NOVARTIS

Clinical Trial Results Summary

A clinical trial to study the effects of AIN457 when used along with standard treatment in people with active lupus nephritis

Thank you!

Thank you to the participants who took part in the clinical trial for lupus nephritis. Every participant helped the researchers learn more about **AIN457**, also called secukinumab.

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.

We hope this summary helps the participants to understand their important role in medical research.

Trial information

Trial number: CAIN457Q12301

Drug studied: AIN457, also known as secukinumab

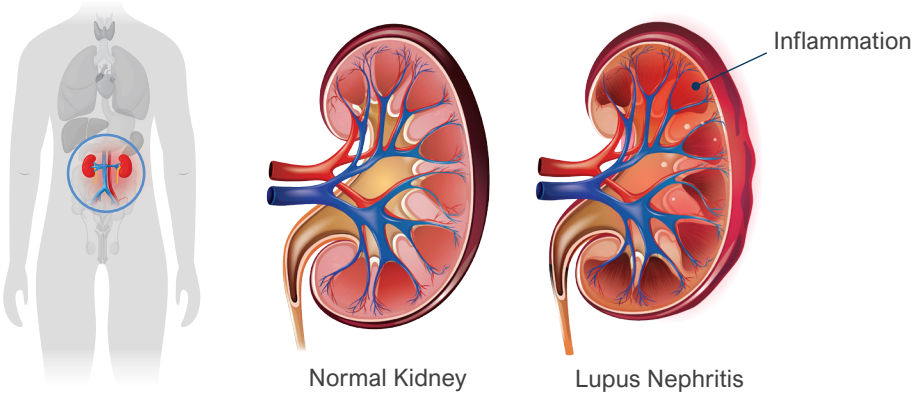
Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings.

What was the main purpose of this trial?

Lupus nephritis is a condition where the immune system attacks the kidneys, causing inflammation. People with **lupus nephritis** have inflamed kidneys, which affects their function and can result in kidney damage. If left untreated, the condition can worsen over time and may gradually lead to kidney failure.

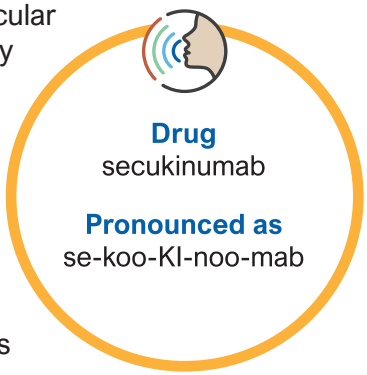


Common symptoms of **lupus nephritis** are:

- Blood in the urine
- Foamy urine due to high amounts of protein
- High blood pressure
- Swelling in the legs, ankles, or feet
- High levels of a waste product called creatinine in the blood

Currently, there are few treatments available for lupus nephritis. **Corticosteroids**, **mycophenolic acid (MPA)**, and **cyclophosphamide (CYC)** are all standard-of-care medicines that lower the body's immune response. They help reduce and manage lupus nephritis symptoms.

Standard-of-care treatments are the widely accepted treatments for a particular disease or disorder. They are usually the treatments recommended by doctors. Even if these treatments are initially effective, lupus flare-ups often occur later on. Therefore, researchers are trying to find new treatments.



In this trial, researchers wanted to learn more about a drug called **AIN457 (secukinumab)**, which is an antibody made in labs. It blocks a protein called **IL-17A**, which the immune system uses to cause inflammation. Researchers wanted to check if blocking the inflammation through **AIN457** would reduce symptoms of **lupus nephritis**. **AIN457** is already approved in the EU and the US for treating other conditions such as psoriatic arthritis, plaque psoriasis, and hidradenitis suppurativa (HS).

In this trial, researchers wanted to learn about the effects of **AIN457** in participants with **lupus nephritis** who are taking standard-of-care medicines.

The main questions that researchers wanted to answer were:

- How many participants had a **complete renal response** to **AIN457** treatment after 52 weeks?
  - ↳ A **complete renal response** means the participant had normal or close-to-normal kidney function test results. For more details, see **page 6**.
- What adverse events did participants have during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial.

How long was this trial?

The trial began in July 2020 and ended in September 2023. The trial was designed so that each participant could take part for up to 118 weeks.

