Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis

Treatment Studied: VAY736 (ianalumab)

Protocol Number: CVAY736X2101

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 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 the results of the trial with you and the public. An independent non-profit organization called CISCRP prepared this summary of the trial results for you. We hope it helps you understand your 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.

What has happened since the trial ended?

The whole trial took about 7 years to finish. The time each participant spent in the trial depended on their test results. The trial started in December 2010 and ended in January 2018.

The trial included 65 participants in Germany. After the trial ended, the sponsor reviewed the data and created a report of the results. This is a summary of that report.

Why was the research needed?

In some diseases, the body's immune system is overactive. When that happens, the immune system attacks the body. The immune system is made up of different kinds of cells. One of these is a white blood cell called a B lymphocyte, also known as a B cell.

The trial drug VAY736 was designed to lower the activity of the immune system by removing B cells. Researchers think that removing B cells could help decrease pain and inflammation in people with immune system diseases like rheumatoid arthritis, also called RA.

VAY736 is an antibody. Antibodies are normally made by the immune system to identify substances like bacteria and viruses that are not made by the body. Sometimes, researchers can use antibodies as medicines to treat certain conditions.

This was the first time VAY736 was given to humans. So, learning more about how safe VAY736 is to take was a main focus of this trial. The researchers also compared 2 ways of giving the participants VAY736. First, they gave VAY736 through a needle put into a vein, also called an IV infusion. Next, they gave the participants VAY736 through a needle put under the skin, also called an injection.

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

- What medical problems did the participants have during this trial?
- Was the amount of VAY736 in the blood different when given as an injection under the skin compared to as an IV infusion?
- How much VAY736 got into the participants' blood after getting multiple doses through an injection under the skin?

To answer the questions in this trial, the researchers asked for the help of participants with RA who had been getting methotrexate treatment for at least 16 weeks, but who were otherwise healthy. Methotrexate is a common treatment for people with RA. The men and women in the trial were 27 to 64 years old when they joined.

What kind of trial was this?

This trial had 3 parts. Each participant was only in 1 part of the trial.

Part 1 of the trial was "double-blind". This means that none of the participants, trial doctors, trial staff, or sponsor staff knew what treatment each participant took. Some trials are done this way because knowing what treatment the participants are taking can affect the results of the trial. When the trial ended, the sponsor found out which treatment each participant took so they could create a report of the results. The sponsor staff did not know the identity of any of the participants.

In this part of the trial, the researchers compared VAY736 to a placebo. A placebo looks like the trial drug but does not have any medicine in it. Using a placebo helps researchers better understand the actual effect of a trial drug.

Parts 2 and 3 of the trial were “open-label”. This means that the participants, the trial doctors, the trial staff, and the sponsor knew what the participants were taking. The sponsor staff did not know the identity of any of the participants. These parts of the trial were done this way because knowing what treatments the participants were taking would not affect the results of the trial.

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

This was also a “dose-escalation” trial. This means that in Parts 1 and 2, a group of participants started out taking a low dose of VAY736. The researchers looked at the results for these participants. Then, the researchers decided whether to increase the dose in the next group of participants. Researchers use dose-escalation trials to learn about the safety of a specific dose before participants are given a higher dose.

What happened during the trial?

Before the treatment started in any of the parts, the trial doctors did tests to make sure the participants could take part in the trial. For all parts, the participants came to the trial site 24 hours before getting their trial treatment and stayed for 1 night.

During Part 1, a total of 41 participants got VAY736 or the placebo:

- 31 participants got a single dose of VAY736
- 10 participants got a single dose of the placebo

Doses of VAY736 were measured in milligrams per kilogram of body weight, also called mg/kg. Both trial treatments were given through an IV infusion. This infusion lasted about 4 hours.

This was the first time VAY736 was given to humans. So, the main focus of this part of the trial was to learn more about the safety of VAY736.

During Part 2, a total of 12 participants got a single dose of VAY736 through an injection under the skin:

- 6 participants got 0.6 mg/kg VAY736
- 6 participants got 2.0 mg/kg VAY736

This part of the trial focused on:

- learning more about the safety of VAY736
- testing another way of giving the participants VAY736

Researchers compared the results from Part 2 to Part 1.

