NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of AIN457 in people with thyroid eye disease

Thank you!

Thank you to the participants who took part in the clinical trial for thyroid eye disease. 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: CAIN457ADE16

Drug studied: AIN457, also known as secukinumab

Sponsor: Novartis

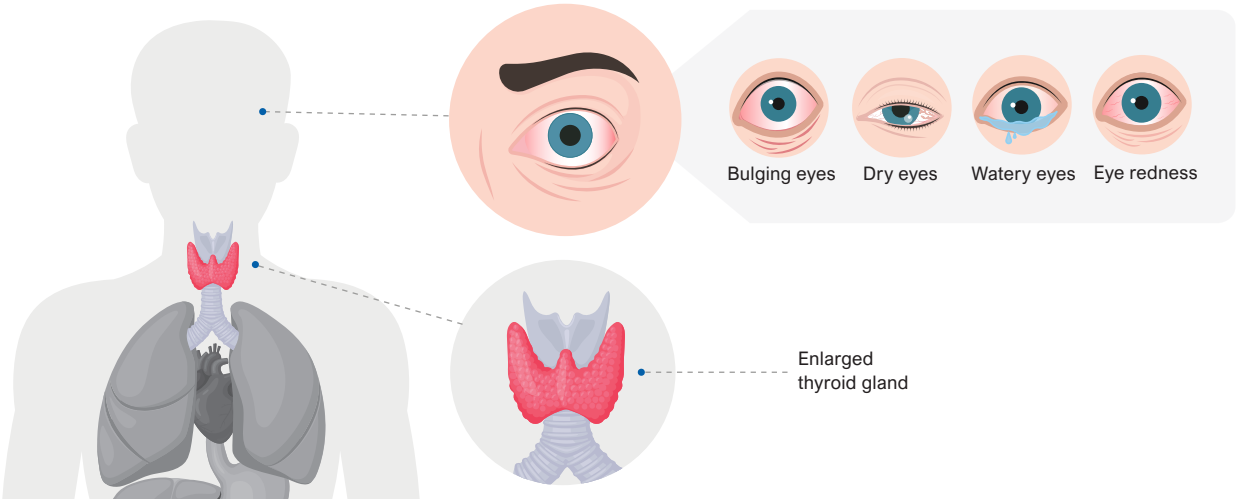
If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

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?

Autoimmune diseases cause the body's immune system to mistakenly attack normal healthy cells, tissues, and organs. **Thyroid eye disease (TED)** is a rare autoimmune disorder that causes inflammation in the eye muscles and the fatty tissue behind and around the eyes. These changes can affect eye position and eyelid appearance, and cause swelling in the face. This may lead to the face having an unnatural expression. As a result, TED can also impact mental health.

TED is commonly seen in people with **Graves' disease**. Graves' disease is also an autoimmune disorder that affects the thyroid gland and leads to the overproduction of thyroid hormones.



Common symptoms of **TED** are:

- Bulging eyes
- Blurry vision or double vision
- Feeling of grittiness in the eyes
- Watery eyes
- Sensitivity to light
- Dry eyes
- Pain behind the eyes or pain when moving the eyes

There are a few treatments available for TED. Steroids are one of the most common drugs given for managing TED symptoms. However, they may have unwanted side effects with long-term use. Radiation therapy may lower inflammation. Eyelid, eye muscle, and eye socket surgeries are other forms of treatment but they are not as convenient. TED can sometimes come back, or relapse, even after treatment. As a result, there is a need to find new treatments.

Antibodies are normally made by the body's immune system to fight infections. The trial drug, **AIN457**, is a type of antibody made in labs. It blocks a protein called IL17-1, which the immune system uses to cause inflammation. **AIN457** is already approved in the EU and the US for treating other autoimmune disorders, such as psoriasis.

In this trial, researchers wanted to learn about the effects of **AIN457** in participants with **TED**.

The main questions that researchers wanted to answer were:

- How many participants achieved a response after 16 weeks of treatment?
- 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 November 2021 and ended in May 2023. The trial was designed so that each participant could take part for up to 26 months. However, the trial ended early after 19 months.

The trial ended earlier than planned because the early results showed the treatment may not work as expected in people with the studied disease. The decision was not due to any 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?

28 participants from Germany with thyroid eye disease (TED) received treatment in this trial. Participants' ages ranged from 29 to 77 years. Their average age was 56 years.

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

Gender

- 7 Men
- 21 Women

Race

- 28 White

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

- Were at least 18 years old
- Had active, moderate to severe TED
- Started having TED symptoms within a year of the first study visit
- Were not at risk of losing their sight
- Did not need urgent treatment
- Did not have any other eye disorders

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 the effect of the trial drug.

- Participants on **placebo** received injections at the same timepoints as participants on **AIN457** during the first 12 weeks of treatment.
- During the first 16 weeks, the participants, trial doctors, and trial staff did not know whether the participants received **AIN457** or **placebo**. Doing a trial this way helps to make sure that the results are looked at with fairness across all treatments.
- After Week 16, participants who did not respond to treatment or relapsed could continue treatment with **AIN457** for another 16 weeks. In that case, the participants and the trial staff knew they were taking **AIN457** treatment.
- No rescue medications were given during this trial. However, If TED worsened, participants received other TED treatments or procedures based on the trial doctors' decision.