However, the trial ended earlier than planned because the early results showed the treatment did not work as expected in people with **lupus nephritis**. Researchers did not observe any new safety concerns with **AIN457**.

When the trial ended, researchers created a report of the trial results. This summary is based on that report.

Who was in this trial?

275 participants with active **lupus nephritis** received treatment in this trial. Participants' ages ranged from 18 to 68 years. Their average age was 34 years.

The number of participants by gender and race are shown below.

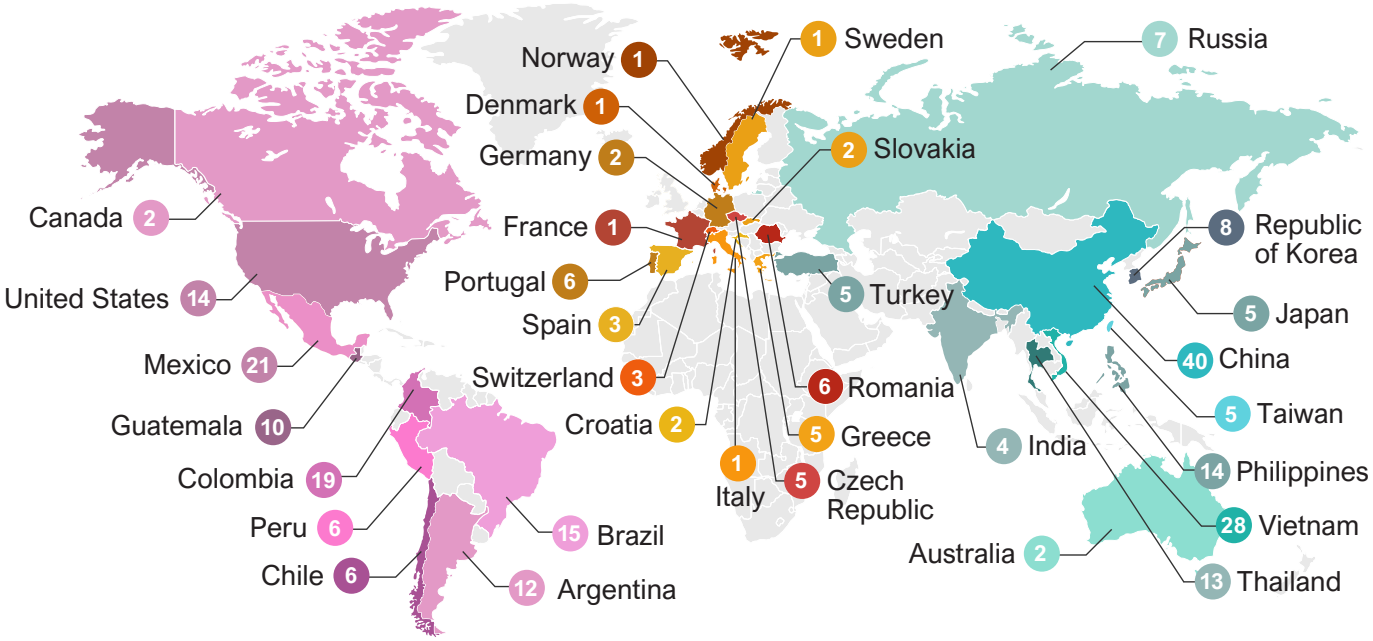
Gender

35 Men	240 Women

Race

123 Asian	94 White	42 American Indian or Alaska Native
15 Black or African American	1 More than 1 race	

275 participants from **34 countries** took part in the trial. The map below shows the number of participants who took part in each country.



Participants **could take part** in this trial if they:

- Were between 18 and 75 years old.
- Had **lupus nephritis** with a kidney biopsy confirming active disease. Kidney biopsy is a medical test that looks at the tissue samples to check the extent of kidney inflammation.
- Did not have kidney problems that require dialysis or a kidney transplant.
- Did not receive prior treatment with **AIN457** or other drugs that worked similarly.

What treatments did the participants receive?

Researchers studied the following treatments:

AIN457: 300 milligrams (mg), given as an injection under the skin.

