NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of secukinumab (AIN457) in participants with Ankylosing Spondylitis

Protocol number: CAIN457FDE03

Thank You!

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. Thank you for taking part in this trial for the drug AIN457, also known as secukinumab. You helped researchers learn more about how secukinumab works in people with Ankylosing Spondylitis.

As a clinical trial participant, you belong to a large community of people around the world. Your invaluable contribution to medicine and healthcare is greatly appreciated.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings. Researchers and health authorities, such as the Food and Drug Administration (FDA) in the United States and the European Medicines Agency (EMA) in Europe, look at the results of many clinical trials to understand which drugs work and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

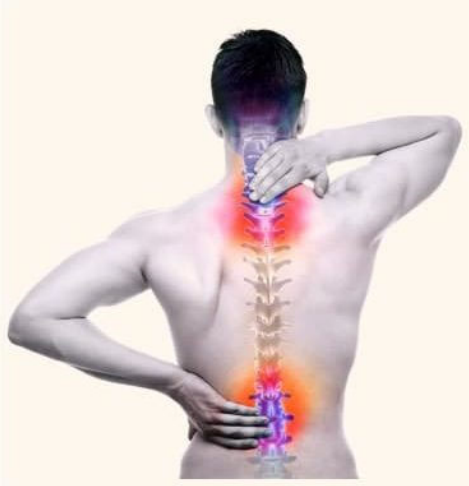
How long was this trial?

This trial was designed so that an individual participant could take part for 6 months. The trial started in May 2016 and ended in September 2019. The entire duration, from enrolling the first participant to the last participant completing the trial was 3 years and 4 months.

The researchers completed this trial as planned. When the trial ended, the researchers collected information on the trial treatments, secukinumab (pronounced se-cu-KIN-umab) and placebo, and created a report of the trial results. This summary is based on that report.

Why was the research needed?

Researchers were looking for a better way to treat Ankylosing Spondylitis, or AS. AS is a rare form of arthritis that causes pain and stiffness in the spine. It is a lifelong condition that starts in the lower back and cause swelling (inflammation) across the whole body. It can further spread to the neck and other parts of the body.



Source: Spondylitis Association of America (spondylitis.org)

Early symptoms of AS include pain in the lower back and hips, especially in the morning. Pain in the neck and feeling tired are also common. As the disease progresses, these symptoms can worsen.

Drugs called non-steroidal anti-inflammatory drugs, or NSAIDs, are often prescribed to relieve pain and reduce swelling (inflammation) in the joints of patients with AS.

NSAIDs are approved for treating conditions such as arthritis. However, NSAIDs can cause side effects when used for a long time and may not be suitable for some patients with AS.

Researchers wanted to see if giving secukinumab in addition to NSAIDs enabled participants to reduce the amount of NSAIDs they were taking, without reducing the beneficial secukinumab treatment effects on their AS symptoms.

Trial drugs

The drugs given in this trial were:

Secukinumab

A drug that blocks the activity of a protein in the body called interleukin 17A, or IL 17A, which causes swelling, redness, and pain when produced in excess. IL 17A is known to play an important role in the body's response in AS.

Placebo

It looks like the trial drug but contains no medicine. Placebo helps researchers better understand if the effects seen in the participants who received the trial drug are actually caused by the trial drug, secukinumab.

Trial purpose

In this trial, researchers looked at the effects of secukinumab in patients with AS. The main question the researchers wanted to answer in this trial was:

How many participants who took secukinumab had at least 20% improvement in their AS symptoms after 12 weeks of treatment compared to placebo?

For this, ASAS20 response was measured. An ASAS20 response is defined as an improvement of at least 20% in the symptoms of AS.

The other question researchers wanted to answer in this trial was:

- Did participants who took secukinumab take lower amounts of NSAIDs to relieve their AS symptoms following up to 24 weeks of treatment?

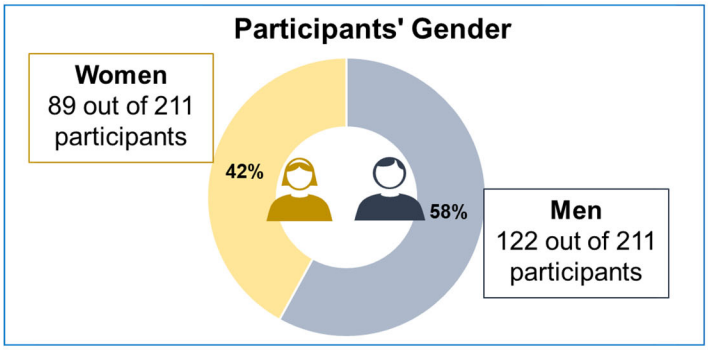
Who was in this trial?

