Clinical Trial Results Summary

Research Sponsor: Novartis

Drug Studied: VAY736 (ianalumab)

Trial Number: CVAY736X2203

Plain Language Title: A trial to learn about the effects of VAY736 and its safety in participants with pemphigus vulgaris

Thank you

Thank you to the participants who took part in the clinical trial for the trial 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 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 wanted to learn if VAY736 helped decrease lesions and other symptoms in participants with pemphigus vulgaris, also known as PV. Lesions are blisters caused by inflammation and reddening of the skin.

The researchers also studied the safety of VAY736 in these participants.

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

- Did VAY736 decrease the number and size of lesions?
- 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.

Who was in the trial?

13 men and women with PV participated in this clinical trial.

What treatments did the participants take?

This trial had 2 parts. During Part 1, the participants received 1 of these treatments 1 time:

- Low dose of VAY736.
- High dose of VAY736.
- Placebo: A placebo looks like the trial drug but does not have any trial drug in it.

During Part 2 of the trial, the participants who had received the placebo during Part 1 had the option to receive the high dose of VAY736 1 time.

Throughout the trial, the participants continued taking certain medicines they had already been taking for their PV symptoms.

What were the main results of the trial?

Overall, the researchers learned that 12 weeks after the participants received treatment:

- The participants in all treatment groups had a decrease in the number and size of their lesions. This decrease was largest in the low dose VAY736 group. Because there were a small number of participants in the trial, the researchers could not determine if VAY736 caused this decrease.
- Most of the participants had medical problems during the trial. The most common medical problems were headache and pain in the mouth or throat. Some of the medical problems were serious. None of the participants left the trial due to a medical problem.

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

What was the purpose of the trial?

Researchers are looking for a better way to treat people with PV. In this trial, the researchers wanted to learn if VAY736 would affect lesions and other symptoms in participants with PV. The researchers also wanted to learn more about the safety of VAY736.

Research shows that the immune system plays a role in PV. The immune system normally protects the body from injury and invaders, like bacteria and viruses. In people with PV, the immune system mistakenly attacks cells in the skin and areas like the lining of the mouth, which causes inflammation.

Before a trial drug can be approved for patients to take, researchers do clinical trials to find out how safe it is and how it works.

What is inflammation?

Inflammation is one of the ways your immune system protects your body from illness and infection. Inflammation:

- Causes swelling, redness, and sometimes pain.
- In people with PV, it can lead to the formation of blisters called lesions, which can damage the skin.

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

- Did VAY736 decrease the number and size of lesions?
- What medical problems did the participants have during the trial?

Who was in the trial?

To answer the questions in this trial, the researchers asked for the help of men and women with PV.

Everyone in this trial was 29 to 70 years old when they joined. The average age of the participants was 49 years.

The trial included 13 participants in Austria, Bulgaria, Taiwan, and the United States.

What trial treatments did the participants receive?

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

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.

This trial had 2 parts.

The chart below shows the trial treatments the participants received.

	Part 1			Part 2
	Group 1	Group 2	Group 3	
	7 participants	2 participants	4 participants	3 participants
	Low dose VAY736: 3 mg/kg	High dose VAY736: 10 mg/kg	Placebo	High dose VAY736: 10 mg/kg
	Through an IV infusion			
	1 time			

A placebo looks like the trial drug but has no trial drug in it.

Part 1

To help make sure the results were looked at fairly, the researchers used the following approach:

- A computer program was used to randomly choose the trial treatment.
- 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.
  - Everyone found out the treatment each participant received 24 weeks after treatment.

Part 2

During Part 2:

- The participants who received VAY736 during Part 1 did not receive any additional trial treatment during Part 2.
- The participants who received the placebo during Part 1 had the option to receive the high dose of VAY736 1 time. During Part 2, everyone knew what the participants were receiving.

Throughout the trial, the participants could continue taking certain medicines they had already been taking for their PV symptoms.

What happened during the trial?

The trial started in December 2013 and ended in September 2019. The longest time a participant was in the trial was about 5 years.

Throughout the trial, the participants answered surveys about their PV symptoms and overall health.

The researchers stopped the trial early after studying the initial results. This was because the researchers were not sure that VAY736 would help people with PV more than treatments that were already being studied in other trials. The decision to stop the trial was not related to safety.

What were the main 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.

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.

For the below results on lesions and PV severity, the researchers focused only on Part 1 of the trial. The results from both Parts 1 and 2 are included in the medical problems section later in this summary.

