Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis

Drug Studied: VAY736 (ianalumab)

Protocol Number: CVAY736X2201

Thank you!

Thank you for taking part in the clinical trial for the drug VAY736, also called ianalumab. You and all of the participants helped researchers learn more about how VAY736 works in people with primary Sjögren's syndrome, also called PSS.

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 doctor or staff at your trial site.

What has happened since the trial ended?

You were in this trial for up to 3 years. But, the entire trial lasted about 3.5 years. This is because participants started and stopped at different times. The trial started in May 2014 and ended in February 2018.

The trial included 27 participants from a trial site 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?

Researchers are looking for a better way to treat people who have PSS. Before a drug can be approved for patients, researchers do clinical trials to find out how safe it is and how well it works. The information collected from many clinical trials is needed to find out if VAY736 improves the health of people with PSS.

In people with PSS, the body's immune system is overactive. When that happens, the immune system attacks the body, including the glands that make fluids like tears, saliva, or sweat. People with PSS have dryness of the mouth, eyes, and other areas. They also have pain and tiredness that severely affect their daily lives.

In this trial, the researchers wanted to find out if VAY736 works in a small number of participants with PSS. They also wanted to find out about the safety of VAY736 in participants with PSS. To do this, the researchers compared VAY736 with 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.

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

- Did VAY736 make the participants' PSS symptoms less severe?
- Did the participants feel that other aspects of their PSS changed after getting VAY736?
- Did the trial doctors think the participants' overall health changed after taking VAY736?
- How long and at what level was VAY736 in the participants blood?
- What medical problems did the participants have?

What kind of trial was this?

To answer the questions in this trial, the researchers asked for the help of men and women with PSS. The participants in this trial were 25 to 70 years old.

This was a "dose escalation" trial. This means that each participant got only 1 dose of the trial drug. Different groups of participants were given different doses of VAY736. The researchers checked to make sure that the dose was safe before giving the next higher dose to the next group of participants.

This trial was done in 2 time periods. The first 24 weeks of the trial was the "double-blind" period. This means none of the participants, trial staff, or sponsor staff knew what trial drug each participant got. Some trials are done this way because knowing what trial drug the participants are getting can affect the results of the trial. Doing a trial this way helps make sure the results are looked at fairly.

A computer program was used to randomly assign the trial drug each participant got during the double-blind period. Researchers do this so that comparing the results of each trial drug is done as fairly as possible.

After 24 weeks, the participants, trial staff, and sponsor staff found out what treatment each participant got during the double-blind period. The participants who got the placebo during the double-blind period were given the choice to get a single dose of VAY736. The rest of this trial was "open-label". This means the participants, trial staff, and sponsor staff knew the treatment each participant received. All participants stayed in the open-label period until their B cell levels returned to normal.

When the trial ended, the sponsor created a report of the trial results. The sponsor staff did not know the identity of any of the participants.

What happened during the trial?

Before treatment started, the participants visited the trial site 2 times. The trial doctors did tests and checked the health of the participants to make sure they could take part in the trial.

During the double-blind period, the participants got a single dose of drug through a needle into a vein. This is called an intravenous dose, also called an IV dose. The dose each participant got was measured in milligrams per kilogram of body weight, also called mg/kg. The participants got 1 of 3 treatments:

- 6 participants got 3 mg/kg of VAY736
- 12 participants got 10 mg/kg of VAY736
- 9 participants got the placebo

After getting the single dose, the participants visited the trial site at least 10 times over 24 weeks.

Throughout the entire trial, the trial doctors took blood, urine, and saliva samples and checked the participants' PSS symptoms and overall health. At some of these visits, the participants filled out questionnaires about their PSS symptoms and had their B cell levels checked.

After the first 24 weeks of the trial, participants who got the placebo in the double-blind period had the choice to restart the trial, and get a single 10 mg/kg dose of VAY736.

