NOVARTIS

Clinical trial results summary

A clinical trial to learn more about the effects and safety of AIN457 in people with axial spondyloarthritis

Protocol number: CAIN457H3301

Thank You!

Novartis, the sponsor of this clinical trial, would like to thank you for taking part in this trial for the drug AIN457, also known as secukinumab. You helped researchers learn more about how AIN457 works in people with axial spondyloarthritis.

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.

Important note: This summary only shows the results of one clinical trial. Other clinical trials may have different findings. Researchers and health authorities 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.

Why was the research needed?

Researchers are looking for a better way to treat axial spondyloarthritis (axSpA). AxSpA is a type of arthritis that causes inflammation (swelling, pain, and stiffness) in the joints, mainly in the spine. Short-term inflammation is one way that the body protects and heals itself from injury and infection. In axSpA, inflammation is long-term and caused by an autoimmune disease. Autoimmune means the body's immune system (its natural defense system against illness and infection) attacks healthy cells in the body by mistake. AxSpA can cause:

- Constant and ongoing **inflammatory back pain**
- Tiredness
- Trouble carrying out day-to-day tasks

AIN457 is a drug that lowers inflammation and is used to treat other types of arthritis. AIN457 binds to and lowers the activity of a protein in the body called interleukin 17a (IL-17a). High levels of IL-17a may cause inflammation and pain. Researchers want to learn if AIN457 could control pain caused by axSpA. To do this, they designed this clinical trial to learn about the effects and safety of AIN457 in people with axSpA.

Trial drugs

The drugs given in this trial were:

AIN457: a drug that is approved for use in many countries to treat other inflammatory diseases, including other types of arthritis.

- AIN457 is also known as **secukinumab** (sek-ue-KIN-ue-mab).

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

Trial purpose

The purpose of this trial was to learn about the effects and safety of AIN457 in people with axSpA. It focused on AIN457's effect on inflammatory back pain after a short period of time (8 weeks). This focus was based on input from patient organizations that identified low levels of back pain as the most important treatment effect for patients with axSpA.

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

- Did more participants who took AIN457 report low inflammatory back pain compared to participants who took the placebo?
- Did more participants who took AIN457 report low axSpA symptoms compared to participants who took the placebo? The axSpA symptoms included back pain, pain in other joints, tiredness, tenderness, and morning stiffness.

Researchers also checked participants' health throughout the trial to look for any medical problems.

How long was this trial?

This trial was designed so that each participant could take part for about 6 months. The trial started in June 2017 and ended in February 2019.

The researchers completed this trial as planned. When the trial ended, the researchers collected information on the trial treatments and created a report of the trial results. This summary is based on that report.

Who was in this trial?

380 participants began this trial – 235 men and 145 women. Participants could take part in this trial if they had axSpA and:

- Rated their inflammatory back pain as high, which was defined as a score higher than 4 on a scale from 0 (no pain) to 10 (most severe pain). The average score was about 7 out of 10.
- Rated their other axSpA symptoms as high, which was defined as a score of 4 or higher on a scale from 0 (no problem) to 10 (worst problem). The average score was about 7 out of 10.
- Had taken at least 2 types of non-steroidal anti-inflammatory drugs (NSAIDs) that didn't work to treat their axSpA. NSAIDs, such as ibuprofen and aspirin, are medicines that can lower pain and inflammation.

Participants' ages ranged from 18 to 80 years. They were 42 years old on average. They identified their race as Caucasian (White), Asian, and Other.

Participants took part at 66 trial sites in Belgium, Bulgaria, Croatia, Czech Republic, Estonia, Finland, Greece, Ireland, Italy, Latvia, Lithuania, Poland, Russia, Spain, Sweden, Switzerland, and the United Kingdom.

The number of participants that took part in each country

What kind of trial was this?

This was a double-blind trial. This means that none of the participants, trial doctors, or trial staff knew what treatment the participants were taking. 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?