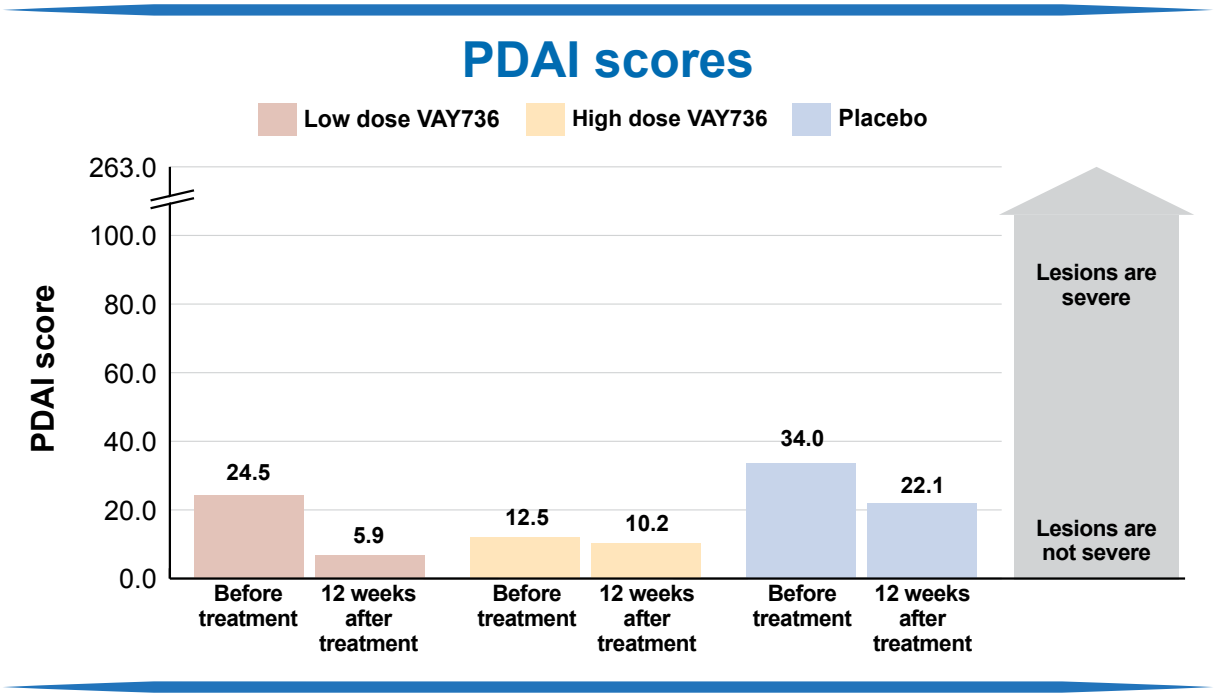
Did VAY736 decrease the number and size of lesions?

The participants in all treatment groups had a decrease in the number and size of their lesions. This decrease was largest for the low dose VAY736 group. Because there were a small number of participants in the trial and other medications used at the same time, the researchers could not be sure if VAY736 caused this decrease.

To answer this question, the researchers used the Pemphigus Disease Area Index, also known as the PDAI. The PDAI is a test made up of several scores. The scores are based on the number and size of the lesions on a person's skin, scalp, and mouth. The scores are added together to calculate a person's overall PDAI score, which is on a scale from 0 to 263. **The higher a person's PDAI score is, the worse their lesions are.**

The trial staff recorded the participants' PDAI scores throughout the trial. The researchers compared the participants' scores before they received the trial treatment to their scores 12 weeks after they received treatment.

The chart below shows these results.



The participants in all treatment groups had a decrease in PDAI scores. The low dose VAY736 group showed the largest decrease in PDAI scores. But, the researchers could not be sure if VAY736 caused this decrease because:

- The number of participants was too small.
- Some participants continued medicines they were already taking for their PV symptoms.

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 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.

Most of the participants had adverse events during the trial. Some of the adverse events were serious. None of the participants left the trial due to an adverse event. The most common adverse events were headache and pain in the mouth or throat.

A lot of research is needed to know whether a trial 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. The results below include information for both parts of the trial.

Summary of adverse events

	Part 1			Part 2
	Low dose VAY736 (Out of 7 participants)	High dose VAY736 (Out of 2 participants)	Placebo (Out of 4 participants)	High dose VAY736 (Out of 3 participants)
Non-serioius adverse events	85.7% 6 of 7	100.0% 2 of 2	75.0% 3 of 4	100.0% 3 of 3
Serious adverse events	14.3% 1 of 7	0.0% 0 of 2	25.0% 1 of 4	33.3% 1 of 3
Left the trial or stopped receiving treatment due to adverse events	0.0% 0 of 7	0.0% 0 of 2	25.0% 1 of 4	0.0% 0 of 3

What were the serious adverse events?

Part 1

15.4% of the participants had serious adverse events. This was 2 out of 13 participants. There were 7.7% of participants who left the trial due to serious adverse events. This was 1 out of 13 participants. This participant was in the placebo treatment group and had the serious adverse event of a worsening of their PV.

Part 2

33.3% of the participants had serious adverse events. This was 1 out of 3 participants. None of the participants left the trial due to serious adverse events.

