NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects and safety of secukinumab (AIN457) 300 mg compared to 150 mg in participants with ankylosing spondylitis

Protocol number: CAIN457FUS06

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 secukinumab, also known as AIN457. You helped researchers learn more about how secukinumab works in people with ankylosing spondylitis.

This summary only shows the average results of a single clinical trial. Other clinical trials may have different findings. Websites listed at the end of the summary may have more information about this trial. 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 were looking for a better way to treat ankylosing spondylitis (AS). AS is an inflammatory disease that affects the joints in the body. It often causes pain and stiffness in the spine. It is a lifelong condition that mostly starts in the lower back or neck and can further spread to other parts of the body.

Secukinumab (pronounced as *se-cu-KIN-umab)* 150 milligram (mg) is an approved treatment for AS. However, some people continue to have active AS symptoms after treatment with this dose.

In this trial, researchers wanted to gather more information about the safety and potential benefits of taking secukinumab 300 mg in participants with AS who are not adequately treated with secukinumab 150 mg. While this trial was in progress, secukinumab 300 mg was approved for the treatment of AS.

The main question the researchers wanted to answer in this trial was:

How many participants, who had an inadequate response to secukinumab 150 mg at Week 16, achieved inactive disease after treatment with secukinumab 300 mg compared to secukinumab 150 mg at Week 52?

'Inactive disease' means relief from signs and symptoms (e.g., pain and stiffness) of AS.

Trial drugs

The drugs given in this trial were:

Secukinumab: It is an approved treatment for AS and certain other conditions. It was given as an injection under the skin.

Placebo: It looked like the trial drug but did not have any medicine in it. Using a placebo helps researchers better understand the effect of a trial drug by making sure that the changes were not happening by chance. In this trial, placebo was used to keep participants, the trial doctors, and the trial staff from knowing the dose of secukinumab participants were receiving.

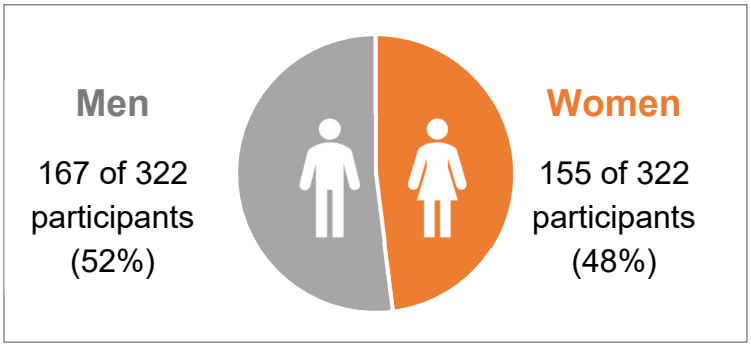
Who was in this trial?

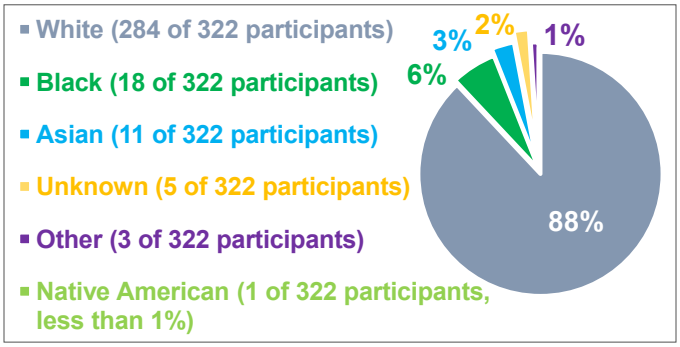
The participants could take part in this trial if they:

- were at least 18 years of age,
- had moderate to severe AS based on their AS symptoms and x-ray findings, and
- had moderate to very severe back pain.

A total of 322 participants from 65 trial sites in the United States of America participated in this trial.

The average age of participants was 48 years. Participants' age ranged from 20 to 83 years.





How was this trial done?

Before Treatment

The trial doctors checked if participants could take part in this trial.

