Clinical Trial Results

NOVARTIS

Research Sponsor: Novartis
Drug Studied: Secukinumab
Protocol Number: CAIN457AUS02 (VIP-S)

Thank you!

Thank you to the participants who took part in the clinical trial CAIN457AUS02 (VIP-S) for the drug secukinumab, also called AIN457. All of the participants helped researchers learn more about how secukinumab affects inflammation in patients who have moderate to severe plaque psoriasis. Plaque psoriasis is a skin disease that causes red, swollen scaly patches to form on the skin.

Novartis sponsored this trial and believes it is important to share the results of the trial with the participants and the public. An independent non-profit organization called CISCRP prepared this summary of the trial results. We hope it 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 doctor or staff at your trial site.

What has happened since the trial ended?

The participants were in the trial for about 1 year. But the entire trial took 2 years to finish because the participants entered the trial and started treatment at different times. The trial started in February 2016 and ended in February 2018.

The trial included 91 participants and was conducted only in the United States. 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?

Inflammation is the normal reaction of the body in response to injuries or things from outside the body, like infections. People who have psoriasis have a response that causes too much inflammation, which may affect healthy tissue. This inflammation can cause red, scaly patches called “plaques” to form on the skin. Inflammation can also happen in other parts of the body, including veins and arteries. Researchers do not know what causes this inflammation. Long-term inflammation can also cause other health problems, like heart and blood vessel problems.

Secukinumab is used in some countries to treat patients who have moderate to severe plaque psoriasis. Secukinumab helps control the part of the immune system that leads to inflammation and the growth of skin plaques.

In this trial, the researchers wanted to find out more about how secukinumab affects inflammation in the aorta of participants who have plaque psoriasis. The aorta is the biggest vessel in the body and carries blood away from the heart. Inflammation in the aorta has been linked with a higher risk of medical problems, like heart attacks.

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

- Did secukinumab reduce inflammation in the aorta?
- How did secukinumab affect other measures of heart and blood vessel disease risk?
- What medical problems did the participants have?

To do this, the researchers compared secukinumab 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.

What kind of trial was this?

To answer the questions in this trial, the researchers asked for the help of men and women who had moderate to severe plaque psoriasis that could not be controlled with other treatments. The participants in this trial were between 22 and 83 years old.

This trial was done in 2 parts, Part 1 and Part 2. Part 2 happened after Part 1 had ended.

Part 1

Part 1 was “double-blind”. This means that none of the participants, trial staff, or sponsor staff knew what treatment each participant got during this part.

During Part 1:

- 46 participants got secukinumab
- 45 participants got the placebo

Both secukinumab and the placebo were given as injections through a needle under the skin. A computer program was used to randomly assign the treatment each participant got during this part. Researchers do this so that comparing the results of each treatment is done as fairly as possible.

Part 2

Part 2 was “open-label”. This means the participants, trial staff, and sponsor staff knew what treatment each participant got during this part. During Part 2, all the participants got secukinumab.

After the entire trial ended, the participants learned whether they got secukinumab or the placebo during Part 1.

What happened during the trial?

Before the treatment started, the trial doctors did tests to make sure the participants could take part in the trial. This part of the trial took up to 4 weeks. During this time, the participants:

- had a physical exam
- gave blood and urine samples
- completed surveys
- told the trial doctors about any medical problems they had and what other medications they were taking
- stopped taking certain medications
- had a picture taken of their aorta

To take a picture of each participant's aorta, the trial doctors used a scan called a "positron emission tomography with computed tomography" scan, also called a PET/CT scan.

After the trial doctors finished these tests, the participants learned if they could participate in the trial. If they could participate, they continued to Part 1 of the trial.

Throughout and at the end of the trial, the doctors continued checking participants' health by performing tests and asking them how they were feeling.

The figures below show how the trial was done.

