NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of taking AIN457 while following a treatment strategy called treat-to-target in people with axial spondyloarthritis

Thank you!

Thank you to the participants who took part in the clinical trial for axial spondyloarthritis. Every participant helped the researchers learn more about the trial drug **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 helps the participants understand their important role in medical research.

Trial information

Trial number: CAIN457HDE01

Drug studied: AIN457 (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 shows the results of a single clinical trial. Other clinical trials may have different findings.

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects of AIN457 given as the first **biologic treatment** for axial spondyloarthritis with a 'treat to target' approach compared to standard treatment.

What is a biologic treatment?

A biologic treatment is made using material such as proteins from living organisms.

Axial spondyloarthritis (axSpA) is a condition affecting the joints and tissues that attach muscles to bones, called tendons, of the spine and the pelvis. It can also affect organs such as the eyes, skin, and gut. When the disease is active, it causes inflammation in the body that can cause symptoms like pain in the back, joints, heel, and abdomen, feeling tired, sleep problems, and more.

AIN457, also called secukinumab, is an approved biologic treatment for inflammatory conditions including axSpA. It helps reduce pain and improve other symptoms related to mobility, inflammation, and quality of life.

In this trial, AIN457 was given as the 'first-line' or starting biologic treatment for axSpA with a treat-to-target approach.

The **treat-to-target (T2T)** approach is a specific treatment strategy that involves setting a treatment goal, like low disease activity, based on a person's signs and symptoms. Doctors perform regular testing to assess the person's signs and symptoms and, adjust the treatment plan and dose to reach the goal.

In this trial, participants who did not benefit from AIN457 with a T2T approach were given a higher dose of AIN457. They were switched to adalimumab if they did not benefit from the higher dose of AIN457. **Adalimumab** is another biologic treatment commonly used for axSpA.

Standard treatment for axSpA follows the 'routine care' approach where doctors treat people based on the current guidelines and the doctor's judgment.

The trial's purpose was to answer these main questions:

- Was AIN457 given as the first biologic treatment for axSpA with a T2T approach better than the standard treatment?
- What adverse events did the 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 June 2019 and ended in September 2022. It was planned for the participants to be in this trial for up to 1 year and 1 month after receiving the trial treatment.

Who was in this trial?

304 participants with axSpA received treatment in this trial. Participants' ages ranged from 18 to 82 years. Their average age was 39 years.

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

Gender

- 194 **Men**
- 110 **Women**

Race

- 1 **Asian**
- 1 **Black** or **African American**
- 242 **White**
- 1 **Multiple races**
- 59 **Other**

The participants could take part in this trial if they:

- Were at least 18 years old and diagnosed with axSpA
- Had active inflammation in the joint linking the spine and the pelvis, despite taking specific drugs called non-steroidal anti-inflammatory drugs (NSAIDs) for relief
- Stopped taking other treatments called disease-modifying anti-rheumatic drugs (**DMARD**s), except methotrexate and sulfasalazine, 4 weeks before getting the trial treatment
- Did not have another ongoing inflammatory condition

59 participants from France and 245 participants from Germany took part in this trial.

What treatments did the participants receive?

The treatments in this trial were:

AIN457 was taken as one 150 milligrams (mg) injection or two 150 mg (total dose of 300 mg) injections under the skin.

Adalimumab was taken as a 40 mg injection under the skin.

Standard treatment could include all approved **DMARD**s for axSpA including biologics such as adalimumab and AIN457.

Each participant, the trial doctors, and the trial staff knew the treatment the participant received.

What happened during this trial?

Before treatment — 8 weeks

Trial doctors checked the participants' health and axSpA to ensure they could take part in this clinical trial. 304 participants joined the trial.