Placebo: Looks like the trial drug but does not have any active drug in it. Using a placebo helps researchers better understand and confirm the effect of the trial drug.

Along with **AIN457** or **placebo**, all participants received the standard-of-care treatments assigned by the trial doctors.

- Participants either received mycophenolic acid (MPA) or cyclophosphamide (CYC). Alternatively, participants could have received **mycophenolate mofetil (MMF)**, which is another form of MPA.
- They either received MPA as a tablet or CYC as an injection into the vein.
- Participants assigned to MPA took it every day during the entire treatment period.
- Participants assigned to CYC received it once every 2 weeks for 12 weeks. After that, they switched to daily MPA for the rest of the treatment period.
- Participants could also take corticosteroids every day for the entire treatment period.

In this trial, none of the participants, researchers, trial doctors, or trial staff knew what treatments the participants were receiving. Some trials are done this way because knowing what treatment the participants receive can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness across all treatments.

What happened during this trial?

Before treatment

Up to 6 weeks

Trial doctors checked the participants' health to make sure they could be in this clinical trial. If a participant was chosen to receive MPA and they were not already taking MPA, they had to start taking it for 4 weeks before the start of treatment with **AIN457**.

During treatment

Up to 104 weeks

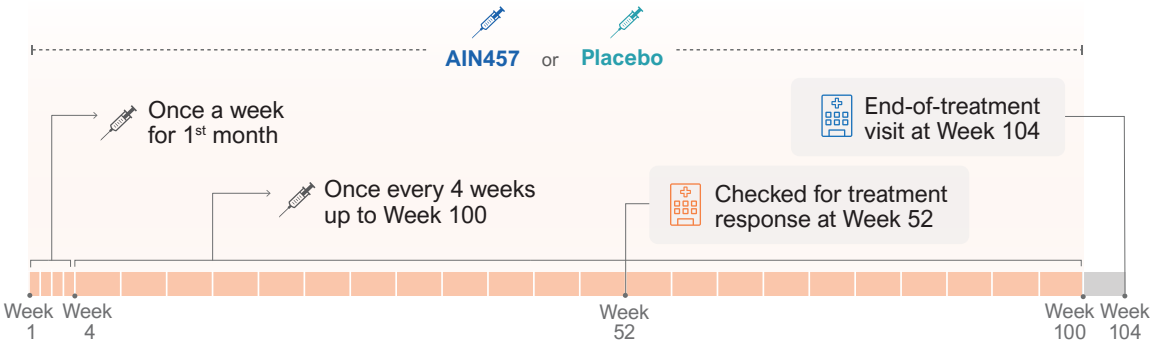
A total of **275 participants** received either **AIN457** or **placebo**. They were randomly assigned to 1 of 2 treatment groups by a computer.

AIN457, 300 mg
137 participants

Placebo
138 participants

Participants received treatment once a week for the 1st month. Then, they were treated every 4 weeks up to Week 100. They also had an end-of-treatment visit at Week 104.

Participants receiving **AIN457** or **placebo** followed the same treatment timeline as shown below:



After treatment

Up to 12 weeks after last dose

Participants had a follow-up visit 12 weeks after their last dose of **AIN457** or **Placebo**. Participants who completed the treatment period were given the option to continue the treatment in a separate extension trial, **CAIN457Q12301E1**.

Those who joined the extension study had their first visit at Week 104 of this study.

Trial doctors checked participants for their overall health throughout the trial.

What were the main results of this trial?

How many participants had a complete renal response to AIN457 treatment after 52 weeks?

After 52 weeks of treatment, **AIN457** did not show better treatment response compared to **placebo**.

Researchers wanted to know how many participants had a **complete renal response** at Week 52. Trial doctors checked 2 types of measurements – **eGFR** and **UPCR**.

Complete Renal Response

Estimated glomerular filtration rate (eGFR) shows how well the kidneys are filtering waste from the blood.

Urine-to-protein creatinine ratio (UPCR) is a measure of kidney function that is used to detect kidney damage or disease. It compares the amount of protein to creatinine in a urine sample.

- A higher UPCR may indicate kidney damage or failure.