Part 1 – Double-blind treatment

12 weeks

• The participants got secukinumab or the placebo once a week for the first 5 weeks	• During this time, the participants did not get trial treatment • The doctors checked the health of the participants	• The participants got 1 dose of their prior treatment, either secukinumab or placebo	• During this time, the participants did not get trial treatment • The doctors checked the health of the participants to make sure they could join Part 2
5 weeks	**3 weeks**	**1 week**	**3 weeks**

Part 2 – Open-label treatment

• The participants who got the placebo in Part 1 got secukinumab once a week for 4 weeks • The participants who got secukinumab in Part 1 got secukinumab once in the first week. Then, they got the placebo once a week for the next 3 weeks	• The participants got secukinumab once every 4 weeks
4 weeks	**36 weeks**

What were the results of the trial?

This is a summary of the overall results of 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. Medical decisions should not be made based on the results of a single trial without first talking to a doctor. Always talk to a doctor before making any changes to medications or treatment plans.

Did secukinumab reduce inflammation in the aorta?

No. Overall, secukinumab did not reduce inflammation in the aorta.

To answer this question, the trial doctors looked at the PET/CT scans done at the start of the trial. Then, they looked at the PET/CT scans done at the end of Part 1, which lasted 12 weeks.

Before each PET/CT scan, the trial doctors injected the participants with a small dose of a radioactive material called radiotracer. This radiotracer was not considered to be harmful and helped the doctors see certain organs and tissues, such as the aorta and veins. The doctors looked at how much of the radiotracer was in the aorta and compared it to how much was in the blood in the veins. This is known as the "target to background ratio", also called the TBR. A higher TBR means there is a high amount of inflammation in the aorta.

At the end of Part 1, the researchers measured the change in the TBR in:

- 43 of the 46 participants who got secukinumab
- 42 of the 45 participants who got the placebo

The researchers were not able to study the TBR results for 3 participants in both treatment groups. This was because these 6 participants left the trial before the researchers could study the results.

The researchers estimated that the average TBR score increased by 0.017 in the secukinumab group and increased by 0.070 in the placebo group. The difference between the groups was too small for researchers to know if secukinumab reduced inflammation in the aorta compared to the placebo.

How did secukinumab affect other measures of heart and blood vessel disease risk?

The researchers wanted to find out if secukinumab affected cholesterol, blood sugar, and other proteins in the blood. These substances can show if a person is at risk for medical problems like heart disease, diabetes, and strokes. They measured these substances before the participants started treatment and at the end of Part 1. The researchers were only able to study the below results for 40 of the 46 participants who got secukinumab and 41 of the 45 participants who got the placebo. This was because some of the participants left the trial before the researchers could study the below results.

For most of these substances, the researchers did not see differences between the participants who got secukinumab and the participants who got the placebo. But there were differences between the 2 groups in measures of cholesterol.

Cholesterol plays an important part in making sure that the body works properly. But there are different types of cholesterol. One type is “low-density lipoprotein” cholesterol, also called LDL cholesterol. LDL cholesterol is “bad” cholesterol and can clog arteries and blood vessels. “High-density lipoprotein” cholesterol, also called HDL cholesterol, is “good” cholesterol. It helps remove bad cholesterol from the blood.

The researchers measured the participants’ LDL cholesterol, HDL cholesterol, and total cholesterol in “milligrams per deciliter”, also called mg/dL. They found that LDL cholesterol and total cholesterol increased slightly in the participants who got secukinumab and decreased in the participants who got the placebo. After 12 weeks of treatment:

LDL cholesterol:

- went up by an average of 10.0 mg/dL in the participants who got secukinumab
- went down by an average of 6.3 mg/dL in the participants who got the placebo

HDL cholesterol:

- went down by an average of 0.8 mg/dL in the participants who got secukinumab
- went down by an average of 1.1 mg/dL in the participants who got the placebo

Total cholesterol:

- went up by an average of 10.6 mg/dL in the participants who got secukinumab
- went down by an average of 8.5 mg/dL in the participants who got the placebo

The researchers found that these differences in cholesterol did not cause the participants to have medical problems. These differences did not affect the other trial results.

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 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 section is a summary of the adverse events that happened during Part 1 and during the trial overall. The overall trial lasted about 52 weeks.

How many participants had adverse events?

