Clinical Trial Results Summary

A clinical trial to learn about the effects and safety of the secukinumab auto-injector in participants with moderate to severe plaque psoriasis

Protocol number: CAIN457A2325

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 the effects and safety of secukinumab auto-injector in people with moderate to severe plaque psoriasis.

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 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.

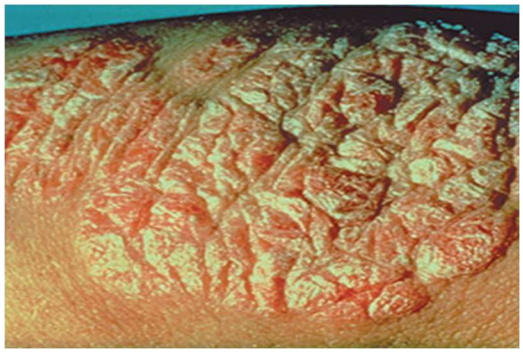
How long was this trial?

This trial was designed so that an individual participant could take part for about 1 year. The trial started in December 2018 and ended in August 2020. The entire duration, from enrolling the first participant to the last participant completing the trial was 1 year and 7 months.

The researchers completed this trial as planned and created a report of the trial results. This summary is based on that report.

Why was the research needed?

Plaque psoriasis is a long-term skin condition, in which overproduction of skin cells leads to their rapid buildup causing scaling on the skin surface. These scales are whitish silver in color and develop in thick red patches, also called plaques or skin lesions. Psoriasis can appear anywhere on the body but mainly affects the elbows, knees, hands, feet, face, scalp, and lower back.



Source: National Psoriasis Foundation (psoriasis.org)

Currently, many treatment options are available for plaque psoriasis. However, these treatment options sometimes either do not work or are unable to completely cure the condition.

In this trial, researchers wanted to learn about the effects and safety of secukinumab (pronounced as se-cu-KIN-umab) when participants with moderate to severe plaque psoriasis injected the secukinumab into themselves using an auto-injector device.

Secukinumab is available as a 1-mL 150 mg pre-filled syringe. Since the approved dose is 300 mg in patients with plaque psoriasis, 2 injections are needed to deliver the appropriate dose. The 2-mL auto injector is a medical device used for delivering the required dose with a single injection.

Trial drugs

The drugs taken in this trial were:

Secukinumab

Secukinumab is already approved in the United States, European Union, Japan, Switzerland, and other countries for the treatment of moderate to severe plaque psoriasis in adult patients. Interleukin 17A (IL-17A) is a protein, present in high levels in psoriatic patients causing swelling, redness, pain, and itch. Secukinumab binds to IL-17A and reduces its activity, thereby reducing swelling, redness, pain, and itch.

Placebo

The placebo devices looked like trial drug devices (see below) but did not have any medicine in it. Using a placebo help researchers better understand the effect of a trial drug by making sure that the changes were not happening by chance.

In this trial, participants injected themselves 2 times with a 1-mL pre-filled syringe containing 150 mg of secukinumab or matching placebo, or participants injected themselves once with a 2-mL auto-injector containing 300 mg of secukinumab or matching placebo.

Auto-injector

The 2-mL auto-injector is a medical device used for self-injecting a single, preloaded dose of a drug. It typically consists of a spring-loaded syringe which works when the device is pushed firmly against the body.

Pre-filled syringe

The 1-mL pre-filled syringe is also used to self-inject secukinumab and is already available in the market for use with secukinumab. A pre-filled syringe is a disposable syringe that is supplied with already loaded drug to be self-injected.

Throughout the trial, participants were not allowed to take any other medicine that could interfere with their immune system or have an effect on their psoriasis.

Researchers also advised participants to limit exposure to ultraviolet (UV) light such as sunlight to avoid any effect on their psoriasis.

Trial purpose

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

? How many participants who took secukinumab auto-injector had at least **75%** improvement in their skin compared with placebo after 12 weeks of treatment?