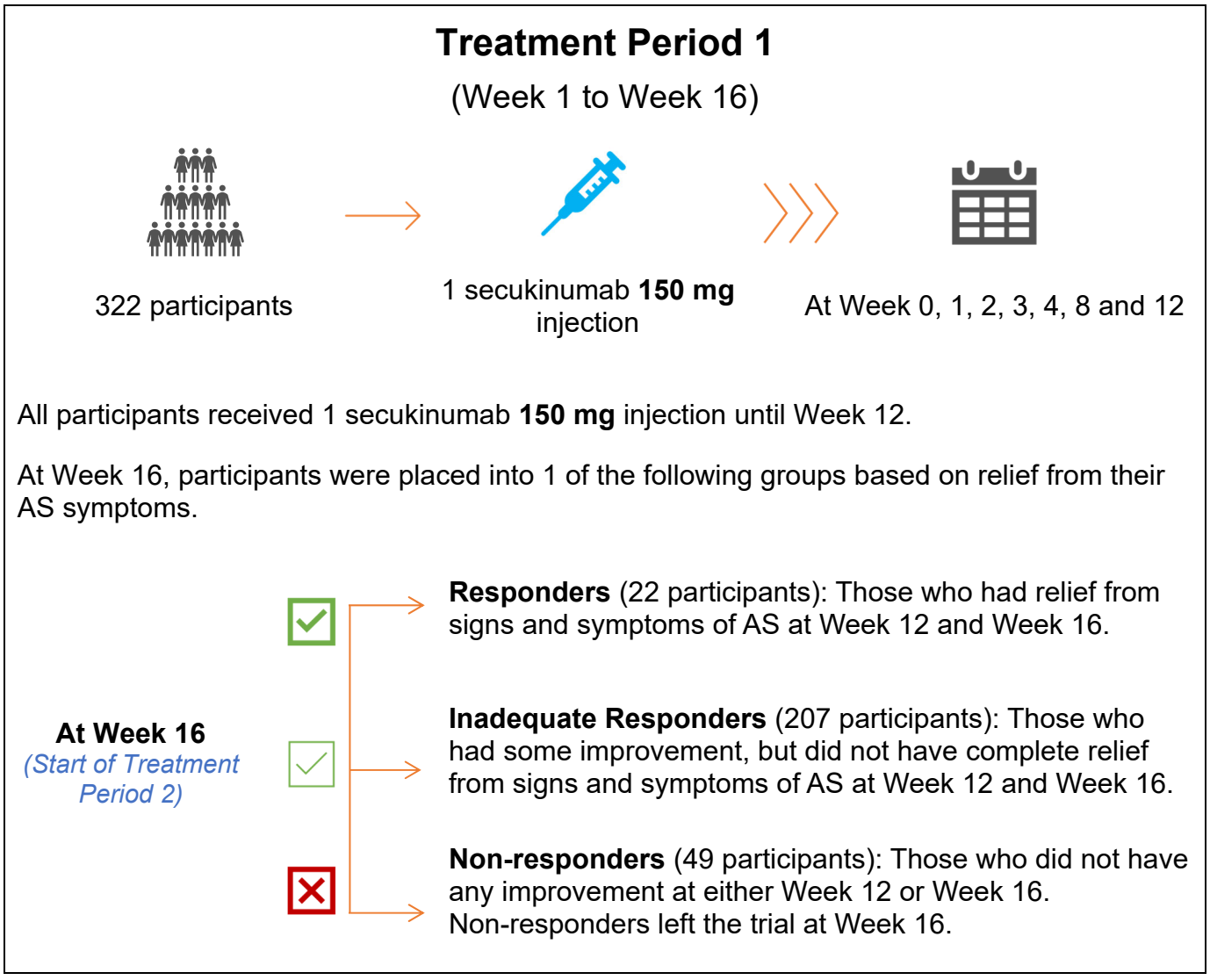
During Treatment

This trial had 2 periods: **Treatment Period 1** and **Treatment Period 2**.

In this trial, researchers wanted to learn more about the effects of taking secukinumab 300 mg compared to secukinumab 150 mg. They studied the participants who had an inadequate response with secukinumab 150 mg to AS in Treatment Period 1.