During treatment — 36 weeks

Participants were randomly assigned to 1 of 2 groups:

Group 1: AIN457 (T2T) – 155 participants

Start of the trial treatment	**Loading dose**: Weekly injections of 150 mg AIN457 until Week 4 (5 injections in total) **Maintenance dose**: Monthly injections of 150 mg AIN457 starting at Week 8			
At Week 12 Tests were done to check participants' response to treatment	**Responders (R)** 83 participants		**Non-responders (NR)** 65 participants	
	Monthly injections of 150 mg AIN457 until Week 20		Monthly injections of 300 mg AIN457 until Week 20	
At Week 24 Tests were repeated to check participants' response to treatment	**R** 62 participants	**NR** 17 participants	**R** 25 participants	**NR** 31 participants
	Monthly injections of 150 mg AIN457 until Week 32	Monthly injections of 300 mg AIN457 until Week 32	Monthly injections of 300 mg AIN457 until Week 32	Bi-monthly injections of 40 mg adalimumab until Week 34

Keywords

Loading dose = a high dose to increase the levels of a drug in the blood and have the desired effects faster

Maintenance dose = a lower dose to continue having the desired levels of the drug in the blood

Responders = those who had enough improvement in their signs and symptoms of axSpA compared to the start of the study

Non-responders = those who did not have enough improvement in their signs and symptoms of axSpA compared to the start of the study

Note: Participants could stop taking their treatment or leave the trial at any time during the study.

During treatment 36 weeks

Group 2: Standard treatment (routine care) – 149 participants

Participants were given treatment according to local practice standards by the trial doctor. The treatment could be adjusted when participants visited their trial site during their regular visits to the doctors.

Researchers checked all participants' axSpA and general health throughout the trial.

After treatment 20 weeks

All participants returned to their trial site once after receiving their last dose of treatment for follow-up at Week 56.

What was the main result of this trial?

Was AIN457 given as the first biologic treatment for axSpA with a T2T approach better than the standard treatment?

No, AIN457 given as the first biologic treatment for axSpA with a T2T approach was not better than the standard treatment.

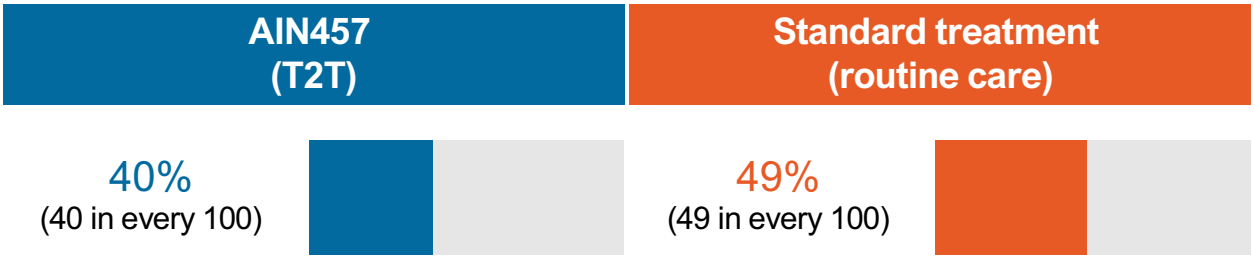
To answer this question, researchers checked whether the participants had the **ASAS40 response** at Week 24. They used complex tests to calculate the percentage of participants who had this response.

Researchers found that a lower percentage of participants in the AIN457 T2T group had the ASAS40 response after 24 weeks of treatment compared with the standard treatment group. However, the difference between the 2 groups was not meaningful enough to confirm this finding.

What is ASAS40 response?

ASAS40 response means an improvement of at least 40% in the symptoms of axSpA based on several questionnaires that assess the level of pain and a person's ability to perform daily activities.

Percentage of participants who had ASAS40 response at Week 24



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 20 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.

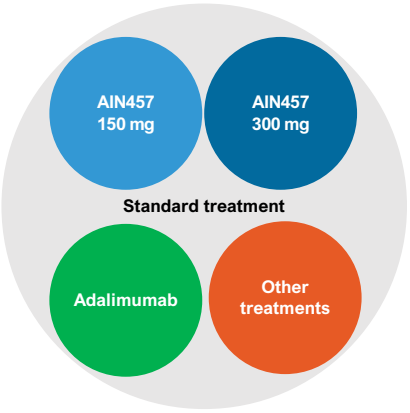
Most participants (221 out of 303) had adverse events. 16 participants had adverse events that were considered serious. No participant died during the trial. 15 participants stopped treatment due to an adverse event. The researchers concluded that there were no new safety concerns about AIN457 from this trial.

How many participants had adverse events?