*To answer this question, researchers used a scale called the **Psoriasis Area Severity Index score**, or **PASI score**. It measures the severity of redness, scaling and thickness of the psoriasis plaques, and how much of the body area is affected. A participant was considered a PASI 75 responder if a reduction of **75%** or more occurred in their PASI score compared to the start of the trial.*

? How many participants who took secukinumab using an auto-injector had a **clear or almost clear** skin compared with placebo after 12 weeks of treatment?

*To answer this question, researchers used a 5-point scale called **Investigator's Global Assessment** (**IGA**). It measures the severity of psoriasis lesions and the participants' response to the treatment. A participant was considered a **0 or 1 responder** if they had clear or almost clear skin after treatment.*

The other questions researchers wanted to answer in this trial were:

- What was participants' experience with the use of the secukinumab auto-injector?
- Did participants' quality of life change after treatment with secukinumab auto-injector as compared to placebo?

Who was in this trial?

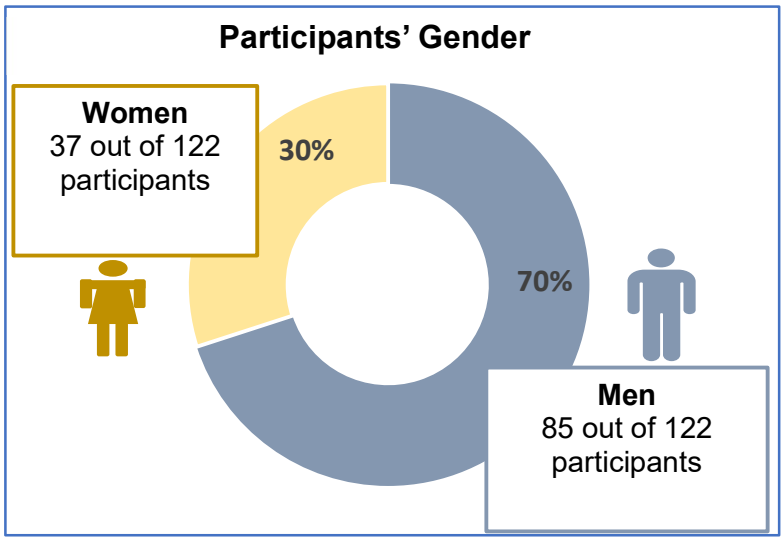
The participants could take part in this trial if they:

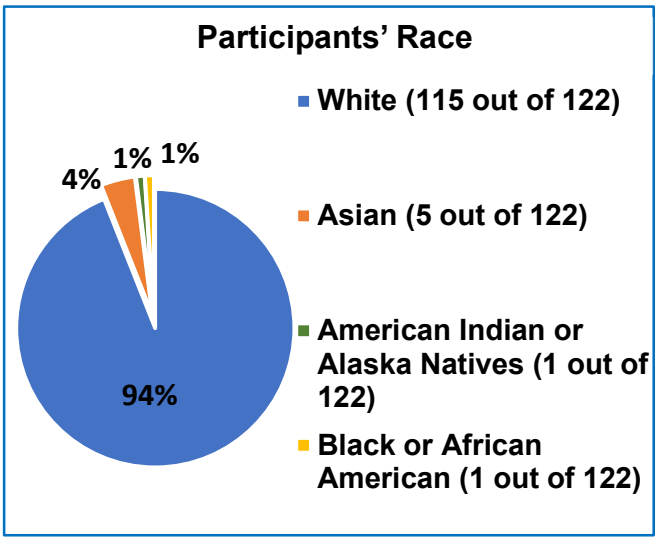
- were 18 years or older in age,
- had moderate to severe plaque psoriasis lasting for at least 6 months before starting trial treatment, and
- had plaque psoriasis that could not be successfully treated with medicines that were applied on the skin, light therapy, or other psoriasis medications taken by mouth.