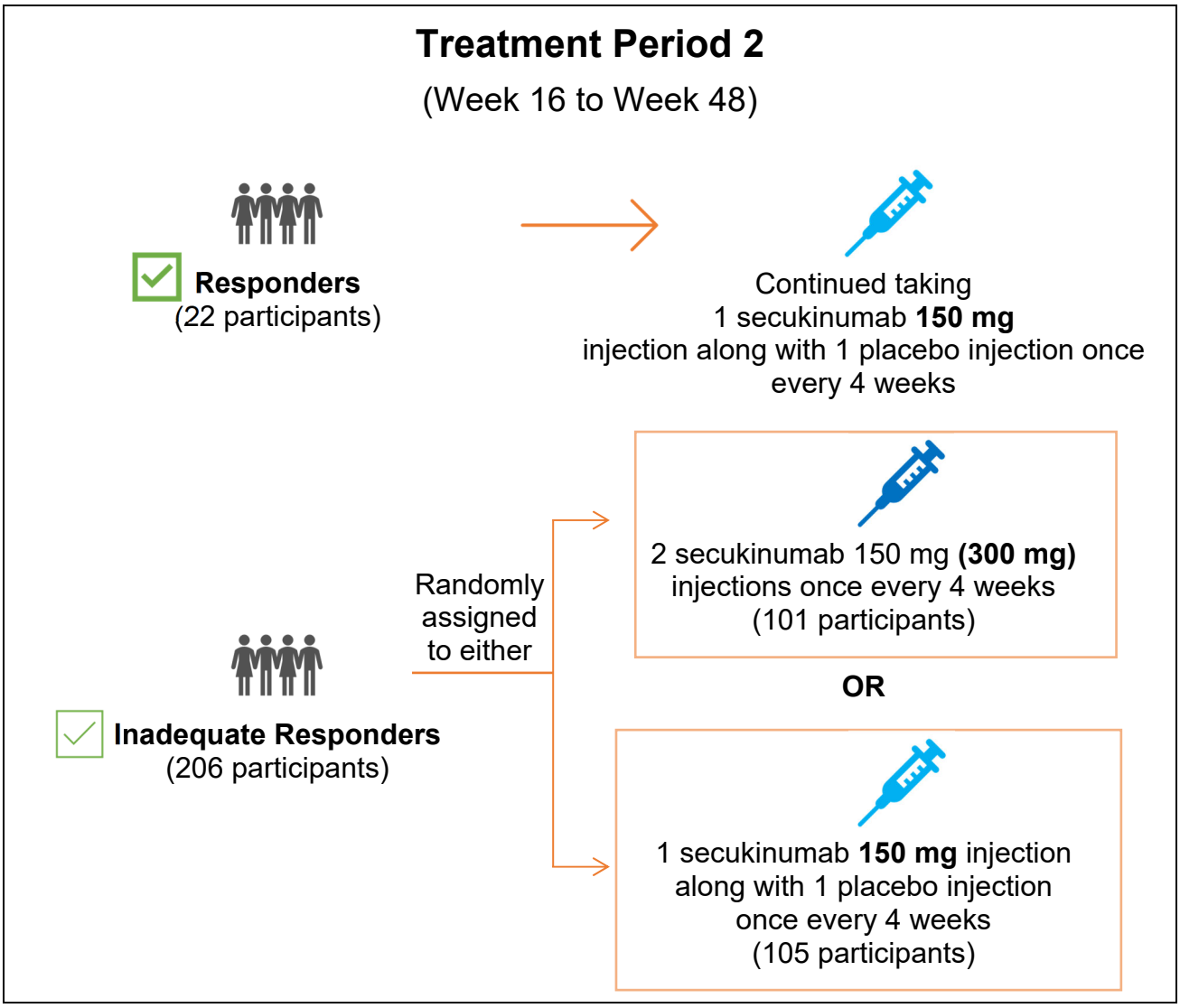
Treatment Period 1

During this period, both the researchers and the participants knew what treatment was given to the participants.



Treatment Period 2

During this period, none of the participants, trial doctors, or trial staff knew what treatment participants were receiving.



