Clinical Trial Results Summary

Research Sponsor: Novartis

Drug Studied: VAY736 (ianalumab)

Trial Number: CVAY736X2202

Plain Language Title: A trial to learn about the effects of VAY736 on the brain and about its safety in participants with relapsing-remitting multiple sclerosis

Thank you!

Thank you to the participants who took part in the clinical trial for the drug VAY736, also known as ianalumab. All of the participants helped the researchers learn more about how VAY736 works and how safe it is to take.

Novartis sponsored this trial and reviewed the results of the trial when it ended. Novartis believes it is important to share what was learned from the results of this trial with the participants and the public. An independent organization prepared this summary of the trial results.

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 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 studied how a drug called VAY736 affected the brain in participants with a disease called relapsing-remitting multiple sclerosis. This disease is also known as RRMS.

The researchers also learned more about the safety of VAY736 in these participants.

What treatments did the participants take?

This trial had 2 parts:

- During Part 1, the participants received either VAY736 or a placebo. A placebo looks like the trial drug but does not have trial drug in it.
- During Part 2, the participants who had received the placebo in Part 1 had the option to get VAY736.
- The participants who received VAY736 in Part 1 did not receive any additional treatment in Part 2.

Who took part in the trial?

There were 8 men and women with RRMS who participated in this clinical trial.

What did the researchers want to learn?

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

- Did VAY736 lower the number of new lesions in the brain?
- What medical problems did the participants have during the trial?

Keeping track of the participants' medical problems helped the researchers learn about the safety of VAY736.

What were the main results of the trial?

- This trial ended early, so the number of participants in each treatment group was small. The researchers could not reach any clear conclusions about the effect of VAY736 on the brain. The decision to stop was not related to safety.
- Most of the participants had medical problems during this trial, and none of the medical problems were serious. The most common medical problems were headache, nausea, and fast heart rate.

More details about the results of this trial can be found on page 6.

Why was the research needed?

Researchers are looking for better treatments for patients with relapsing-remitting multiple sclerosis, also known as RRMS. Before a drug can be approved, researchers do clinical trials to find out how safe it is and how it works. In this trial, the researchers studied how the trial treatment called VAY736 affected the brain lesions in participants with RRMS. The researchers also wanted to learn more about the safety of VAY736.

The immune system is made up of cells and proteins that work together to protect the body from injury and invaders, like bacteria and viruses. In people with RRMS, the immune system mistakenly attacks a layer of cells that helps cover and protect nerves in the body. When the layer is damaged, signals between the brain and the rest of the body are slowed down or blocked. People with RRMS may also have areas of inflammation that can lead to tissue damage in their brain. These areas are known as “brain lesions”.

What is inflammation?

Inflammation is one of the ways the immune system protects and helps the body heal when it lasts a short time.

Inflammation in multiple sclerosis leads to:

- build-up of white blood cells, proteins, and fluid in the brain and spinal cord
- tissue damage and health issues when it lasts a long time

Research shows that the immune system has a role in RRMS. There are different kinds of cells in the immune system. One of these is a white blood cell called a B cell. Researchers think that removing B cells could help decrease the number of brain lesions in people with RRMS. The trial treatment, VAY736, was designed to lower the activity of the immune system by removing B cells.

What was the purpose of the trial?

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- Did VAY736 lower the number of new lesions in the brain?
- What medical problems did the participants have during the trial?

What treatments did the participants take?

This trial had 2 parts. During Part 1, the participants received either VAY736 or the placebo:

- VAY736 was measured in milligrams per kilogram of body weight, also known as mg/kg. This meant that the amount of VAY736 the participants received depended on their body weight.
- A placebo looks like the trial drug but does not have any trial drug in it.

Both treatments were given through a needle put into a vein, also known as an IV infusion.

The researchers used a computer program to randomly choose the treatment each participant received in Part 1. This helped make sure that comparing the results of the treatments was as fair as possible.