A total of 122 participants from 6 countries participated in this trial.

Country	Number of Participants
United States	38
Iceland	22
Poland	17
Germany	17
Canada	15
Spain	13

The average age of participants was 44 years. Participants' age ranged from 18 to 72 years. The majority of participants were men and 94% (115 out of 122) participants were White.





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 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.

At each visit during this trial, the participants gave themselves 3 injections – 1 injection using the 2-mL auto-injector and 2 injections using the 1-mL pre-filled syringe, containing either secukinumab or placebo. This was to ensure that no one knew who received which treatment.

What happened during this trial?

Treatment Period 1

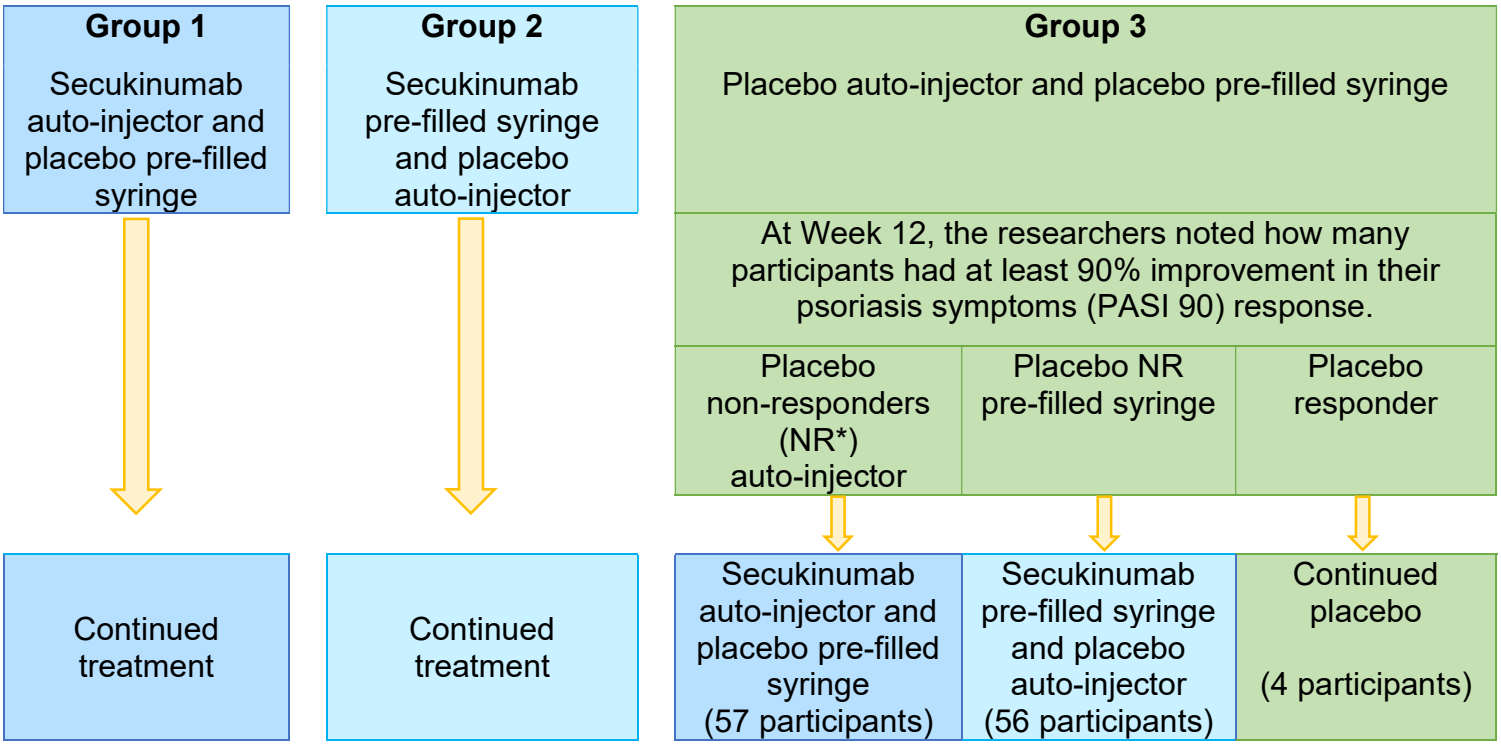
During Treatment Period 1, 122 participants were randomly assigned to 1 of 3 treatment groups.