During Part 3, a total of 12 participants got 60 mg of VAY736 through an injection under the skin:

- Participants returned to the trial site about once every 2 weeks to get a dose of VAY736.
- Participants got 6 total doses of VAY736.

This part of the trial focused on:

- learning more about the safety of VAY736
- measuring how much VAY736 was in the blood after multiple doses of VAY736

After treatment, the participants in each part visited the trial site until their B cells levels returned to normal. Once this happened, they visited the site 1 more time.

Throughout the trial, the trial doctors:

- checked the participants' overall health
- took blood and urine samples from the participants
- checked B cell levels in the blood
- asked the participants about any other medicines they were taking and how they were feeling
- checked the participants' RA symptoms

The chart below shows the treatments the participants got in this trial.

Part 1	Part 2	Part 3
31 participants got anywhere from 0.0003 mg/kg to 10.0 mg/kg of VAY736. 10 participants got the placebo.	6 participants got 0.6 mg/kg of VAY736. 6 participants got 2.0 mg/kg of VAY736.	12 participants got 60 mg of VAY736.
VAY736 through an IV infusion or a placebo through an IV infusion	VAY736 through an injection under the skin	VAY736 through an injection under the skin
1 time	1 time	6 times
Safety of VAY36	Safety of VAY736 Testing another way of getting VAY736 (comparing the results from Part 2 to Part 1)	Safety of VAY736 How much VAY736 was in the blood after getting multiple doses

What were the results of the trial?

This is a summary of the overall results of your trial, not your individual results. The results presented here are for a single trial. Other trials may provide new information or different results. You should not make medical decisions based on the results of a single trial. Always talk to a doctor before making any changes to your medications or treatment plans.

What medical problems did the participants have 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, 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 a medical problem. During a trial, all medical problems are reported and written down, whether or not they are caused by the trial drug. So, when new drugs are being studied, researchers keep track of all medical problems that participants have.

This was the first time VAY736 was given to humans. So, learning more about how safe VAY736 is to take was the main focus of this trial.

How many participants had adverse events overall?

Across all parts of the trial:

- Most of the participants had at least 1 adverse event.
- No participants left the trial because of an adverse event.
- Most of the adverse events happened during the first 24 hours after getting VAY736.
- 8 serious adverse events were reported by 5 participants in Parts 1 and 2. No serious adverse events happened in Part 3.

The section below provides more details about the adverse events that happened during each part of this trial.

How many participants had adverse events in each part?

Part 1

- 87.8% of the participants had adverse events during Part 1. This was 36 of the 41 participants.
- 7.3% of the participants had serious adverse events during Part 1. This was 3 of the 41 participants.

The table below shows how many participants in each treatment group had adverse events during Part 1.

Adverse events during Part 1 of this trial

	Placebo (Out of 10 participants)	VAY736 (Out of 31 participants)	Total (Out of 41 participants)
How many participants in Part 1 had adverse events?	80.0% (8)	90.3% (28)	87.8% (36)
How many participants in Part 1 had serious adverse events?	0.0% (0)	9.7% (3)	7.3% (3)

Part 2

- 100.0% of the participants had adverse events during Part 2. This was all 12 of the participants.
- 16.7% of the participants had serious adverse events during Part 2. This was 2 of the 12 participants.

The table below shows how many participants in each treatment group had adverse events during Part 2.

Adverse events during Part 2 of this trial

	0.6 mg/kg VAY736 (Out of 6 participants)	2.0 mg/kg VAY736 (Out of 6 participants)	Total (Out of 12 participants)
How many participants in Part 2 had adverse events?	100.0% (6)	100.0% (6)	100.0% (12)
How many participants in Part 2 had serious adverse events?	16.7% (1)	16.7% (1)	16.7% (2)

Part 3

- 100.0% of the participants had adverse events during Part 3. This was all 12 of the participants.
- None of the participants had serious adverse events during Part 3.

The table below shows how many participants in each treatment group had adverse events during Part 3.

Adverse events during Part 3 of this trial

	60 mg VAY736 (Out of 12 participants)
How many participants in Part 3 had adverse events?	100.0% (12)
How many participants in Part 3 had serious adverse events?	0.0% (0)

In all parts of the trial, none of the participants left the trial because of an adverse event.