Researchers randomly assigned (like tossing a coin) inadequate responders to 1 of 2 doses of secukinumab (150 mg or 300 mg). Responders and inadequate responders who were maintained on secukinumab 150 mg also received matching placebo injections. Non-responders left the trial at Week 16.

After Treatment

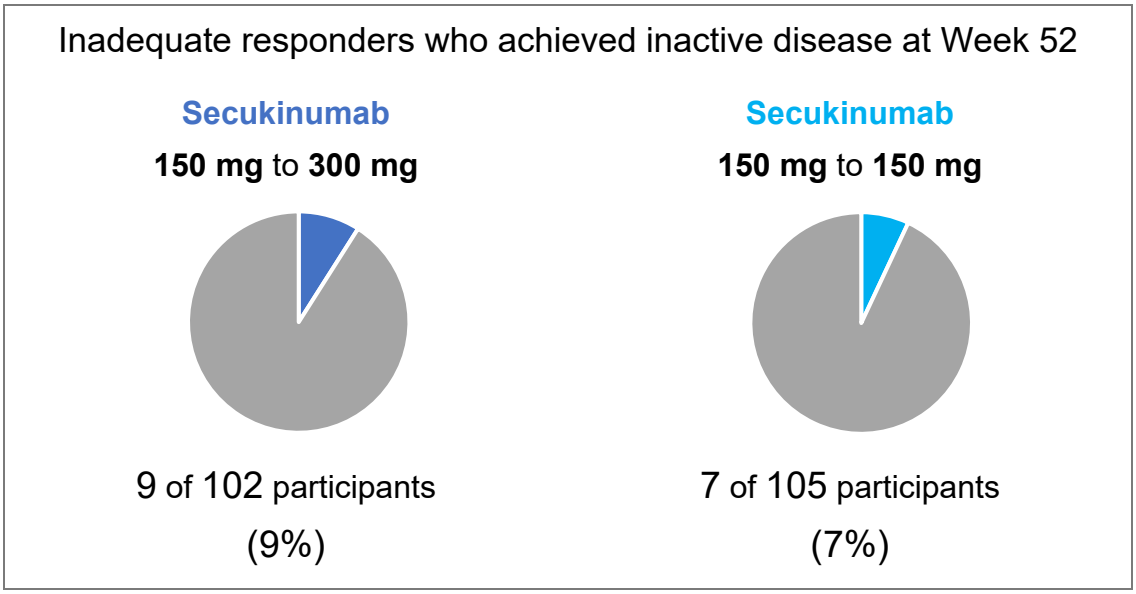
All participants attended an end of treatment visit at the trial site at Week 52, 4 weeks after the last treatment at 48 weeks. No trial treatment was given during the Week 52 visit.

Researchers closely monitored the overall health of the participants throughout the trial. Researchers completed this trial as planned.

What were the main results of this trial?

How many participants, who had an inadequate response to secukinumab 150 mg at Week 16, achieved inactive disease after treatment with secukinumab 300 mg compared to secukinumab 150 mg at Week 52?

Researchers used a score called **Ankylosing Spondylitis Disease Activity Score** (**ASDAS**) to measure response to treatment only for inadequate responders. The score was based on levels of pain, stiffness, mobility, and fatigue experienced by a participant. The lower the score, the better was their response to treatment. The number of inadequate responders who achieved inactive disease after treatment with secukinumab 300 mg was similar to that with secukinumab 150 mg at Week 52.



What medical problems did the participants have during the trial?

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

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.

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.

How many participants had adverse events?

Number of Participants (%) With Adverse Events

	Treatment Period 1	**Treatment Period 2**		
	Secukinumab 150 mg **Out of 322 participants**	**Secukinumab 150 - 150 mg** (Responders) **Out of 22 participants**	**Secukinumab 150 - 150 mg** (Inadequate responders) **Out of 105 participants**	**Secukinumab 150 - 300 mg** (Inadequate responders) **Out of 101 participants**
At least 1 adverse event	192 (60%)	15 (68%)	72 (69%)	64 (63%)
At least 1 serious adverse event	11 (3%)	0	3 (3%)	7 (7%)
Stopped drug due to adverse event	12 (4%)	1 (<1%)	4 (4%)	4 (4%)
Death	0	0	0	0

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 5% of participants in any group are presented below.