This trial had a screening period, 2 treatment parts (Part 1 and Part 2), and a follow-up period.

Screening period
Up to 3 months before taking either AIN457 or placebo, trial doctors checked participants' health and axSpA symptoms to make sure they could be in this clinical trial. 380 participants could take part in this trial.

Treatment Part 1 – 8 weeks long
Participants were randomly assigned to take 1 of 2 treatments:

- **150 mg (milligrams) AIN457** one time a week (75% of participants)
- A **placebo** one time a week (25% of participants)

Participants took their assigned treatment by giving themselves an injection under the skin, usually in the thigh or belly area at the start of treatment and at weeks 1, 2, 3, and 4. After each treatment and 4 weeks after their last treatment (week 8), participants visited the trial site to rate the severity of their axSpA symptoms.

Treatment Part 2 – 16 weeks long
Participants from Treatment Part 1 were reassigned to take 1 of 2 treatments:

- **150 mg AIN457** every 4 weeks
- **300 mg AIN457** every 4 weeks

All participants who took AIN457 in Treatment Part 1 and had low inflammatory back pain at week 8 were assigned to take the 150 mg dose of AIN457.

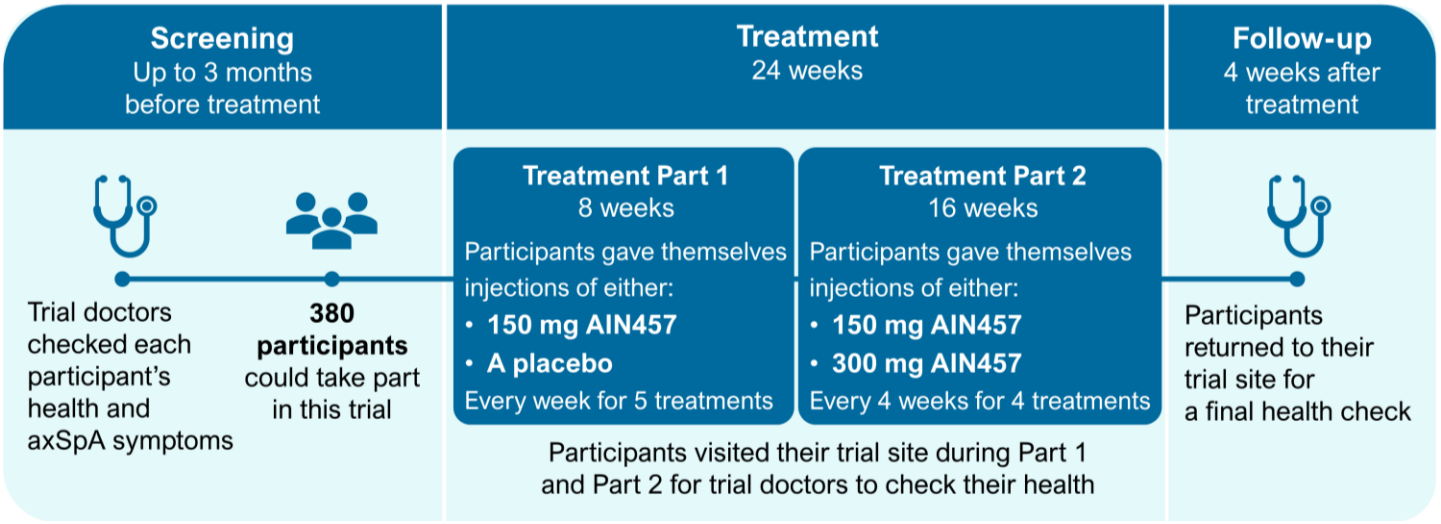
All other participants, including those who took the placebo, were evenly assigned to either the 150 mg dose or the 300 mg dose of AIN457.

Participants took their assigned treatment a total of 4 times and visited the trial site to rate the severity of their axSpA symptoms.