What were the most common serious adverse events in each part?

Part 1

In Part 1, the following 4 serious adverse events happened:

- Shortness of breath during exercise
- Overactive parathyroid glands
- Parathyroid tumor that wasn't cancer
- Bone pain

Part 2

In Part 2, the following 4 serious adverse events happened:

- Stomach hernia, a condition where part of the stomach pushes up through the diaphragm
- Acid reflux
- Bursitis, a condition where there is swelling of the fluid-filled pads that cushion joints
- Soft tissue injury due to a fall

Part 3

None of the participants in Part 3 had serious adverse events.

None of the participants died during any part of this trial.

What were the most common adverse events in each part?

The researchers wanted to study the most common adverse events that happened within 24 hours of the participants getting trial treatment. This is because some adverse events are considered common when a drug is given that causes B cell levels to decrease quickly. The researchers also studied the most common adverse events that happened more than 24 hours after the participants got the trial treatment.

For all parts of the trial, most of the adverse events happened within first 24 hours of getting VAY736.

Part 1

In Part 1, the most common adverse event within 24 hours of trial treatment was a headache. The most common adverse event more than 24 hours after trial treatment was the common cold.

The tables below show the adverse events that happened in at least 10% of the participants in Part 1.

Adverse events within 24 hours of trial treatment in Part 1 of this trial

Adverse event	Placebo (Out of 10 participants)	All VAY736 groups combined (Out of 31 participants)	Total (Out of 41 participants)
Headache	40.0% (4)	41.9% (13)	41.5% (17)
Body temperature increased	0.0% (0)	41.9% (13)	31.7% (13)
Chills	0.0% (0)	19.4% (6)	14.6% (6)
Fever	0.0% (0)	19.4% (6)	14.6% (6)
Feeling cold	0.0% (0)	16.1% (5)	12.2% (5)
Nausea	0.0% (0)	16.1% (5)	12.2% (5)

Adverse events more than 24 hours after trial treatment in Part 1 of this trial

Adverse event	Placebo (Out of 10 participants)	All VAY736 groups combined (Out of 31 participants)	Total (Out of 41 participants)
Common cold	10.0% (1)	48.4% (15)	39.0% (16)
Headache	30.0% (3)	16.1% (5)	19.5% (8)

The adverse events during Part 1 helped the researchers learn more about the type of symptoms that happen when there is a fast drop in B cell levels, caused by VAY736 treatment. So, the adverse events that happened within 24 hours of getting VAY736 in Part 1 became known as “injection-related reactions” for the rest of the trial.

Part 2

In Part 2, the most common adverse event within 24 hours of trial treatment was an injection-related reaction. The most common adverse event more than 24 hours after trial treatment was the common cold.

The tables below show the adverse events that happened in at least 10% of the participants in Part 2.

Adverse events within 24 hours of trial treatment in Part 2 of this trial

Adverse event	0.6 mg/kg VAY736 (Out of 6 participants)	2.0 mg/kg VAY736 (Out of 6 participants)	Total (Out of 12 participants)
Injection-related reaction	50.0% (3)	83.3% (5)	66.7% (8)
Headache	66.7% (4)	16.7% (1)	41.7% (5)

Adverse events more than 24 hours after trial treatment in Part 2 of this trial

Adverse event	0.6 mg/kg VAY736 (Out of 6 participants)	2.0 mg/kg VAY736 (Out of 6 participants)	Total (Out of 12 participants)
Common cold	33.3% (2)	33.3% (2)	33.3% (4)
RA flare-up	33.3% (2)	16.7% (1)	25.0% (3)

Part 3

In Part 3, the most common adverse event within 24 hours of trial treatment was an injection-related reaction. None of the adverse events in Part 3 happened more than 24 hours after getting trial treatment.

The table below shows the adverse events that happened in at least 10% of the participants in Part 3.

Adverse events within 24 hours of trial treatment in Part 3 of this trial

	60 mg VAY736 (Out of 12 participants)
Injection-related reaction	83.3% (10)
Headache	25.0% (3)

Was the amount of VAY736 in the participants' blood different when given as an injection under the skin compared to an IV infusion?

Yes. The researchers found that there was less VAY736 that got into the blood when participants got it through an injection under the skin compared to getting it through an IV infusion.