Group 1	Group 2	Group 3
Secukinumab in 1 x 2 mL auto-injector and Placebo in 2 x 1 mL pre-filled syringe (41 participants)	Secukinumab in 2 x 1 mL pre-filled syringe and Placebo in 1 x 2 mL auto-injector (41 participants)	Placebo in 1 x 2 mL auto-injector and Placebo in 2 x 1 mL pre-filled syringe (40 participants)

All participants visited the trial site and gave themselves 3 injections at the start of the treatment period and at Weeks 1, 2, 3, 4, and 8.

Treatment Period 2

At Week 12, participants who were on placebo and showed at least a 90% improvement in their psoriasis symptoms (PASI 90) continued on placebo. If not, they were switched to one of the secukinumab treatment groups.



Non-responders are participants who did not have 90% improvement in their skin after treatment.

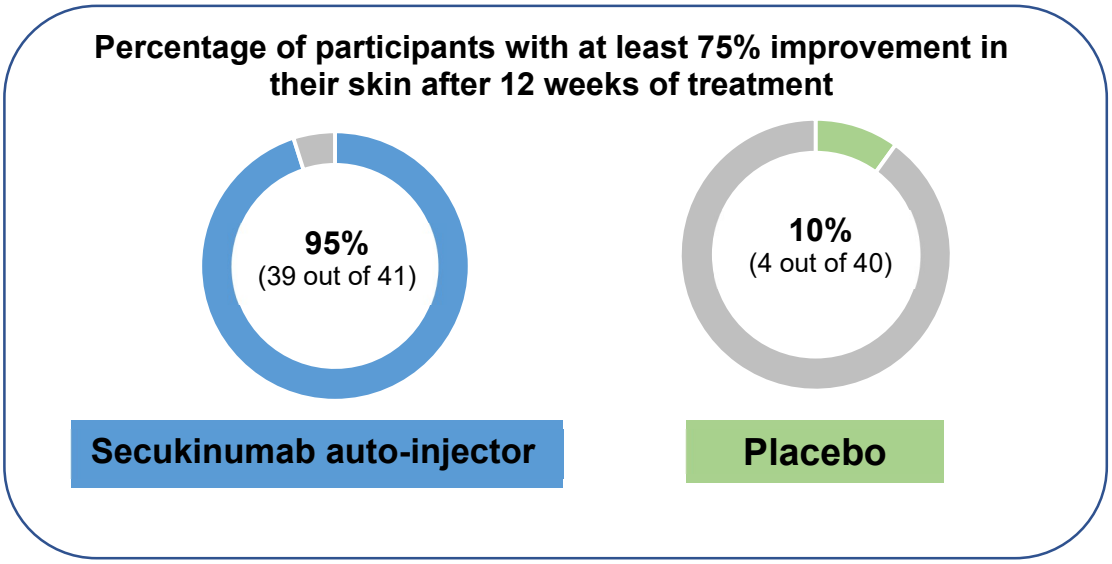
4 participants responded to placebo treatment and therefore continued to receive placebo until the end of the study. All other placebo participants switched to secukinumab at Week 12 and continued secukinumab treatment until the end of the study.

The researchers continued to measure the extent and severity of the participants' psoriasis symptoms using standard measurement scales and participants' health throughout the trial.

What were the key results of this trial?

How many participants who took secukinumab using an auto-injector had at least 75% improvement in their skin compared with placebo after 12 weeks of treatment?