During Part 1, more participants who got secukinumab had adverse events compared to participants who got the placebo.

More participants who got secukinumab for the entire trial had adverse events compared to participants who got the placebo during Part 1 and then secukinumab during Part 2.

The table below shows how many participants had adverse events during all 52 weeks of the trial.

Adverse events during the trial

	Secukinumab (Part 1) and secukinumab (Part 2) (Out of 46 participants)	Placebo (Part 1) and secukinumab (Part 2) (Out of 45 participants)	Total (Out of 91 participants)
How many participants had adverse events?	80.4% (37)	66.7% (30)	73.6% (67)
How many participants had serious adverse events?	10.9% (5)	0.0% (0)	5.5% (5)
How many participants stopped taking the trial drug due to adverse events?	8.7% (4)	2.2% (1)	5.5% (5)

What were the most common serious adverse events?

There were 10.9% of participants who got secukinumab for the entire trial who had a serious adverse event. This was 5 out of 46 participants. None of the participants who got the placebo in Part 1 and secukinumab in Part 2 had a serious adverse event.

None of the participants died during the trial.

The table below shows the serious adverse events that happened during the trial. Each of these serious adverse events happened in 1 participant.

Serious adverse events during the trial

	Secukinumab (Part 1) and secukinumab (Part 2) (Out of 46 participants	Placebo (Part 1) and secukinumab (Part 2) (Out of 45 participants)	Total (Out of 91 participants)
Broken arm	2.2% (1)	0.0% (0)	1.1% (1)
Broken rib	2.2% (1)	0.0% (0)	1.1% (1)
Muscle weakness	2.2% (1)	0.0% (0)	1.1% (1)
Narrowing of the aorta (this can make it difficult for blood to flow)	2.2% (1)	0.0% (0)	1.1% (1)
Stomach pain	2.2% (1)	0.0% (0)	1.1% (1)

What were the most common adverse events?

The most common adverse event during the trial was a cold. This happened in:

- 19.6% of participants who got secukinumab during the entire trial. This was 9 out of 46 participants.
- 15.6% of participants who got the placebo in Part 1 and secukinumab in Part 2. This was 7 out of 45 participants.

The table below shows the most common adverse events that happened during all 52 weeks of the trial.

Most common adverse events during the trial

	Secukinumab (Part 1) and secukinumab (Part 2) (Out of 46 participants)	Placebo (Part 1) and secukinumab (Part 2) (Out of 45 participants)	Total (Out of 91 participants)
Common cold	19.6% (9)	15.6% (7)	17.6% (16)
Infection in the nose and throat, often caused by a virus	13.0% (6)	8.9% (4)	11.0% (10)
Joint pain	10.9% (5)	6.7% (3)	8.8% (8)
Cough	2.2% (1)	8.9% (4)	5.5% (5)
Diarrhea	6.5% (3)	4.4% (2)	5.5% (5)

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 information described above helped the researchers better understand how secukinumab might help reduce inflammation in the aorta in participants who have moderate to severe plaque psoriasis. In this trial, secukinumab did not help reduce inflammation in the aorta.

The researchers also wanted to understand if secukinumab affected the risk of heart and blood vessel diseases in the participants. Overall, the researchers did not find a difference in heart and blood vessel disease risk between secukinumab and the placebo. But, the researchers did find that LDL and total cholesterol increased slightly in the participants who got secukinumab and decreased in the participants who got the placebo.

This summary shows only the main results from this one trial. 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 **"CAIN457AUS02"** into the keyword search box and click **"Search"**. If you have questions about the results, please speak with the trial doctor or trial 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 **"NCT02690701"** into the search box and click **"Search"**.

If more clinical trials are planned, they will be listed on the above public websites or www.novartisclinicaltrials.com. Search for **"AIN457"**.

Full trial title: A Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Effect of Secukinumab on Aortic Vascular Inflammation and Cardiometabolic Biomarkers after 12 Weeks of Treatment, Compared to Placebo, and Up to 52 Weeks of Treatment with Secukinumab in Adult Patients with Moderate to Severe Chronic Plaque-type Psoriasis

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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