Number of Participants (%) With Most Common Non-Serious Adverse Events

	Treatment Period 1	Treatment Period 2		
	Secukinumab 150 mg **Out of 322 participants**	**Secukinumab 150 - 150 mg** (Responders) **Out of 22 participants**	**Secukinumab 150 - 150 mg** (Inadequate responders) **Out of 105 participants**	**Secukinumab 150 - 300 mg** (Inadequate responders) **Out of 101 participants**
Worsening of AS	1 (<1%)	2 (9%)	1 (1%)	5 (5%)
Back pain	6 (2%)	2 (9%)	4 (4%)	4 (4%)
Common cold *(Upper respiratory tract infection)*	15 (5%)	0 (0)	8 (8%)	6 (6%)
Diarrhea *(Diarrhoea)*	18 (6%)	0 (0)	3 (3%)	7 (7%)
Joint pain *(Arthralgia)*	15 (5%)	2 (9%)	10 (10%)	6 (6%)

What were the serious adverse events?

Treatment Period 1 (Secukinumab150 mg)

Serious adverse events happened in 11 out of 322 (3%) of participants. The serious adverse events that happened in at least 1 participant were:

- **stomach pain** *(abdominal pain)*
- **inflammation in the gut** *(colitis)*
- **inflammation and sores in the gut** *(ulcerative colitis)*
- **constipation**
- **acid reflux** *(gastroesophageal reflux disease)*
- **slowed or stopped motion of the gut that moves the food along** *(ileus)*
- **skin infection** *(cellulitis)*
- **pus within a tooth** *(tooth abscess)*
- **broken or cracked hip bone** *(acetabulum fracture)*
- **broken backbone** *(lumbar vertebral fracture)*
- **type 1 diabetes** *(type 1 diabetes mellitus)*
- **back pain**
- **a long-lasting disease in which the immune system attacks its tissues** *(systemic lupus erythematosus)*
- **breast cancer**
- **migraine** *(migraine)*
- **fit** *(seizure)*
- **fainting** *(syncope)*

Treatment Period 2

Secukinumab 150 mg - 150 mg (responders): No serious adverse events happened in the 22 participants in this group.

Secukinumab 150 mg -150 mg (inadequate responders): Serious adverse events happened in 3 out of 105 (3%) participants in this group. The serious adverse events that happened in at least 1 participant were **increase in calcium in the blood** *(hypercalcemia)*, **skin cancer** *(basal cell carcinoma),* and **prostate cancer**.

Secukinumab 150 mg -300 mg (inadequate responders): Serious adverse events happened in 7 out of 101 (7%) participants in this group. The serious adverse events that happened in at least 1 participant were:

- **irregular heartbeat** *(atrial fibrillation)*
- **hardening of the arteries** *(coronary artery disease)*
- **stomach pain** *(abdominal pain)*
- **cancer of the liver** *(hepatic cancer)*
- **vomiting**
- **chest pain**
- **infection in any part of the urinary system** *(urinary tract infection)*
- **decrease in calcium in the blood** *(hypocalcemia)*

- **decrease in magnesium in the blood** *(hypomagnesemia)*
- **shortness of breath** *(dyspnea)*
- **collapse of a small bone in the backbone** *(compression fracture)*
- **broken backbone** *(lumbar vertebral fracture)*
- **bruise of the lung** *(pulmonary contusion)*
- **broken or cracked rib** *(rib fracture)*
- **road traffic accident**
- **accumulation of blood in the chest due to an injury** *(traumatic hemothorax)*
- **migraine** *(migraine)*
- **nerve pain** *(neuralgia)*
- **bladder cancer**
- **collapsed lungs** *(pneumothorax)*

How many participants stopped trial drug due to adverse events?

Treatment Period 1

During this period, 12 out of 322 (4%) of participants stopped secukinumab early due to adverse events. The most common adverse events that led to stopping secukinumab were **inflammation and sores in the intestine** *(ulcerative colitis)* and **rash**.