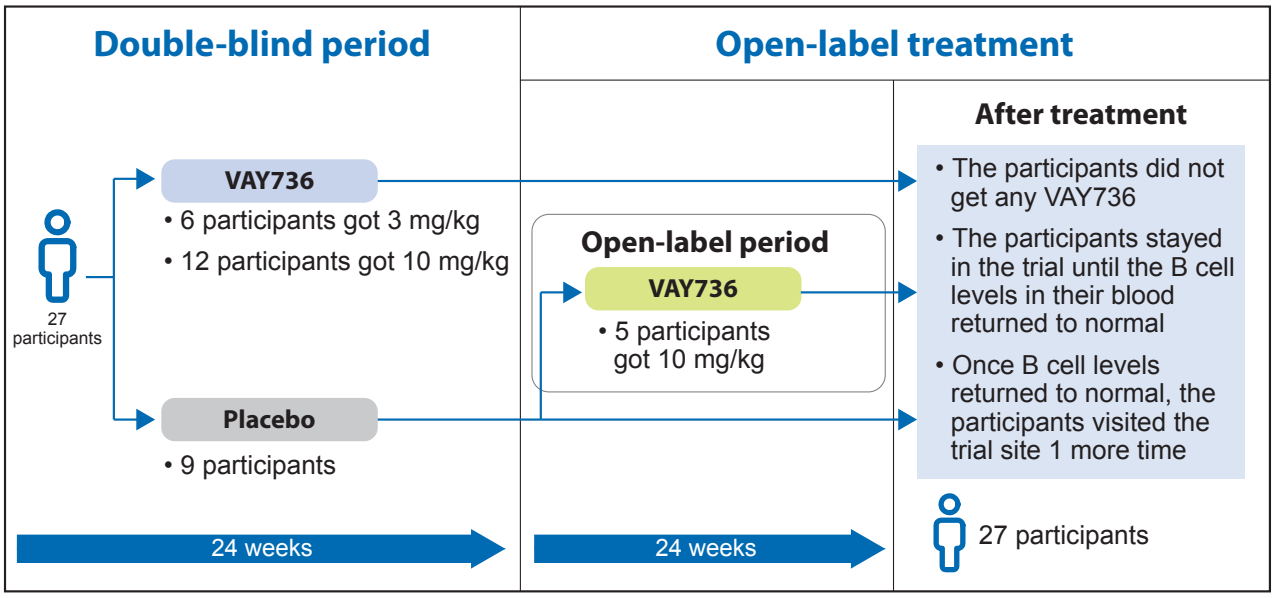
After the double-blind period finished:

- 6 participants out of 18 who got any dose of VAY736 in the double-blind period finished the trial within 24 weeks
- 12 participants out of 18 who got any dose of VAY736 in the double-blind period stayed in the trial because their B cell levels did not return to normal after 24 weeks
- Of the 9 participants who got the placebo:
  - 4 participants finished the trial after the double-blind period ended
  - 5 participants chose to get a single, open-label dose of 10 mg/kg VAY736

The 5 participants who got open-label VAY736 kept visiting the trial site because their B cells did not return to normal within 24 weeks of getting VAY736.

After treatment, the trial doctors took more blood, urine, and saliva samples and checked the participants' PSS symptoms and overall health. The participants filled out questionnaires about their primary Sjögren's syndrome symptoms and had their B cell levels checked.

The graphic below shows how the trial was done.



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.

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

Did VAY736 make the participants' PSS symptoms less severe?

After 12 weeks, there were slight reductions in the participants' PSS symptoms in all treatment groups. The researchers were more interested in the difference between VAY736 and the placebo than in the difference between the 2 VAY736 doses. So, the researchers combined the 2 VAY736 treatment groups into 1 group when looking at the results.

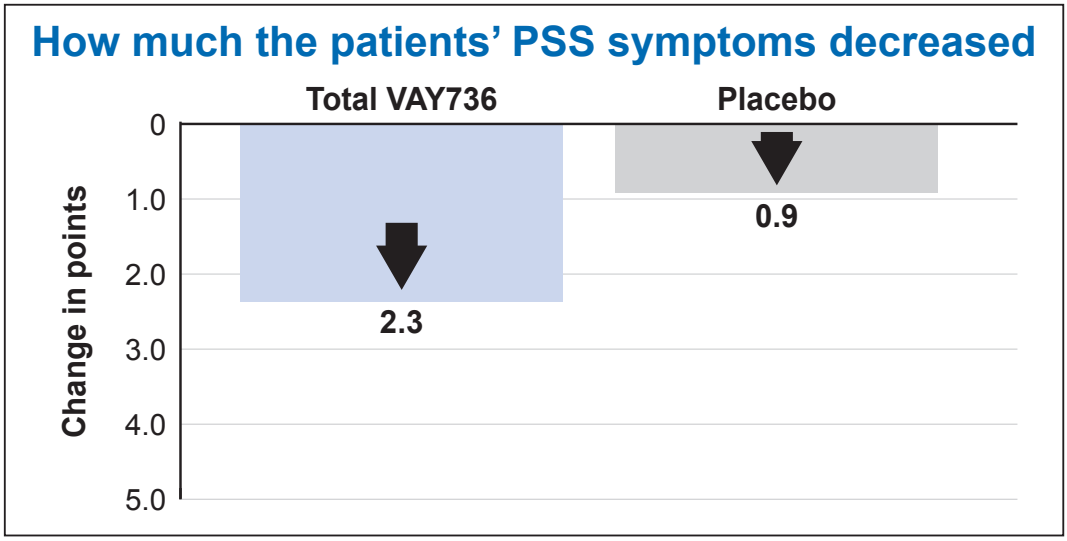
There was a slightly larger reduction in PSS symptoms for the participants who got VAY736 compared to the participants who got the placebo. But, the differences between the treatment groups were too small for the researchers to know if they were caused by the trial drug.