During both parts of the trial, participants could also continue taking certain other treatments for axSpA, such as NSAIDs, certain pain medicines, certain arthritis medicines, and corticosteroids. Trial staff took blood and urine samples at some of the trial visits.

Follow-up period
Participants returned to their trial site for a final visit 4 weeks after taking their last treatment from Treatment Part 2. Trial staff took blood and urine samples at this visit.

How researchers designed this trial:



What were the main results of this trial?

This is a summary of the overall results for all participants. 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. More details on the results can be found on the websites listed at the end of this summary.

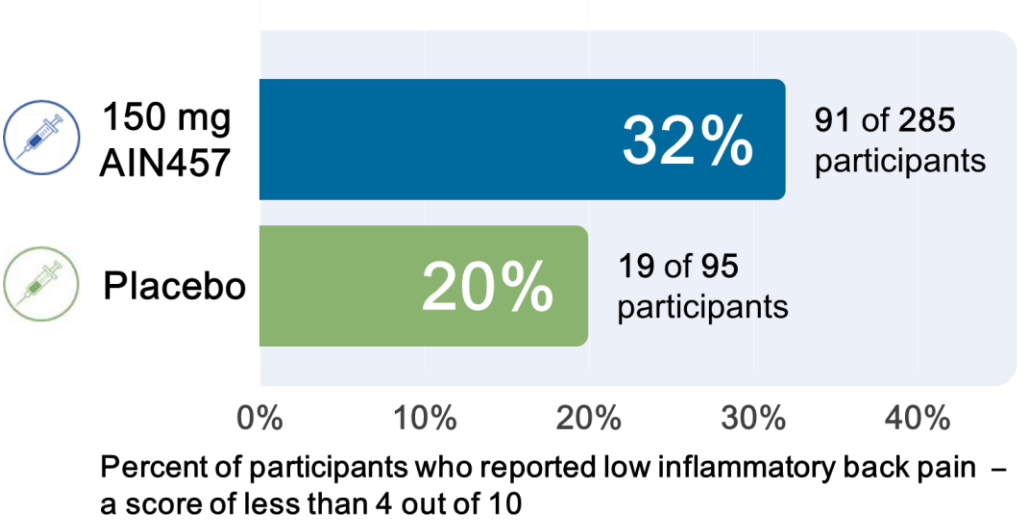
Did more participants who took AIN457 report low inflammatory back pain compared to participants who took the placebo in Part 1?

To learn if participants reported low inflammatory back pain after they took AIN457, participants rated their inflammatory back pain on a scale from 0 (no pain) to 10 (most severe pain). **The inflammatory back pain score** was a participant's average score. Low inflammatory back pain was defined as a score of less than 4.

Researchers compared participants who took AIN457 and reported low inflammatory back pain to participants who took the placebo and reported low inflammatory back pain at the end of Treatment Part 1 (8 weeks).

More participants who took AIN457 reported low inflammatory back pain compared to participants who took the placebo. Some participants who took the placebo also reported low inflammatory back pain, which was likely because pain scores are subjective (based on personal feelings) and change over time.

Participants who reported low inflammatory back pain (score of less than 4 out of 10) at 8 weeks during Treatment Part 1



Other participants reported a decrease in their score for inflammatory back pain after treatment, but their score was 4 or higher.

What were the other results of this trial?

Did more participants who took AIN457 report low axSpA symptoms compared to participants who took the placebo in Part 1?

To learn if participants reported low axSpA symptoms, participants rated their axSpA symptoms from the past week on a scale from 0 (no problem) to 10 (worst problem). The symptoms included: back pain, pain in other joints, tiredness, tenderness, and morning stiffness.