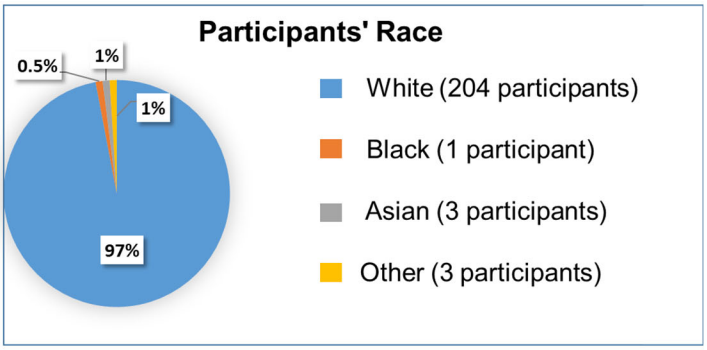
The participants could take part in this trial if they:

- were 18 years of age or above,
- had AS as confirmed by X-ray and a questionnaire to assess AS symptoms,
- had been taking at least 2 different NSAIDs for at least 4 weeks,
- were regularly taking NSAIDs at a dose that was at least half the recommended dose for that particular NSAID or the maximum tolerated dose.

A total of 211 participants at 40 centers in Germany participated in this trial.

The average age of participants was 45 years. Participants' age ranged from 20 to 78 years. The majority of participants, 58% (122 out of 211) were men. 97% (204 out of 211) of the participants were white, as shown below.





What kind of trial was this?

This was a Phase 4 trial. Phase 4 trials are carried out after a new study treatment has been approved for use in patients to learn more about safety, benefits, and risks.

This was a double-blind trial. This means that none of the participants, trial doctors, or trial staff knew what treatment participants were receiving. Some trials are done this way because knowing what treatment each participant is getting can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness towards all treatments.

What happened during this trial?

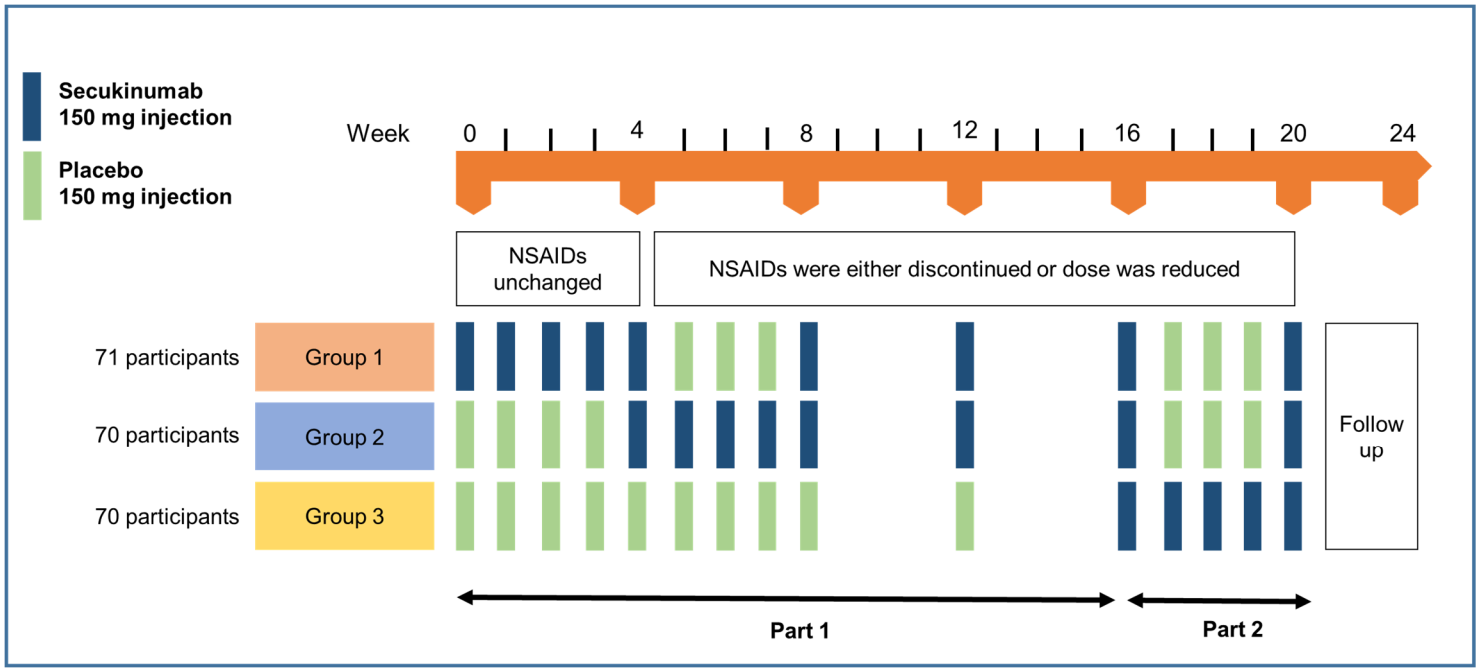
At the start of the trial, the researchers assigned each of the participants randomly into 1 of the 3 treatment groups to receive secukinumab and placebo as shown below:

- **Group 1**: participants in this group took secukinumab 150 milligram (mg) at Weeks 0, 1, 2, 3, 4, 8, 12, 16 and 20 and placebo at Weeks 5, 6, 7, 17, 18, and 19.
- **Group 2**: participants in this group took placebo at Weeks 0, 1, 2 and 3 and secukinumab 150 mg at Weeks 4, 5, 6, 7, 8, 12, 16, and 20 and again took placebo at Weeks 17, 18 and 19.
- **Group 3**: participants in this group took placebo at Weeks 0, 1, 2, 3, 4, 5, 6, 7, 8, and 12 and secukinumab 150 mg at Weeks 16, 17, 18, 19, and 20.

All participants got secukinumab and placebo as injections under the skin during the trial.

All participants received guidance to reduce the dose or discontinue their NSAID intake starting from Week 4 upon an improvement in back pain. Participants could continue or even increase taking their NSAIDs if their pain worsened. From Week 4 onwards, patients had complete flexibility regarding their NSAID-dosage.

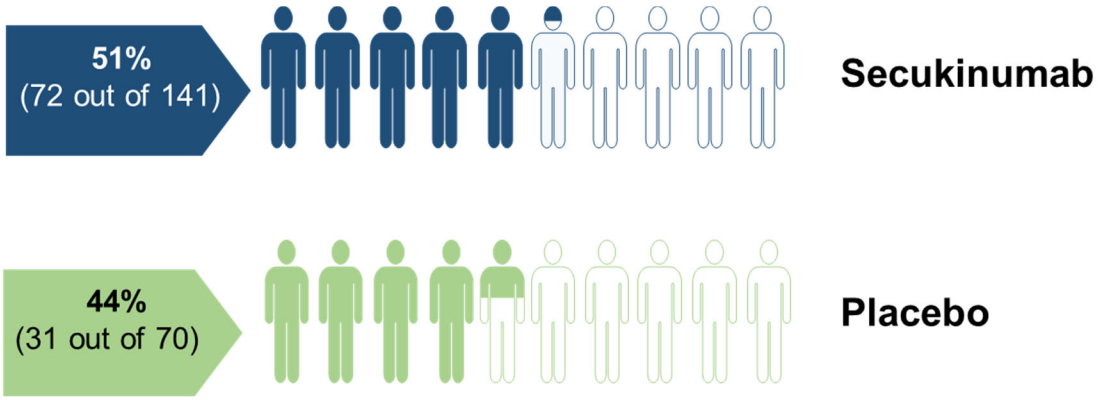
This trial had 2 parts. Part 1 lasted until Week 16. During Part 1, the participants in Group 3 took placebo. Part 2 lasted from Week 16 to Week 20. During Part 2, participants in all 3 groups took secukinumab.



What were the key results of this trial?

This is a summary of the average results for all participants in different treatment groups. It does not show the results of each individual participant. Results of individual participants could be different from the results of the total group of participants. A detailed presentation of the results can be found on the websites listed at the end of this summary.

How many participants who took secukinumab had at least 20% improvement in their AS symptoms after 12 weeks of treatment compared to placebo?



More participants who took secukinumab showed improvement in their AS symptoms compared to those who took placebo. However, the difference was not large enough to confirm the effect of secukinumab in improving participants' AS symptoms.

What were the other results of this trial?