In this trial, participants had a **complete renal response** at Week 52 if:

- their eGFR was normal, or at least 85% of its value at the start of the trial.
- their UPCR from urine collected over 24 hours was close to normal.
- they did not stop treatment before Week 52.
- they did not overuse corticosteroids in the last 8 weeks before Week 52.

Of the 275 total participants, the results below are shown for **182 participants** who had the opportunity to complete 52 weeks of treatment when the decision to end the study was made.

The table below shows the average response of the participants to the treatment. It is presented as a percentage of participants who had a complete renal response.

Average Response at Week 52

	AIN457 91 participants	Placebo 91 participants
Complete renal response at Week 52	26%	39%

Researchers wanted to learn if **AIN457** was better than placebo in treating **lupus nephritis**. However, the results showed that participants who took **AIN457** did not have a higher treatment response than those who took **placebo**.

What adverse events did the participants have?

Trial doctors keep track of all **adverse events** that happen in trials, even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of treatment up to 12 weeks after the last treatment.

An **adverse event** is:

- Any **sign or symptom** that the participants have during a trial
- 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 treatments in the trial.

243 out of 275 participants had adverse events.

- **69 participants** had adverse events that were considered serious.
- **4 participants** left the trial due to an adverse event.
- **2 participants** died.

How many participants had adverse events?

Adverse events are reported for participants who received at least 1 dose of **AIN457** or **placebo**.

Summary of adverse events

Participants who:	AIN457 137 participants	Placebo 138 participants
Had at least 1 serious adverse event	30 of 137 **(22%)**	39 of 138 **(28%)**
Had at least 1 other adverse event	111 of 137 **(81%)**	116 of 138 **(84%)**
Left the trial due to an adverse event	1 of 137 **(1%)**	3 of 138 **(2%)**
Died during the trial	1 of 137 **(1%)**	1 of 138 **(1%)**

What serious adverse events did the participants have?

The table below shows the most common serious adverse events that happened in 3 or more participants in either group.

Serious adverse events	AIN457 137 participants	Placebo 138 participants
COVID-19	3 of 137 **(2%)**	4 of 138 **(3%)**
Lung Infection Pneumonia	5 of 137 **(4%)**	3 of 138 **(2%)**
Acute kidney injury	1 of 137 **(1%)**	4 of 138 **(3%)**
Worsening of lupus nephritis Lupus Nephritis	4 of 137 **(3%)**	5 of 138 **(4%)**

2 participants died during the trial, one from the **AIN457** group and one from the **placebo** group.

What other adverse events did the participants have?

The table below shows the other adverse events that happened in 15 or more participants in either group.

Other adverse events	AIN457 137 participants	Placebo 138 participants
Urinary tract infection	19 of 137 **(14%)**	30 of 138 **(22%)**
COVID-19	25 of 137 **(18%)**	22 of 138 **(16%)**
Infection of the nose and throat Upper respiratory tract infection	19 of 137 **(14%)**	26 of 138 **(19%)**
Diarrhea	23 of 137 **(17%)**	21 of 138 **(15%)**
Headache	21 of 137 **(15%)**	14 of 138 **(10%)**
Joint pain Arthralgia	13 of 137 **(9%)**	19 of 138 **(14%)**

What was learned from this trial?

This trial helped researchers learn about the effects of **AIN457** in people with **lupus nephritis**.

The researchers concluded that:

- **AIN457** did not increase the treatment response as compared to **placebo**.
- Although adverse events were reported for many participants, there were no new or unexpected safety concerns with **AIN457**.

The trial ended earlier than planned because the early results showed the treatment did not work as expected in people with **lupus nephritis**.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website, **www.novctrd.com**.

Follow these steps to find the scientific summary:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Agree to the terms ☑ **I agree** → Search for **CAIN457Q12301**

For more information about this trial go to any of the following websites:

- **clinicaltrials.gov** – search using the number **NCT04181762**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2019-003211-57**

Other trials of AIN457 may also appear on the public websites above. When there, search for **AIN457** or **secukinumab**.

Full clinical trial title: A Two-year, Phase III Randomized, Double-blind, Parallel-group, Placebo-controlled Trial to Evaluate the Safety, Efficacy, and Tolerability of 300 mg s.c. Secukinumab Versus Placebo, in Combination with SoC Therapy, in Patients with Active Lupus Nephritis

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