of the trial?

Overall, the researchers learned that:

- All of the participants had adverse events during this trial, and about half of the adverse events were serious.
- Most of the serious adverse events were considered common for the disease that the participants had in this trial.

Details of medical problems are listed beginning on page 7.

Why was the research needed?

Researchers are looking for a better way to treat patients with blood cancer who need stem cell transplants. Before a drug can be approved for patients to take, researchers do clinical trials to find out how safe it is and how it works. In this trial, the researchers wanted to learn more about the safety of KRP203 in participants who have blood cancer and need a stem cell transplant.

A common treatment for blood cancer is a stem cell transplant. Stem cells can be taken from the blood, bone marrow, or umbilical cord blood. Stem cells can be taken from 1 person and transplanted to another, where they can turn into any common type of cell normally found in the blood. Because stem cells come from a different person, a patient receiving a transplant is at risk for graft versus host disease, also known as GvHD. In GvHD, the transplanted stem cells attack the body after the transplant. This can happen because the stem cells do not recognize the new body. Certain types of white blood cells can cause GvHD.

KRP203 works by keeping those types of white blood cells from moving into the bloodstream and into other parts of the body. Researchers wanted to find out if KRP203 could help prevent GvHD.

What was the purpose of the trial?

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

- What medical problems did the participants have during the trial?
- How much and how quickly KRP203 got into the participants' blood?
- How many participants survived for at least 6 months after their last treatment without having GvHD?

What treatments did the participants take?

There were 2 parts in this trial. Each participant was in only 1 part.

During Part 1, the participants took KRP203 and a drug called cyclosporine A. Each dose of KRP203 was 3 milligrams, also known as mg.

During Part 2, the participants could take 1 mg or 3 mg of KRP203 in addition to 2 standard treatments to help prevent GvHD. All of the treatments were taken as a pill by mouth.

They took either:

- KRP203, cyclosporine A, and methotrexate
- KRP203, tacrolimus, and methotrexate

The researchers used a computer program to randomly choose the treatment each participant took during Part 2. This helped make sure that comparing the results of the treatments was as fair as possible.

The chart below shows the treatments the participants took.

Part 1	Part 2	
• 10 participants	• 6 participants	• 7 participants
• 3 mg KRP203 • Cyclosporine A	• 1 mg KRP203 • Cyclosporine A • Methotrexate	• 3 mg KRP203 • Tacrolimus • Methotrexate

- Started taking treatments 10 days before stem cell transplant
- Took treatments once a day for up to 111 days

Who took part in the trial?

To answer the questions in this trial, the researchers asked for the help of men and women with blood cancer who had a stem cell transplant. They were 49 years old on average and all between 23 and 63 years old.

The trial included 23 participants in 3 countries: France, Germany, and Switzerland.

What type of trial was this?

This trial studied the trial drug's safety by giving different amounts of the drug to a small number of people.

In this trial, each participant knew what treatment they were taking. The trial staff and sponsor staff also knew what each participant was taking.

What happened during the trial?

Each participant was in the trial for up to 2 years. The trial started in June 2013 and ended in August 2018.

The researchers made the decision to stop this trial early. This was because the sponsor decided to stop all research on KRP203 in GvHD. The decision to stop was not related to safety.

The chart below shows what happened during the trial.

Before the participants took the trial drug

- The trial doctors checked to make sure the participants could join the trial.

Up to 50 days

While the participants were taking the trial drug

Each participant was only in 1 part

Part 1

- The participants took KRP203 and cyclosporine A once a day.
- The participants received their stem cell transplant 10 days after starting their first treatment.

Part 2

- The participants took KRP203 and methotrexate along with either cyclosporine A or tacrolimus once a day.
- The participants received their stem cell transplant 10 days after starting their first treatment.

- The trial doctors took blood and urine samples from each participant.
- The trial doctors checked each participant's health and if they had GvHD.

Each part was up to 111 days

After taking the last dose

- The participants had up to 5 more visits for up to 2 years after their stem cell transplant to have their health checked.

Up to 2 years

What did researchers learn from the results of the 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.

Other trials may provide new information or different results. Always talk to a doctor before making any healthcare decisions.

For more information about this trial, please see the scientific summary that can be found on the website noted at the end of the summary.

What medical problems happened during the trial?

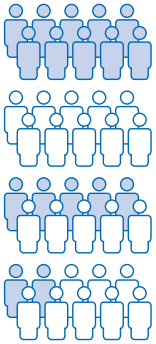
Medical problems that happen in clinical trials are called **"adverse events"**. An adverse event is any unwanted sign or symptom that participants have during a trial. An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care.

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. The trial 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 during this trial.