The researchers wanted to know if VAY736 made the participants' PSS symptoms less severe. To find out, the trial doctors measured how severe the participants' PSS symptoms were before getting the trial drug, and 12 weeks after getting the trial drug. They did this using the EULAR Sjögren's Syndrome Disease Activity Index, also called the ESSDAI. Lower scores meant the PSS symptoms were less severe. The researchers looked at the data after 12 weeks to decide whether or not to continue the trial.

The researchers learned that after 12 weeks, on average:

- The PSS symptoms in the participants who got VAY736 decreased by 2.3 points.
- The PSS symptoms in the participants who got the placebo decreased by 0.9 points.

The chart below shows these results.



Did the participants feel that other aspects of their PSS changed after getting VAY736?

Overall, the participants in all treatment groups felt that their PSS symptoms changed after 12 weeks. But, some of the differences between the treatment groups were too small for the researchers to know if these differences were caused by the trial drug.

The researchers wanted to know if VAY736 changed the participants' PSS symptoms throughout the trial. To find out, they used 4 questionnaires.

The table below shows what these questionnaires are.

Name	Description	What the score shows
EULAR Sjögren's Syndrome Patient Reported Index (also called the ESSPRI)	Measured how severe the participants' main PSS symptoms of pain, dryness, and tiredness were during the trial	A low score in the ESSPRI meant the participants' PSS symptoms were less severe
Multidimensional Fatigue Inventory (also called the MFI)	Measured the participants' tiredness	A low score in the MFI meant the participants were less tired
Patient Global Assessment version of the Visual Analog Scale (also called the VAS)	Measured the participants' overall condition	A low score in the Patient Global Assessment VAS meant the participant had a healthier overall condition
36-Item Short Form Health Survey (also called the SF-36)	Measured the participants' physical, emotional, and social well-being	A high score in the SF-36 meant the participants had a healthier well-being

Overall, the scores showed that the participants who got VAY736 or the placebo had fewer PSS symptoms after getting the study treatment. Some of these effects lasted longer than 12 weeks for participants who got 10 mg/kg of VAY736. The participants who got 10 mg/kg of VAY736 generally had larger differences than participants who got 3 mg/kg compared to the placebo. But, the differences between the treatment groups were too small for the researchers to know if these differences were caused by the trial drug.

Did the trial doctors think the participants' overall health changed after getting VAY736?

Yes. The trial doctors thought that the participants' overall health changed after getting VAY736.

To answer this question, the trial doctors filled out the doctor's version of the VAS before each participant got the trial drug, and 12 weeks after they got the trial drug. A decrease in the participants' VAS scores after 12 weeks showed that the participants' overall condition was getting healthier.

The researchers compared the results from the participants who got VAY736 with the results from the participants who got the placebo. They found that there was a bigger decrease in the trial doctors' VAS scores for the participants who got VAY736 compared with the VAS scores for the participants who got the placebo.

How long and at what level was VAY736 in the participants' blood?

To answer this question, the trial doctors took blood samples from the participants after they got a single dose of VAY736. The trial doctors did this over the course of the entire trial.

The researchers wanted to know about how long VAY736 was in the participants' blood. The researchers found that:

- For all treatments, it took about 2 hours for VAY736 to reach its highest level in the blood. This was at the end of the infusion.

The researchers also wanted to know about how much VAY736 got into the participants' blood. The researchers found that:

- Overall, higher amounts of VAY736 were in the blood of participants that got 10 mg/kg compared to those who got 3 mg/kg.

What medical problems did the participants have?

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 adverse events may or may not be caused by the trial drug.

A lot of research is needed to know whether a trial drug causes an adverse event. During a trial, all adverse events 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 adverse events that participants have.

This section is a summary of the adverse events that happened during both parts of this trial.

How many participants had adverse events?

Most of the participants in the trial had at least 1 adverse event. Most of the adverse events happened within the first 24 hours of getting the trial drug. None of the participants in the trial stopped getting the trial drug because of adverse events.

The table below shows how many participants had adverse events during the double-blind period of this trial.