The table below shows the serious adverse events that happened during this trial. No other serious adverse events were reported, including no deaths.

Serious adverse events

	Part 1			Part 2
	Low dose VAY736 (Out of 7 participants)	High dose VAY736 (Out of 2 participants)	Placebo (Out of 4 participants)	High dose VAY736 (Out of 3 participants)
Duodenal ulcer (Melena)	14.3% (1 of 7)	0.0% (0 of 2)	0.0% (0 of 4)	0.0% (0 of 3)
Worsening of PV (Pemphigus flare)	0.0% (0 of 7)	0.0% (0 of 2)	25.0% (1 of 4)	0.0% (0 of 3)
Clouding of the lens in the eye (Cataract)	0.0% (0 of 7)	0.0% (0 of 2)	0.0% (0 of 4)	33.3% (1 of 3)

What were the non-serious adverse events?

The most common non-serious adverse events that happened were headache and pain in the mouth or throat, which is also known as oropharyngeal pain.

The table below shows the non-serious adverse events that happened in **at least 2 participants**. There were other non-serious adverse events during the trial, but those happened in fewer participants.

For more information about the adverse events in this trial, visit novctrd.com. Use clinical trial number **CVAY736X2203** to find the scientific summary.

Most common adverse events

	Part 1			Part 2
	Low dose VAY736 (Out of 7 participants)	High dose VAY736 (Out of 2 participants)	Placebo (Out of 4 participants)	High dose VAY736 (Out of 3 participants)
Headache	28.6% (2 of 7)	50.0% (1 of 2)	0.0% (0 of 4)	33.3% (1 of 3)
Pain in the mouth or throat (Oropharyngeal pain)	28.6% (2 of 7)	50.0% (1 of 2)	0.0% (0 of 4)	33.3% (1 of 3)
Cough	42.9% (3 of 7)	0.0% (0 of 2)	0.0% (0 of 4)	0.0% (0 of 3)
Common cold (Nasopharyngitis)	14.3% (1 of 7)	0.0% (0 of 2)	25.0% (1 of 4)	33.3% (1 of 3)
Unable to sleep (Insomnia)	28.6% (2 of 7)	0.0% (0 of 2)	0.0% (0 of 4)	0.0% (0 of 3)
Dizziness	14.3% (1 of 7)	50.0% (1 of 2)	0.0% (0 of 4)	0.0% (0 of 3)
Infection of the nose, throat, and airways (Upper respiratory tract infection)	14.3% (1 of 7)	50.0% (1 of 2)	0.0% (0 of 4)	0.0% (0 of 3)
Sores on body caused by a virus (Herpes simplex)	14.3% (1 of 7)	0.0% (0 of 2)	0.0% (0 of 4)	33.3% (1 of 3)

What other results were learned?

Did VAY736 affect other symptoms of PV?

To answer this question, researchers used two measures. They compared the participants' scores before treatment and 12 weeks after treatment.

The first measure the researchers used is called the Autoimmune Bullous Skin Disorder Intensity Score, also known as the ABSIS. Like the PDAI, the ABSIS is a test made up of a series of scores. These scores are based on the percentage of a person's body that has lesions, as well as the pain they feel while eating or drinking. The higher a person's ABSIS score is, the worse their lesions and pain are.

Overall, the researchers found that the participants in all treatment groups had less lesions on their body. This decrease was largest for the placebo group. The researchers did not see a meaningful difference between the treatment groups.

The second measure the researchers used is called the Investigator's Global Assessment, also known as the IGA. Researchers use the IGA to calculate how severe a person's PV was.

Overall, the researchers found that the participants in all treatment groups had a decrease in the severity of their PV. This decrease was largest in the low dose VAY736 group.

For both measures, researchers could not be sure if VAY736 caused these decreases because:

- there were a small number of participants in the trial
- participants were allowed to continue other medications during the trial

What was learned from this trial?

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

More research is needed to find out which treatments can be used for patients with PV. 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"** at the top right of the page.
- After accepting the terms, go to the bottom left of the page and click **"Study number"** from the drop-down menu.
- Type **"CVAY736X2203"** 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 website listed below.

- www.clinicaltrials.gov Once you are on the website, type **"CVAY736X2203"** into the **"Other terms"** search box and click **"Search"**.

www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search"**, then type **"2013-001217-33"** in the search box, and click **"Search"**.

If more clinical trials are planned, they will be listed on the above public websites or at www.novartisclinicaltrials.com. Search for **"VAY736"** or **"ianalumab"** or **"pemphigus vulgaris"**.

Full trial title: A randomized, partial-blind, placebo-controlled trial evaluating the efficacy, safety, pharmacokinetics and pharmacodynamics of VAY736 in the treatment of patients with pemphigus vulgaris

Protocol number: CVAY736X2203

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.

1-888-669-6682 (US) • +41613241111 (EU)
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