After 12 weeks of treatment, more participants who took secukinumab using an auto-injector had improvement in their skin compared to participants who took placebo.

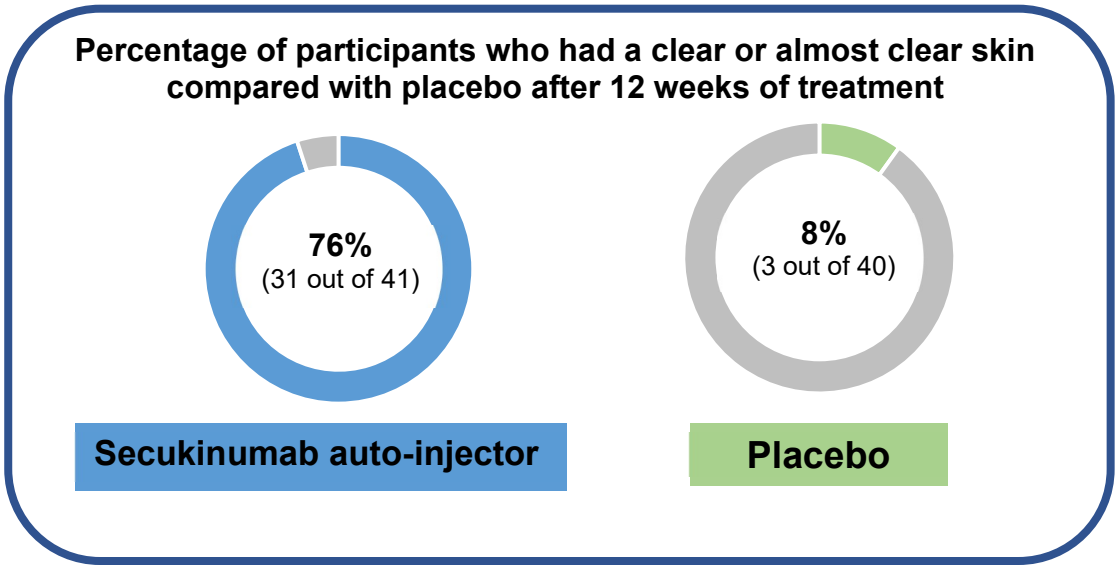


How was this measured?

To answer this question, researchers used a scale called the **Psoriasis Area Severity Index score**, or **PASI score**. It measures the severity of redness, scaling and thickness of the psoriasis plaques, and how much of the body area is affected. A participant was considered a PASI 75 responder if a reduction of 75% or more occurred in their PASI score after 12 weeks of treatment compared to the start of the trial.

How many participants who took secukinumab using an auto-injector had a clear or almost clear skin compared with placebo after 12 weeks of treatment?

After 12 weeks of treatment, more participants who took the secukinumab using an auto-injector had clear or almost clear skin compared to participants who took the placebo.



How was this measured?

To answer this question, researchers used a 5-point scale called **Investigator's Global Assessment** (**IGA**). It measures the severity of psoriasis lesions and the participants response to the treatment.

A participant was considered a 0 or 1 responder if there was clear or almost clear skin after 12 weeks of treatment compared to the start of the trial.

What were the other results of this trial?

What was participants' experience with the use of the secukinumab auto-injector?

To answer this question, researchers used a questionnaire called the **self-Injection assessment questionnaire** (**SIAQ**). The SIAQ measures the overall participant experience with the use of an auto-injector.

The SIAQ results showed the participants were able to follow instructions for use and felt comfortable using the auto-injector.

Did participants' quality of life change after treatment with secukinumab auto-injector as compared to placebo?

To answer this question, researchers used a questionnaire called **Dermatology Life Quality Index** (**DLQI**) **questionnaire**, which measures the impact of skin disease on the participants' quality of life. A participant was considered a 0 or 1 responder if the disease did not affect his/her quality of life.