The researchers wanted to compare how much VAY736 got into the blood when the participants got it through an injection under the skin in Part 2 compared to getting it through an IV infusion in Part 1.

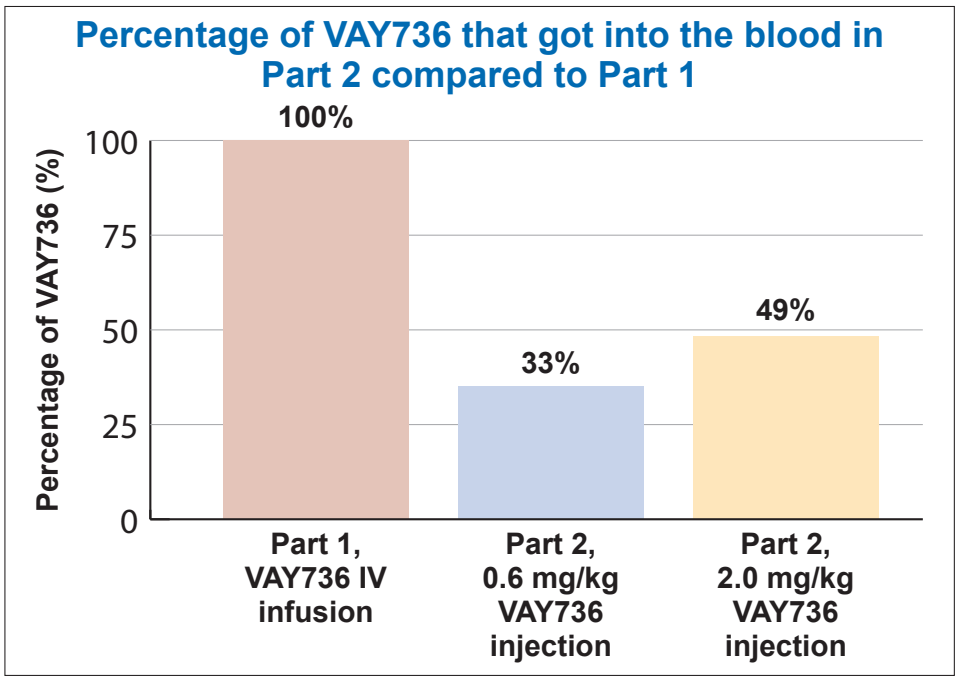
After getting an injection under the skin of 0.6 mg/kg of VAY736:

- the amount of VAY736 in the blood was 33% of the amount of VAY736 that was in the blood after getting the IV infusion.

After getting an injection under the skin of 2.0 mg/kg of VAY736:

- the amount of VAY736 in the blood was 49% of the amount of VAY736 that was in the blood after getting the IV infusion.

The graph below shows the amount of VAY736 that got into the blood in Part 2 compared to Part 1.



How much VAY736 got into the participants' blood after getting multiple doses through an injection under the skin?

In Part 3, participants got VAY736 6 times through an injection under the skin every 2 weeks. The researchers wanted to know how much VAY736 got into the participants' blood after the first dose on Day 1 and the last dose on Day 71. To answer this question, the researchers measured the amount of VAY736 in the blood at different times during Part 3.

Overall, the researchers found that:

- The amount of VAY736 was higher on Day 71 compared to Day 1.
- It took about 72 hours, or about 3 days, after the injection to reach the highest level in the blood.

More information can be found about this trial on the websites listed at the end of this summary.

How has this trial helped patients and researchers?

This was the first time VAY736 was given to humans. The information described above helped the researchers better understand how safe VAY736 was to take. The information above also helped the researchers understand how much VAY736 stays in the blood.

The results presented here are for a single trial in participants with RA. This summary shows only the main results from this one trial in a small number of participants. Other trials may provide new information or different results. It takes volunteers in many trials all around the world to advance medical science.

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). Once on the site, click **"READ MORE"** under **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **"CVAY736X2101"** into the keyword search box and click **"Search"**. If you 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 **"NCT02675803"** into the **"Other terms"** search box and click **"Search"**.

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

Full trial title: A dose escalation study to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of VAY736 in rheumatoid arthritis patients

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.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation.

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