During Part 2, the participants who received the placebo in Part 1 had the option of receiving VAY736. The participants who received VAY736 in Part 1 did not receive any additional treatment in Part 2. There was 1 participant in Part 1 and 1 participant in Part 2 who received VAY736 and had a reaction to the infusion that caused the trial doctors to stop their infusions early. This meant that these 2 participants did not get a full dose of VAY736. These participants still completed the rest of the trial.

The chart below shows the treatments the participants were planned to receive.

	Part 1		Part 2
	• 4 participants	• 4 participants	• 4 participants who got the placebo in Part 1
	• 10 mg/kg of VAY736	• Placebo	• 10 mg/kg of VAY736
	• Through an IV infusion		
	• A single dose		

Who took part in the trial?

To answer the questions in this trial, the researchers asked for the help of patients with RRMS. Everyone in the trial was 19 to 45 years old when they joined. The average age of the participants was about 37 years old.

The trial included 8 participants in 3 countries: Czech Republic, Ukraine, and the United States.

What type of trial was this?

This trial studied the trial drug's safety and how well it worked in a small number of people.

In Part 1 of this trial, none of the participants, trial staff, or sponsor staff knew what treatment each participant received.

Some trials are done this way because knowing what treatment the participants are receiving can influence the results. Not knowing what treatment the participants receive helps make sure the results are looked at fairly.

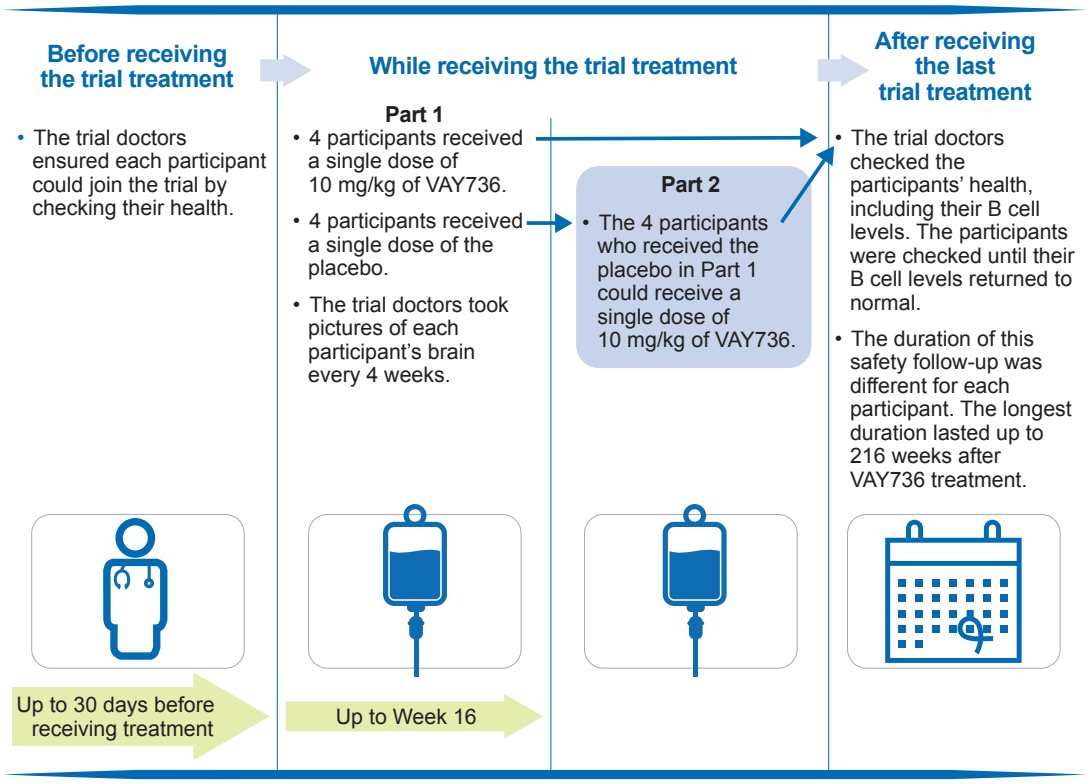
In Part 2 of this trial, each participant knew they were receiving VAY736. The trial staff and sponsor staff also knew what each participant received.