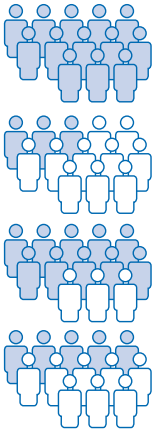
Adverse events summary

Part 1



- 100.0% had adverse events. This was 10 out of 10 participants.
- None of the participants left the trial due to adverse events
- 50.0% had serious adverse events. This was 5 out of 10 participants.
- 2 participants died from serious adverse events.

Part 2



- 100.0% had adverse events. This was 13 out of 13 participants.
- 23.0% of participants left the trial due to adverse events. This was 3 out of 13 participants.
- 77.0% had serious adverse events. This was 10 out of 13 participants.
- 5 participants died from serious adverse events.

What were the most common serious adverse events?

In this trial, most of the serious adverse events happened more than 30 days after the stem cell transplant. The serious adverse events in this trial are considered common for people who have blood cancer and get a stem cell transplant. This summary lists the serious adverse events that happened in 2 or more participants. There were other serious adverse events, but these happened in fewer participants.

For more information about the serious adverse events in this trial, please see the scientific summary that can be found on the website noted at the end of the summary.

Part 1

All the serious adverse events that happened in Part 1 occurred in only 1 participant each.

There were 2 participants who died from serious adverse events. These serious adverse events were:

- myelodyplastic syndrome, a disorder in which the bone marrow does not make enough healthy blood cells
- acute myeloid leukemia, a type of blood cancer

Part 2

All of the serious adverse events in Part 2 that happened in 2 or more participants took place more than 30 days after the transplant. The chart below shows these serious adverse events. There were other serious adverse events, but these happened in fewer participants.

Serious adverse events during Part 2 (more than 30 days after transplant)

	1 mg of KRP203, cyclosporine A, and methotrexate (Out of 6 participants)	3 mg of KRP203, tacrolimus, and methotrexate (Out of 7 participants)
Temporary GvHD in the intestine	33.0% (2)	14.0% (1)
Diarrhea	0.0% (0)	29.0% (2)
General worsening of physical health	17.0% (1)	14.0% (1)

There were 5 participants who died from serious adverse events. These serious adverse events were:

- pneumonia aspiration, a condition where something is breathed into the lungs instead of being swallowed
- liver failure, a condition where the liver stops working like it should
- return of lymphoma, a cancer affecting the immune system
- myelofibrosis, a rare type of bone marrow cancer
- hodgkin's disease, a type of blood cancer

What were the most common adverse events?

The tables below show the most common adverse events that happened in both parts:

- from the start of treatment until just before the transplant
- from the transplant up to 30 days after the transplant
- more than 30 days after the transplant

The most common adverse events in this trial were:

- nausea and vomiting from the start of treatment until just before the transplant
- vomiting and inflammation of the mouth and lips from the transplant up to 30 days after the transplant
- chronic GvHD and swelling in the lower limbs more than 30 days after the transplant

The adverse events below happened in at least 20.0% of the participants in either part of the trial. There were other adverse events, but these happened in fewer participants.

From start of treatment until just before the transplant

	Part 1	Part 2	
	3 mg of KRP203 and cyclosporine A (Out of 10 participants)	1 mg of KRP203, cyclosporine A, and methotrexate (Out of 6 participants)	3 mg of KRP203, tacrolimus, and methotrexate (Out of 7 participants)
Nausea	20.0% (2)	67.0% (4)	43.0% (3)
Vomiting	40.0% (4)	33.0% (2)	14.0% (1)
Increased weight	0.0% (0)	50.0% (3)	43.0% (3)
Increased creatinine in the blood (a sign of kidney damage)	0.0% (0)	33.0% (2)	14.0% (1)
Slow heart rate	20.0% (2)	0.0% (0)	0.0% (0)

From the transplant up to 30 days after the transplant

	Part 1	Part 2	
	3 mg of KRP203 and cyclosporine A (Out of 10 participants)	1 mg of KRP203, cyclosporine A, and methotrexate (Out of 6 participants)	3 mg of KRP203, tacrolimus, and methotrexate (Out of 7 participants)
Vomiting	60.0% (6)	33.0% (2)	43.0% (3)
Inflammation of the mouth and lips	10.0% (1)	67.0% (4)	71.0% (5)
High blood pressure	10.0% (1)	67.0% (4)	57.0% (4)
Nausea	20.0% (2)	17.0% (1)	29.0% (2)
Fever	0.0% (0)	17.0% (1)	57.0% (4)
Low platelet level	0.0% (0)	50.0% (3)	29.0% (2)
Temporary GvHD in the intestine	30.0% (3)	17.0% (1)	0.0% (0)
Back pain	0.0% (0)	33.0% (2)	29.0% (2)
Bone pain	0.0% (0)	33.0% (2)	29.0% (2)
Increased levels of C-reactive protein (a sign of inflammation)	0.0% (0)	33.0% (2)	29.0% (2)
Diarrhea	0.0% (0)	33.0% (2)	29.0% (2)
Trouble breathing	10.0% (1)	17.0% (1)	29.0% (2)
Headache	0.0% (0)	17.0% (1)	43.0% (3)
Low magnesium levels	0.0% (0)	33.0% (2)	29.0% (2)
Not enough healthy red blood cells	0.0% (0)	33.0% (2)	14.0% (1)
Tiredness	0.0% (0)	17.0% (1)	29.0% (2)
A buildup of fluid between the tissues that line the lungs and the chest	20.0% (2)	0.0% (0)	14.0% (1)
A condition in which fluid and proteins leak out of tiny blood vessels, into surrounding tissues	20.0% (2)	0.0% (0)	0.0% (0)