Did participants who took secukinumab take lower amounts of NSAIDs to relieve their AS symptoms following up to 24 weeks of treatment?

To do this, researchers measured the amount of NSAIDs taken by the participants during the trial taking into account the type of NSAID, the total daily dose, and number of days participants took the NSAIDs.

There was a reduction in the amount of NSAIDs taken by participants in all the treatment groups following up to 24 weeks of treatment. This reduction in NSAIDs was slightly more for participants who took secukinumab compared to placebo, but the researchers could not confirm if the difference was an effect of secukinumab treatment.

What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called "adverse events".

A lot of research is needed to know whether a drug causes an adverse event. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug. When new drugs are being studied, researchers keep track of all adverse events participants have.

This section is a summary of the adverse events that happened during this trial. The websites listed at the end of this summary may have more information about all the adverse events that happened in this trial.

An adverse event is an unwanted sign, symptom, or disease that participants have during a trial. These problems may or may not be caused by the trial drug.

An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care.

How many participants had adverse events?

Not all participants in this trial had adverse events.

During Part 1, 165 out of 211 participants (78%) had 1 or more adverse events. 6 out of 211 participants (3%) stopped the drug early because of adverse events. Serious adverse events happened in 8 out of 211 participants (4%) in the trial. No participant died during Part 1 of the trial.

The 3 treatment groups are shown below:

- **Group 1**: secukinumab 150 milligram (mg) at Weeks 0, 1, 2, 3, 4, 8, 12, 16 and 20 and placebo at Weeks 5, 6, 7, 17, 18 and 19.
- **Group 2**: placebo at Weeks 0, 1, 2 and 3 and secukinumab 150 mg at Weeks 4, 5, 6, 7, 8, 12, 16 and 20 and again took placebo at Week 17, 18 and 19.
- **Group 3**: placebo at Weeks 0, 1, 2, 3, 4, 5, 6, 7, 8 and 12 and secukinumab 150 mg at Weeks 16, 17, 18, 19 and 20.

Number of Participants (%) with Adverse Events during Part 1

	Group 1 (Out of 71 participants)	**Group 2** (Out of 70 participants)	**Group 3** (Out of 70 participants)
At least 1 adverse event	53 (75%)	57 (81%)	55 (79%)
At least 1 serious adverse event	4 (6%)	3 (4%)	1 (1%)
Stopped drug due to adverse event	3 (4%)	3 (4%)	0

During Part 2, 71 out of 211 participants (34%) had 1 or more adverse events. 2 out of 211 participants (1%) stopped the drug early because of adverse events. Serious adverse events happened in 2 out of 211 participants (1%) in the trial. No participant died during Part 2 of the trial.

Number of Participants (%) with Adverse Events during Part 2

	Group 1 (Out of 71 participants)	**Group 2** (Out of 70 participants)	**Group 3** (Out of 70 participants)
At least 1 adverse event	25 (35%)	23 (33%)	23 (33%)
At least 1 serious adverse event	1 (1%)	0	1 (1%)
Stopped drug due to adverse event	1 (1%)	1 (1%)	0

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 5% (5 out of 100) of participants during Part 1 in any treatment group are listed below.

Number of Participants (%) with Most Common Non-Serious Adverse Events during Part 1

	Group 1 (Out of 71 participants)	**Group 2** (Out of 70 participants)	**Group 3** (Out of 70 participants)
Common cold (Nasopharyngitis)	6 (9%)	13 (19%)	14 (20%)
Headache	12 (17%)	10 (14%)	6 (9%)
High blood pressure (Hypertension)	4 (6%)	3 (4%)	4 (6%)
Worsening of Ankylosing Spondylitis (AS)	3 (4%)	1 (1%)	6 (9%)
Inflammation of the bronchial tubes (Bronchitis)	5 (7%)	2 (3%)	3(4%)
Stomach flu (Gastroenteritis)	2 (3%)	4 (6%)	3 (4%)
Nausea	2 (3%)	2 (3%)	5 (7%)
Chest infection (Respiratory tract infection)	2 (3%)	4 (6%)	3 (4%)
Back pain	4 (6%)	1 (1%)	1 (1%)
Stuffy nose (Rhinitis)	4 (6%)	0	2 (3%)

The most common non-serious adverse events that happened in at least 5% (5 out of 100) of participants during Part 2 in any group are presented below.