What happened during the trial?

The time each participant spent in the trial depended on their test results. The trial started in December 2013 and ended in September 2018.

This trial ended earlier than planned, because the sponsor decided to stop all research on VAY736 in RRMS. This was because there were similar treatments to VAY736 already being studied in other trials, and the sponsor did not expect that VAY736 would be better than the other trial drugs at treating RRMS. The decision to stop was not related to safety.

The chart below shows what happened during the trial.



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 changes to your healthcare.

Did VAY736 lower the number of new lesions in the brain?

This trial ended early, so the number of participants in each treatment group was small. The researchers could not reach any clear conclusions about the effect of VAY736 on the brain. The decision to stop was not related to safety.

To answer this question, the trial doctors took pictures of each participant's brain using magnetic resonance imaging, also known as an MRI. An MRI machine uses magnets to create a picture of any part of the body. To see the brain lesions in the pictures, the trial doctors first gave the participants a dye that attaches to areas of high inflammation in the brain.

Even though the researchers could not answer this question, the researchers still learned about the safety of VAY736 and how it works in participants with RRMS.

For more information about these results, 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?

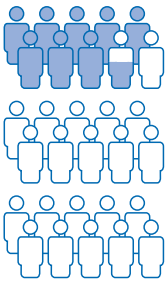
Medical problems that happen in clinical trials are called **"adverse events"**. An adverse event is any unwanted sign or symptom that participants have during a trial. An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care.

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. 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.

Most of the participants had adverse events during this trial, and none of the adverse events were serious. The most common adverse events were headache, nausea, and fast heart rate.

Summary of adverse events



- 87.5% of participants had adverse events. This was 7 out of the 8 participants.
- None of the participants had serious adverse events.
- None of the participants left the trial because of adverse events.

There was 1 participant in Part 1 and 1 participant in Part 2 who received VAY736 and had a reaction to the infusion that caused the trial doctors to stop their infusions early. This meant that these 2 participants did not get a full dose of VAY736. These participants still completed the rest of the trial.

What were the most common serious adverse events?

None of the participants had serious adverse events, and no deaths were reported during this trial.

What were the most common adverse events?

The most common adverse events during this trial were headache, nausea, and fast heart rate.

The adverse events below happened in 2 or more participants during the trial. There were other adverse events, but these happened in fewer participants. The table below includes the 4 participants in Part 2 who previously received the placebo in Part 1.

Most common adverse events in this trial

	Part 1		Part 2
	10 mg/kg of VAY736 (Out of 4 participants)	Placebo (Out of 4 participants)	10 mg/kg of VAY736 (Out of 4 participants)
Headache	75.0% (3)	25.0% (1)	25.0% (1)
Nausea	75.0% (3)	0.0% (0)	25.0% (1)
Fast heart rate	75.0% (3)	0.0% (0)	0.0% (0)
Having no energy	50.0% (2)	0.0% (0)	0.0% (0)
Chills	50.0% (2)	0.0% (0)	0.0% (0)
Fever	25.0% (1)	0.0% (0)	25.0% (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.

What was learned from this trial?

Because the trial ended early, the researchers could not conclude how VAY736 affects brain lesions in these participants. But the information described above still helped researchers learn about the safety of VAY736 and how it works in participants with RRMS.

More research is needed to find out which treatments can be used for patients with RRMS. 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 **"CVAY736X2202"** into the keyword search box, and click **"Search"**.

If you would like to view the website in a language other than English, you can click the "Google Translate" button on the top right of the page.

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 below.

- www.clinicaltrials.gov Once you are on the website, type **"CVAY736X2202"** into the **"Other terms"** search box, and click **"Search"**.
- www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search"**, then type **"CVAY736X2202"** in the search box, and click **"Search"**.

Full trial title: A randomized, partially blind, placebo-controlled, proof-of-concept study to assess the effect of a single infusion of VAY736 on disease activity as measured by brain MRI scans in patients with relapsing-remitting multiple sclerosis

Protocol number: CVAY736X2202

Thank you!

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