More than 30 days after the transplant

	Part 1	Part 2	
	3 mg of KRP203 and cyclosporine A (Out of 10 participants)	1 mg of KRP203, cyclosporine A, and methotrexate (Out of 6 participants)	3 mg of KRP203, tacrolimus, and methotrexate (Out of 7 participants)
Chronic GvHD	70.0% (7)	50.0% (3)	29.0% (2)
Swelling in the lower limbs	40.0% (4)	50.0% (3)	43.0% (3)
Chronic GvHD that lasted in the liver	50.0% (5)	50.0% (3)	14.0% (1)
Temporary GvHD in the skin	30.0% (3)	33.0% (2)	43.0% (3)
Temporary GvHD in the intestine	30.0% (3)	33.0% (2)	29.0% (2)
Increased levels of alanine aminotransferase (a sign of liver damage)	10.0% (1)	67.0% (4)	29.0% (2)
Diarrhea	20.0% (2)	33.0% (2)	29.0% (2)
Nausea	20.0% (2)	50.0% (3)	14.0% (1)
Rash	20.0% (2)	50.0% (3)	14.0% (1)
Chronic GvHD that lasted in the skin	30.0% (3)	0.0% (0)	29.0% (2)
Yeast infection in the mouth	0.0% (0)	50.0% (3)	29.0% (2)
Increased levels of aspartate aminotransferase (a sign of liver damage)	10.0% (1)	50.0% (3)	0.0% (0)
Chronic GvHD that lasted in the intestine	20.0% (2)	33.0% (2)	0.0% (0)
Infection from a virus called a cytomegalovirus	10.0% (1)	0.0% (0)	43.0% (3)
Swelling in the eyelid	20.0% (2)	0.0% (0)	14.0% (1)
Low potassium levels	0.0% (0)	33.0% (2)	14.0% (1)

For more information about the adverse events in this trial, please see the scientific summary that can be found on the website noted at the end of the summary.

How much and how quickly KRP203 got into the participants' blood?

The researchers wanted to know how much KRP203 got into the blood and how quickly it got into the blood after the participants took it. To find out, the trial doctors took blood samples at different times before and after the participants took KRP203.

Overall, the researchers found that:

- The higher the dose of KRP203 the participants took, the higher the level of KRP203 was in the blood.
- KRP203 reached its highest levels in the blood in about 3 to 10 hours after the first treatment.
- KRP203 reached steady levels in the blood about 14 days after the participants started treatment.

This information helps researchers decide when a dose should be given and what dose is safe and effective.

How many participants survived for at least 6 months after their last treatment without having GvHD?

Overall, the researchers found that 52.2% of the participants in this trial survived for at least 6 months after their last treatment without having GvHD. This was 12 out of the 23 participants.

To find this information, the researchers counted the number of participants who:

- survived
- did not have a return of GvHD
- did not have a moderate or severe case of GvHD that lasted either a short or a long time

How has this trial helped patients and researchers?

The information described above helped researchers learn more about how safe KRP203 is in participants with blood cancer who need stem cell transplants. The information also helped researchers learn more about how KRP203 gets into the blood and if it helped the participants survive for at least 6 months after their last treatment without having GvHD.

More research is needed to find out which treatments can be used for patients with GvHD. This summary shows only the main results from this one trial. Other trials may provide new information or different results.

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.

- Go to www.novctrd.com.
- Once on the site, click **"Clinical trial results and trial summary for patients"** at the top right of the page.
- After accepting the terms, go to the bottom left of the page and click **"Search by study number"**.
- Type **"CKRP203A2105"** into the keyword search box and click **"Search"**.

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 website listed below.

- www.clinicaltrials.gov Once you are on the website, type **"CKRP203A2105"** into the **"Other terms"** search box and click **"Search"**.
- If you would like to search by trial title, please use the full trial title listed below.

Full trial title: A Two-part, Single- and Two Arm Randomized, Open-label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy (in Part 2 Only) of KRP203 in Subjects Undergoing Allogenic Hematopoietic Stem Cell Transplant for Hematological Malignancies

Protocol number: CKRP203A2105

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.

NOVARTIS

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

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