Number of Participants (%) with Most Common Non-Serious Adverse Events during Part 2

	Group 1 (Out of 71 participants)	**Group 2** (Out of 70 participants)	**Group 3** (Out of 70 participants)
Common cold (Nasopharyngitis)	7 (10%)	5 (7%)	3 (4%)
Headache	4 (6%)	3 (4%)	1 (1%)

What were the serious adverse events?

The serious adverse events that happened in the participants during Part 1 in any treatment group are listed below:

Each serious adverse event happened only once in each group. The table below lists the serious adverse events by group.

Group 1 (Out of 71 participants)	**Group 2** (Out of 70 participants)	**Group 3** (Out of 70 participants)
• Inflammation in the large intestine (Colitis) • Inflammation in the digestive tract (Crohn's disease) • Swelling of the stomach lining (Gastritis) • Ulcer in the food pipe (Oesophageal ulcer) • Kidney stones (Nephrolithiasis) • A skin condition that causes red, flaky, crusty patches of skin covered with silvery scales (Psoriasis)	• Swelling in the stomach (Abdominal hernia) • Stomach pain (Abdominal pain) • Soft tissue bulging through the stomach muscles (Inguinal hernia)	• Skin infection (Erysipelas)

During Part 2 of the trial, 2 out of 211 participants (1%) had serious adverse events. 1 participant in Group 1 had vaginal cyst and 1 participant in Group 3 had inflammation of the inner tissues of the eye (iridocyclitis).

Full details of serious adverse events that happened during the trial are provided on the websites mentioned on Page 13.

How many participants stopped trial drug due to adverse events?

During Part 1 of the trial, 6 out of 211 participants (3%) stopped the drug early due to adverse events. The most common adverse event that caused the participants to stop the trial drug was inflammation in the large intestine.

During Part 2, 2 out of 211 participants (1%) stopped the drug early due to adverse events.
1 participant in Group 1 had swelling in the joints (arthritis) and 1 participant in Group 2 had blisters on the palms of the hands and soles of the feet (palmoplantar pustulosis).

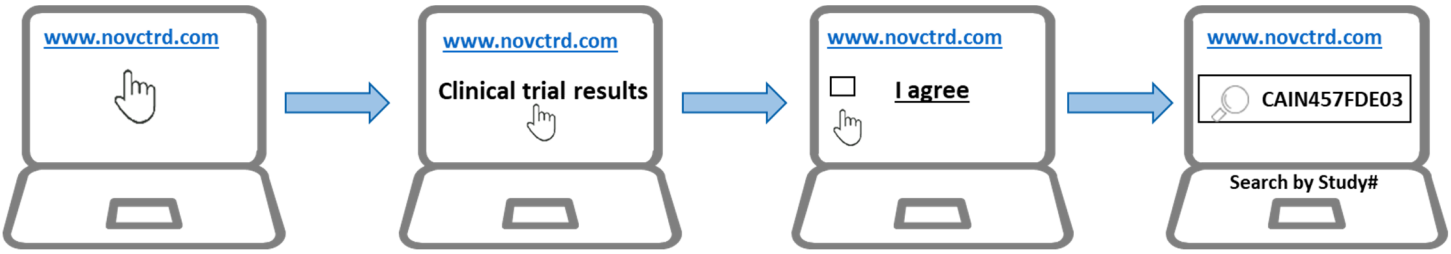
How was this trial useful?

This trial helped researchers learn if giving secukinumab to participants with AS helped in improving the symptoms of AS. It also helped researchers to further understand the effects of secukinumab, when given with NSAIDs, in participants with AS. The response that participants had while taking secukinumab was similar to that seen in other studies done with secukinumab. However, the researchers saw an unusually high response in the placebo group which could not be explained. Therefore the researchers could not confirm a big enough difference in the groups. It shows that secukinumab reduced the amount of NSAIDs without reducing its beneficial treatment effects in participants with AS.

Please remember, this summary only shows the results of a single clinical trial. Other clinical trials may have different results. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

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).



You can find more information about this trial on the following websites:

- www.clinicaltrials.gov Use the NCT identifier NCT02763046 in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search/search Use the EudraCT identifier 2015-004575-74 in the search field.

Full clinical trial title: A randomized, double-blind, placebo-controlled multicenter study of Secukinumab (AIN457) to examine the clinical efficacy and the NSAID-sparing effect of Secukinumab over 16 weeks in patients with ankylosing spondylitis (ASTRUM)

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of people around the world. You helped researchers answer important health questions and test new medical treatments.

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

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