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.

During treatment

Up to 32 weeks

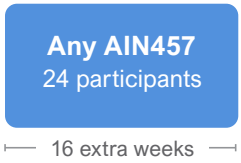
A total of 28 participants received either **AIN457** or **placebo.** They were randomly assigned to 1 of 2 treatment groups by a computer. The treatment period lasted for 16 weeks with doses on Weeks 1, 2, 3, 4, and 12.

After Week 16, study doctors checked participants to see if they responded to treatment or not.

Participants were given the opportunity to continue **AIN457** treatment for another 16 weeks. **Placebo** was no longer given.

There were 24 participants who continued **AIN457** treatment, including those participants who first received **placebo**. These participants were in the Treatment period for a **total of 32 weeks**.

In the remaining 4 participants, 1 participant left the study, and 3 participants did not continue as the study ended early.



After treatment

Up to 24 weeks

AIN457 treatment was stopped as soon as the trial ended but participants were checked for disease symptoms, relapse and adverse events.

Participants who continued the study	Participants who stopped the treatment early
Follow-up period up to Week 56 or 24 weeks after the last dose	Follow-up visit 12 weeks after last dose

What were the main results of this trial?

How many participants achieved a response after 16 weeks of treatment?

None of the participants responded to **AIN457** treatment after 16 weeks.

Researchers used a tool called the **Clinical Activity Score (CAS)** to measure the amount of inflammation around each eye.

In this trial, the more severely affected eye was called the **study eye** while the other eye was called the **fellow eye.**

A participant was considered to have **responded to AIN457 treatment** if:

- their clinical activity score (CAS) went down by 2 points or more in their study eye
- the bulging in their study eye decreased by at least 2 millimeters (mm)
- the condition of their fellow eye did not get worse

The table below shows the results for 28 participants who received at least one dose of **AIN457** or **placebo**.

Some participants left the study before Week 16 or did not have a Week 16 assessment, so their results were considered **missing**.

Treatment response at Week 16

Participants who:	AIN457 14 participants	Placebo 14 participants
Had no response	12 of 14 **(86%)**	11 of 14 **(79%)**
Missing	2 of 14 **(14%)**	3 of 14 **(21%)**

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 the trial treatment up to 24 weeks after the last dose.

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.

23 participants had adverse events.

- 2 participants had adverse events that were considered serious.
- None of the participants died.
- None of the participants stopped the treatment due an adverse event.

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:	Placebo 14 participants	Any AIN457 26 participants
Had at least 1 serious adverse event	1 of 14 **(7%)**	1 of 26 **(4%)**
Had at least 1 other adverse event	12 of 14 **(86%)**	23 of 26 **(88%)**
Stopped the treatment due an adverse event	0 of 14 **(0%)**	0 of 26 **(0%)**
Died during the trial	0 of 14 **(0%)**	0 of 26 **(0%)**

Placebo group includes participants who received **placebo** only for the first 16 weeks.

Any AIN457 group includes all participants who received at least one dose of **AIN457** during any time of the study for up to 32 weeks.

What serious adverse events did the participants have?

A total of 2 participants who received at least 1 dose of **AIN457** or **placebo** had serious adverse events. Both participants required eye socket surgery (orbital decompression surgery).

The table below shows the serious adverse events that happened in 2 participants.

Serious adverse events

	Placebo 14 participants	Any AIN457 26 participants
Worsening of TED Graves disease	0 of 14 **(0%)**	1 of 26 **(4%)**
Eye Inflamation Endocrine ophthalmopathy	1 of 14 **(7%)**	0 of 26 **(0%)**

What other adverse events did the participants have?

The table below shows the other adverse events that happened in at least 2 participants in either group.

Other adverse events

	Placebo 14 participants	Any AIN457 26 participants
COVID-19	6 of 14 **(43%)**	10 of 26 **(38%)**
Headache	2 of 14 **(14%)**	5 of 26 **(19%)**
High blood pressure Hypertension	2 of 14 **(14%)**	3 of 26 **(12%)**
Urinary tract infection	3 of 14 **(21%)**	2 of 26 **(8%)**
Joint pain Arthralgia	0 of 14 **(0%)**	2 of 26 **(8%)**
Fatigue	0 of 14 **(0%)**	2 of 26 **(8%)**

What was learned from this trial?

This trial helped researchers learn about the effects of **AIN457** in people with thyroid eye disease **(TED)**.

The researchers concluded that:

- The desired response with **AIN457** was not achieved in participants at Week 16.
- **AIN457** was well tolerated in participants and no new, unexpected safety concerns were found.

The trial ended earlier than planned because the results showed the treatment may not work as expected in people with the studied disease. The decision was not due to any safety concerns with **AIN457.**

At the time this summary was written, there are no ongoing studies with **AIN457** being done in people with TED.

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 **CAIN457ADE16**

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

- **clinicaltrials.gov** – search using the number **NCT04737330**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2020-001611-24**

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 Multi-center Phase 3 Study to Investigate the Efficacy and Safety of Secukinumab in Adult Patients With Active, Moderate to Severe Thyroid Eye Disease (ORBIT), With a Randomized, Parallel-group, Double-blind, Placebo-controlled, 16-week Treatment Period, and a Follow-up/Retreatment.

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