Adverse events during the double-blind period

	Placebo (Out of 9 participants)	VAY736 (Out of 18 participants)	Total (Out of 27 participants)
How many participants in this trial had adverse events?	88.9% (8)	94.4% (17)	92.6% (25)
How many participants in this trial had serious adverse events?	11.1% (1)	5.6% (1)	7.4% (2)

The table below shows how many participants had adverse events during the open-label period of this trial.

Adverse events during the open-label period

Adverse event	Placebo (Out of 4 participants)	VAY736 (Out of 18 participants)	Open-label VAY736 (Out of 5 participants)	Total (Out of 27 participants)
How many participants in this trial had adverse events?	25.0% (1)	50.0% (9)	100.0% (5)	55.6% (15)
How many participants in this trial had serious adverse events?	0.0% (0)	5.6% (1)	20.0% (1)	7.4% (2)

What were the most common serious adverse events?

A total of 5 serious adverse events happened in 4 participants.

The serious adverse events that happened during this trial were:

- Fluid-filled sac in the ovary
- Groin hernia
- Inflammation of the appendix
- Jaw fracture
- Long-term inflammation of the large intestine

None of the participants died during this trial.

What were the most common adverse events?

The most common adverse event that happened in the participants during the double-blind period was a reaction from getting the trial drug through an IV, also called an infusion-related reaction. This adverse event happened in 83.3% of the participants who got any dose of VAY736. This was 15 out of 18 participants. This adverse event also happened in 11.1% of the participants who got the placebo. This was 1 out of 9 participants.

The table below shows the most common adverse events that happened in 2 or more total participants during the double-blind period. There were other adverse events, but these happened in fewer participants.

Most common adverse events during the double-blind period

Adverse event	Placebo (Out of 9 participants)	VAY736 (Out of 18 participants)	Total (Out of 27 participants)
Infusion-related reaction	11.1% (1)	83.3% (15)	59.3% (16)
Common cold	11.1% (1)	33.3% (6)	25.9% (7)
Headache	22.2% (2)	16.7% (3)	18.5% (5)
Chest pain not related to the heart	22.2% (2)	0.0% (0)	7.4% (2)
Flu	0.0% (0)	11.1% (2)	7.4% (2)
Infection in the stomach or intestines	11.1% (1)	5.6% (1)	7.4% (2)
Pain in the mouth and throat	11.1% (1)	5.6% (1)	7.4% (2)
Rash	11.1% (1)	5.6% (1)	7.4% (2)
Sinus infection	11.1% (1)	5.6% (1)	7.4% (2)
Tooth infection	11.1% (1)	5.6% (1)	7.4% (2)

The most common adverse event that happened in the participants during the open-label period was the common cold. This adverse event happened in 33.3% of total participants. This was 9 out of 27 participants.

The table below shows the most common adverse events that happened in 2 or more total participants during the open-label period. There were other adverse events, but these happened in fewer participants.

Most common adverse events during the open-label period

Adverse event	Placebo (Out of 4 participants)	VAY736 (Out of 18 participants)	Open-label VAY736 (Out of 5 participants)	Total (Out of 27 participants)
Common cold	25.0% (1)	16.7% (3)	100.0% (5)	33.3% (9)
Infusion-related reaction	0.0% (0)	0.0% (0)	60.0% (3)	11.1% (3)
Headache	0.0% (0)	5.6% (1)	20.0% (1)	7.4% (2)
Infection of the middle ear	0.0% (0)	5.6% (1)	20.0% (1)	7.4% (2)
Pink eye	0.0% (0)	5.6% (1)	20.0% (1)	7.4% (2)
PSS getting worse	0.0% (0)	5.6% (1)	20.0% (1)	7.4% (2)

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

How has this trial helped participants and researchers?

The results of this trial helped researchers better understand if VAY736 works in participants with PSS. The results from many trials are needed to find out which treatments can be used for people with PSS. This summary shows only the main results from this 1 trial. This was the first time that participants with PSS got VAY736. This trial was done in a small number of participants. Other trials may provide new information or different results.

If other trials with VAY736 in participants with PSS are planned, you will be able to find them on the websites listed below.

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 **"CVAY736X2201"** 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 websites listed below:

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02149420"** into the **"Other terms"** search box and click **"Search"**.

- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2013-000250-22"** in the 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"** or **"ianalumab"**.

Full Trial Title: A single dose, double-blind, placebo-controlled, parallel study to assess the pharmacodynamics, pharmacokinetics and safety and tolerability of VAY736 in patients with primary Sjögren's syndrome

Thank you!

As a clinical trial participant, you belong to a large community of participants around the world. You helped 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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