Participants who:	AIN457 150 mg 190 participants	AIN457 300 mg 92 participants	Adalimumab 40 mg 116 participants	Other treatments 128 participants
Had at least 1 adverse event	144 (76%)	72 (78%)	88 (76%)	90 (70%)
Had at least 1 serious adverse event	10 (5%)	4 (4%)	5 (4%)	8 (6%)
Stopped treatment due to an adverse event	8 (4%)	2 (2%)	5 (4%)	8 (6%)

Note:

- In this section, the numbers of participants who are reported under AIN457, or adalimumab include those who received these treatments at any point during the trial – regardless of their group. Numbers of participants who received any other treatment in the standard treatment group are provided together under '**Other treatments**'.
- A single participant could be counted under more than 1 treatment group if they had adverse events while taking those treatments.



What serious adverse events did the participants have?

16 participants had serious adverse events. No participant died during this trial. The table below shows the most common serious adverse event that happened in **2% or more** of participants in any treatment group during the trial.

	AIN457 150 mg 190 participants	AIN457 300 mg 92 participants	Adalimumab 40 mg 116 participants	Other treatments 128 participants
Worsening of a type of axSpA called ankylosing spondylitis Ankylosing spondylitis	2 (1%)	0	1 (1%)	2 (2%)

What other adverse events did the participants have?

221 participants had other adverse events. The table below shows the most common other adverse events that happened in **5% or more** of participants in any treatment group during the trial.

	AIN457 150 mg 190 participants	AIN457 300 mg 92 participants	Adalimumab 40 mg 116 participants	Other treatments 128 participants
Common cold Nasopharyngitis	24 (13%)	13 (14%)	7 (6%)	10 (8%)
Diarrhea	16 (8%)	9 (10%)	8 (7%)	11 (9%)
Headache	12 (6%)	7 (8%)	7 (6%)	6 (5%)
Feeling sick Nausea	12 (6%)	6 (7%)	3 (3%)	7 (5%)
Infection of the nose and throat Upper respiratory tract infection	10 (5%)	6 (7%)	6 (5%)	3 (2%)
Joint pain Arthralgia	7 (4%)	6 (7%)	3 (3%)	0
Infection of the respiratory system including the lungs Respiratory tract infection	10 (5%)	3 (3%)	3 (3%)	3 (2%)
Feeling tired Fatigue	7 (4%)	3 (3%)	6 (5%)	5 (4%)

What was learned from this trial?

Researchers learned about the effects of taking AIN457 as the first biologic treatment for axSpA with a T2T approach.

Researchers concluded that AIN457 given as the first biologic treatment for axSpA with a T2T approach was not better than standard treatment. Researchers did not find any new safety concerns with the use of AIN457.

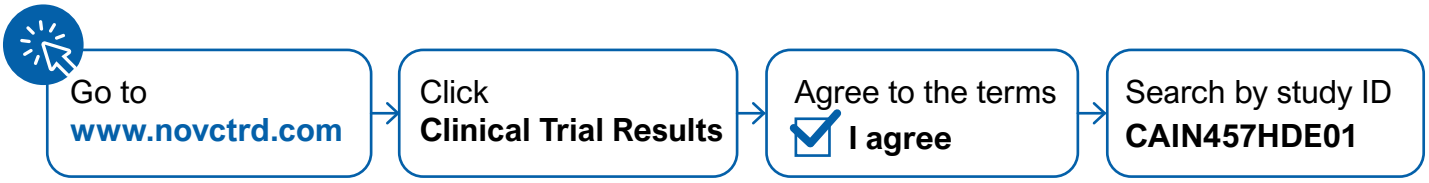
Findings from this study may be used in other studies with AIN457.

There are no plans for future trials to study AIN457 using a T2T approach in people with axSpA.

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:



For more information about this trial, go to any of these websites:

- www.clinicaltrials.gov search using the number **NCT03906136**
- clinicaltrialsregister.eu/ctr-search/search search using the number **2018-003882-32**

If more trials are planned, they will appear on the public websites above. When there, search for AIN457, secukinumab, or axial spondyloarthritis.

Full clinical trial title: A randomized, open label multicenter trial to investigate the efficacy of a treattotarget treatment strategy with secukinumab (AIN457) as a first-line biologic compared to a standard-of-care treatment over 36 weeks in patients with active axial spondyloarthritis (axSpA) – AScalate

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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