Treatment Period 2

Secukinumab 150 mg - 150 mg (responders): During this period, 1 out of 22 participants in this group stopped secukinumab early due to **weakness** *(asthenia)*, **feeling tired** *(fatigue)*, **diabetes type 2** *(type 2 diabetes mellitus),* and **mental confusion** *(disorientation)*.

Secukinumab 150 mg - 150 mg (inadequate responders): During this period, 4 out of 105 (4%) participants in this group stopped secukinumab early due to:

- **inflammation in the digestive tract** *(Crohn's disease)*,
- **increase in a protein called creatinine in the blood** *(blood creatinine increased)*,
- **joint pain** *(arthralgia)*,
- **extra fluid around a joint** *(joint effusion)*,
- **prostate cancer**.

Secukinumab 150 mg - 300 mg (inadequate responders): During this period, 4 out of 101 (4%) participants in this group stopped secukinumab early due to:

- **inflammation in the digestive tract** *(inflammatory bowel disease)*,
- **collapse of a small bone in the backbone** *(compression fracture)*,
- **broken backbone** *(lumbar vertebral fracture)*,
- **bruise of the lung** *(pulmonary contusion)*,
- **broken or cracked rib** *(rib fracture)*,
- **road traffic accident**,
- **accumulation of blood in the chest due to an injury** *(traumatic hemothorax)*,
- **migraine** *(migraine)*,
- **nerve pain** *(neuralgia)*,
- **cancer of the liver** *(hepatic cancer)*,
- **abnormal growth in the kidney** *(renal mass)*.

How was this trial useful?

Researchers learned that the effects of secukinumab 300 mg and 150 mg were similar in participants with AS who were not adequately treated with secukinumab 150 mg. There were no new safety concerns seen in the participants during the trial. The safety results were consistent with previous findings in participants with AS treated with 150 mg and 300 mg secukinumab.

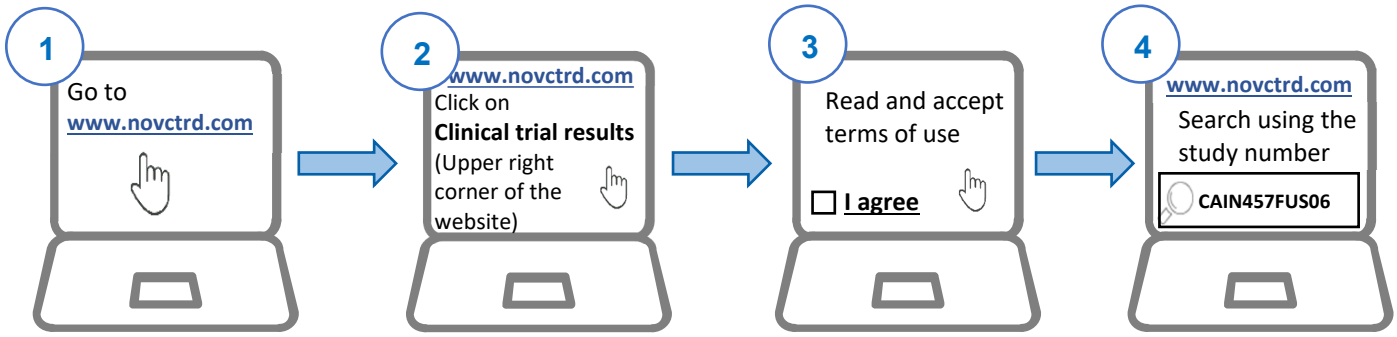
Results from this trial may be used in other clinical trials for people with AS.

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).

Please follow the below steps:



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

- www.clinicaltrials.gov Use the NCT identifier NCT03350815 in the search field.

Full clinical trial title: A randomized, double-blind, parallel-group, multicenter study of secukinumab to compare 300 mg and 150 mg at Week 52 in patients with Ankylosing Spondylitis who are randomized to dose escalation after not achieving inactive disease during an initial 16 weeks of open-label treatment with secukinumab 150 mg (ASLeap)

Trial Dates: The trial started in March 2018 and ended in March 2021.

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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