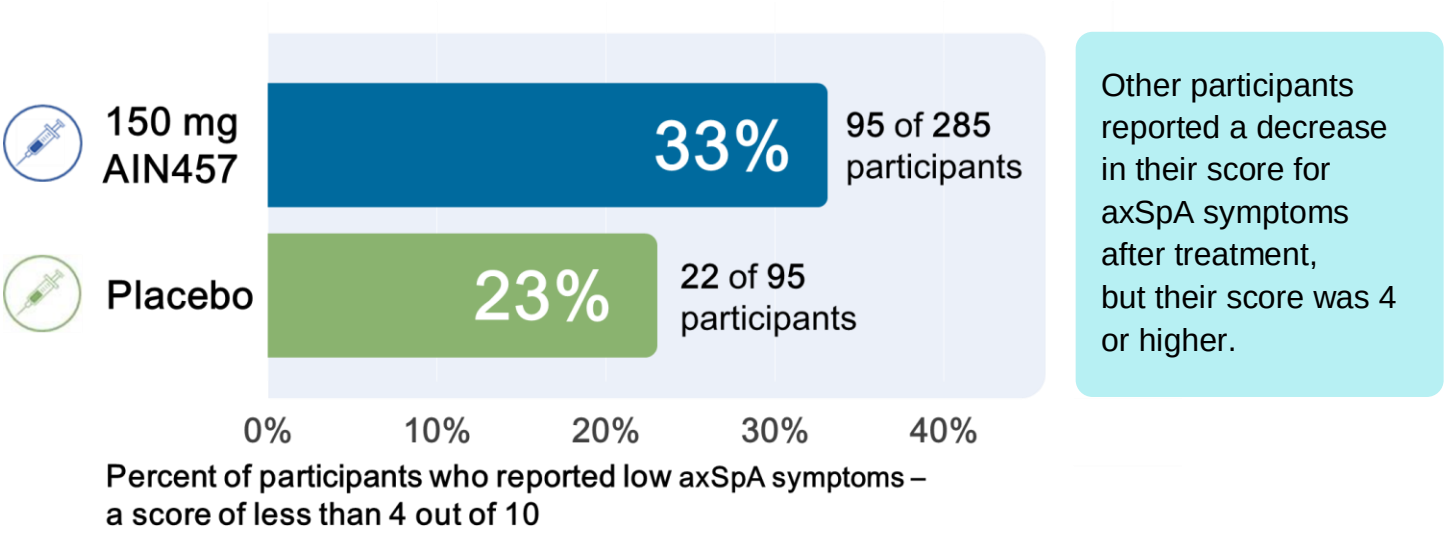
The axSpA symptom score was the average of the symptom scores. Low axSpA symptoms was defined as a score of less than 4.

Researchers compared participants who took AIN457 and reported low axSpA symptoms to participants who took the placebo and reported low axSpA symptoms at the end of Treatment Part 1 (8 weeks).

Researchers found that more participants who took AIN457 reported low axSpA symptoms compared to participants who took the placebo. Some participants who took the placebo also reported low

axSpA symptoms, which was likely because symptom scores are subjective and change over time.

Participants who reported low axSpA symptoms (score of less than 4 out of 10) at 8 weeks during Treatment Part 1



Other participants reported a decrease in their score for axSpA symptoms after treatment, but their score was 4 or higher.

What were the results in Part 2?

Researchers also kept track of participants' inflammatory back pain scores and axSpA symptom scores during Part 2 of this trial. They found that:

- The percent of participants who reported low inflammatory back pain and low axSpA symptoms went up in all groups at the end of Part 2
- Participants who reported low inflammatory back pain at the end of Part 1 were more likely to report low inflammatory back pain and low axSpA symptoms at the end of Part 2 compared to the other groups

What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called "adverse events". An adverse event is an 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 an adverse event. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug.

So, when new drugs are being studied, researchers keep track of all adverse events the participants have.

This section is a summary of the adverse events that happened during the treatment and follow-up periods. The websites listed at the end of this summary have more information about the adverse events that happened in this trial.

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 4% of participants in any group are listed in the tables below.