After 12 weeks of treatment, more participants (71%) who took secukinumab using the auto-injector reported that their psoriasis did not affect their quality of life as compared to participants who took placebo (8%). From Week 12 onwards, this improvement in participants' quality of life remained the same until the end of the trial (Week 52).

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.

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?

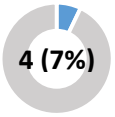
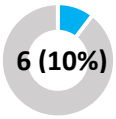
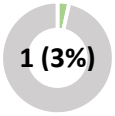
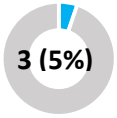
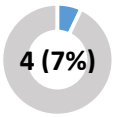
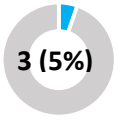
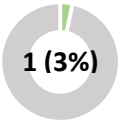
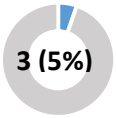
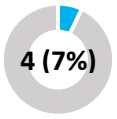
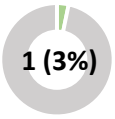
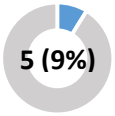
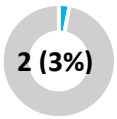
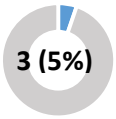
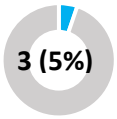
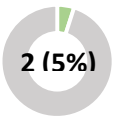
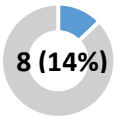
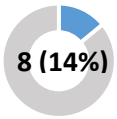
The table below presents the number of participants who had 1 or more adverse events during the entire treatment period (Treatment Period 1 and 2, combined). Adverse events in the placebo arm are expected to be lower since most of the participants were on placebo only for 12 weeks.

	Secukinumab auto-injector (includes placebo NR*)	Secukinumab pre-filled syringe (includes placebo NR*)	Placebo
Total Number of participants	**57**	**58**	**40**
At least 1 adverse event	36 (63%)	43 (74%)	14 (35%)
At least 1 serious adverse event	1 (2%)	4 (7%)	0 (0%)
Stopped drug due to adverse event	0 (0%)	2 (3%)	0 (0%)
Death	0 (0%)	0 (0%)	0 (0%)

**NR: Non-Responders were participants from the placebo group who did not have at least 90% improvement in their skin after 12 weeks of treatment.*

What were the most common non-serious adverse events?

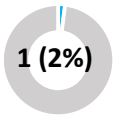
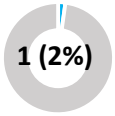
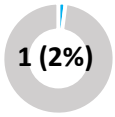
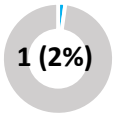
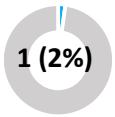
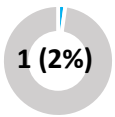
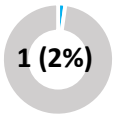
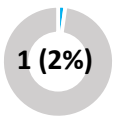
The most common non-serious adverse events that happened in at least 5 out of 100 (5%) of participants in any group are presented below:

Non-Serious Adverse Events	Secukinumab auto-injector (includes placebo *NR)(57 participants)	Secukinumab pre-filled syringe (includes placebo *NR) (58 participants)	Placebo (40 participants)
Common cold (Upper respiratory tract infection)	 4 (7%)	 6 (10%)	 1 (3%)
Feeling sick to the stomach (Nausea)	0 (0%)	 3 (5%)	0 (0%)
Flu (Influenza like illness)	 4 (7%)	 3 (5%)	 1 (3%)
Headache	 3 (5%)	 4 (7%)	 1 (3%)
High blood pressure (Hypertension)	 5 (9%)	 2 (3%)	0 (0%)
Itching (Pruritis)	 3 (5%)	 3 (5%)	 2 (5%)
Nose and throat infection (Nasopharyngitis)	 8 (14%)	 8 (14%)	0 (0%)

**NR: Non-Responders were participants from the placebo groups who did not have 90% improvement in their skin after 12 weeks of treatment.*

What were the serious adverse events?