Most common non-serious adverse events in Treatment Part 1

Treatment assigned	150 mg AIN457	Placebo
	Percent % (out of 285 participants)	Percent % (out of 95 participants)
Headache	4% (10)	1% (1)
Upper respiratory tract infection Such as a cold or the flu	1% (4)	5% (5)

Most common non-serious adverse events in Treatment Part 2

Treatment assigned during Part 2	150 mg AIN457			300 mg AIN457	
	(150 mg in Part 1 with low back pain rating)	(150 mg in Part 1 with high back pain rating)	(Placebo in Part 1)	(150 mg in Part 1 with high back pain rating)	(Placebo in Part 1)
	Percent % (out of 90 participants)	Percent % (out of 94 participants)	Percent % (out of 45 participants)	Percent % (out of 94 Participants)	Percent % (out of 44 participants)
Common cold Nasopharyngitis	1% (1)	3% (3)	4% (2)	4% (4)	5% (2)
Sign of kidney damage Blood creatinine increased	3% (3)	1% (1)	0	0	5% (2)
Throat pain Oropharyngeal pain	4% (4)	2% (2)	0	0	0

What were the serious adverse events?

There were no deaths reported during this trial. During both parts of this clinical trial, 9 participants or 2% of all participants had serious adverse events.

Treatment Part 1

4 participants who took AIN457 had a total of 5 serious adverse events. These were:

- **Abnormal growth in the kidney**
  Renal mass
- **Boil-like swelling near the anus**
  Anal abscess
- **Broken bones in the face**
  Facial bones fracture
- **Heart attack**
  Myocardial infarction
- **Sudden heart attack**
  Acute myocardial infarction

Treatment Part 2

5 participants who took AIN457 had a total of 5 serious adverse events. These were:

- **An inflammatory bowel disease**
  Colitis ulcerative
- **Inflamed pancreas**
  Pancreatitis
- **Kidney failure**
  Renal impairment
- **Partial paralysis**
  Hemiparesis
- **Severe skin cancer**
  Malignant melanoma

None of the participants who took the placebo during Treatment Part 1 had serious adverse events.

How has this trial helped?

This trial helped researchers learn how well AIN457 works to lower inflammatory back pain in people with axSpA after a short period of time. At 8 weeks, more participants who took AIN457 reported low inflammatory back pain and axSpA symptoms compared to participants who took the placebo. The adverse events participants had during this trial were similar to those other participants had during past trials of AIN457.

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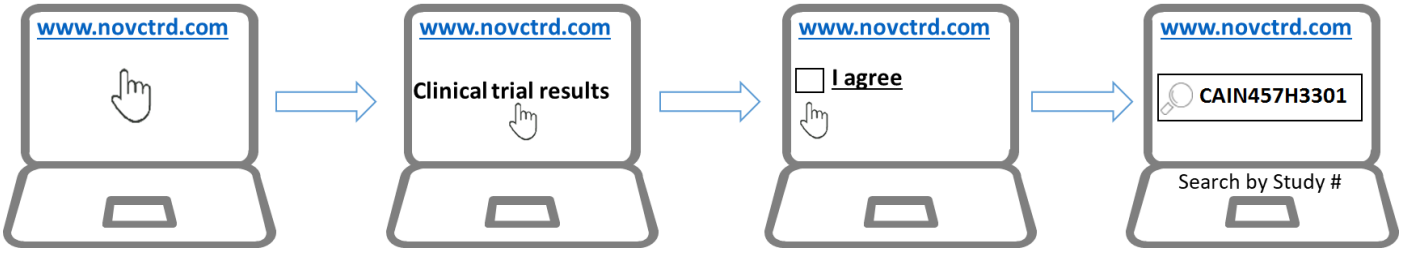
Where can I learn more about this trial?

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 03136861 in the search field.
- www.clinicaltrialsregister.eu. Use the EudraCT identifier 2017-000401-21 in the search field.

Full clinical trial title: A 24-week, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of secukinumab in controlling spinal pain in patients with axial spondyloarthritis

Thank you

Thank you for taking part in this trial. 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.

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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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