The serious adverse events that happened in any group are presented below:

Non-Serious Adverse Events	Secukinumab auto-injector (includes placebo *NR) (57 participants)	Secukinumab pre-filled syringe (includes placebo *NR) (58 participants)	Placebo (40 participants)
COVID-19	**0 (0%)**	 **1 (2%)**	**0 (0%)**
Brain injury (Concussion)	**0 (0%)**	 **1 (2%)**	**0 (0%)**
Infection caused due to the use of device (Device related infection)	 **1 (2%)**	**0 (0%)**	**0 (0%)**
Fainting (Syncope)	**0 (0%)**	 **1 (2%)**	**0 (0%)**
Head injury	**0 (0%)**	 **1 (2%)**	**0 (0%)**
Asthma	**0 (0%)**	 **1 (2%)**	**0 (0%)**
Inflammation of the appendix (Appendicitis)	**0 (0%)**	 **1 (2%)**	**0 (0%)**
Road traffic accident	**0 (0%)**	 **1 (2%)**	**0 (0%)**

**NR: Non-Responders were participants from the placebo groups who did not have 90% improvement in their skin after 12 weeks of treatment.*

How many participants stopped trial drug due to adverse events?

During the trial, 2 out of 58 participants (3%) in **Secukinumab pre-filled syringe** (including placebo non-responders) group stopped the trial drug early due to adverse events of **platelet count decreased** (thrombocytopenia) and **COVID-19 infection**.

How was this trial useful?

This trial helped researchers find out the effects and safety of the secukinumab 300 mg auto-injector in participants with moderate to severe plaque psoriasis.

Researchers found that more participants who took secukinumab using an auto-injector showed improvement in their skin compared to participants who took placebo. More participants who took secukinumab using auto-injector reported that their psoriasis had no effect at all on their quality of life as compared to participants who took placebo.

Researchers found that participants were able to follow instructions for use of auto-injector and felt comfortable using the auto-injector.

Researchers also found that the adverse events that happened during this trial were common in people with moderate to severe plaque psoriasis. No new adverse events related to the use of auto-injector was identified during this trial.

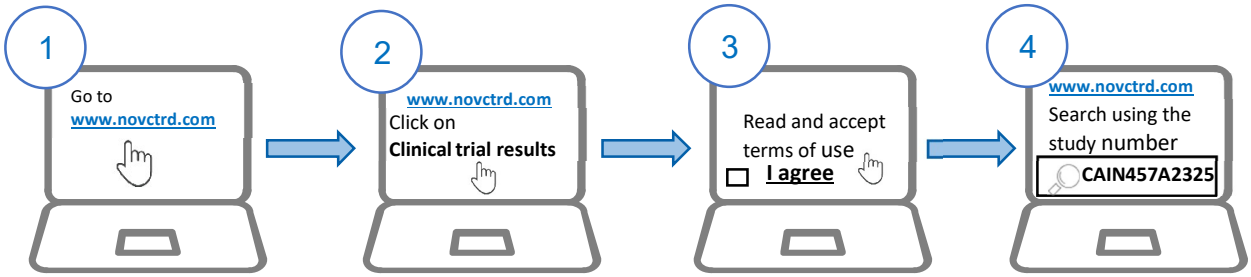
Results from this trial may be used in other clinical trials for people with plaque psoriasis.

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 websites:

- www.clinicaltrials.gov Use the NCT identifier NCT03589885 in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search/search Use the EudraCT identifier 2018-000518-39 in the search field.

Full clinical trial title:

Multicenter, randomized, double-blind, placebo-controlled, 52-week study to demonstrate the efficacy, safety and tolerability of subcutaneous secukinumab injections with
2 mL auto-injectors (300 mg) in adult subjects with moderate to severe plaque psoriasis – MATURE

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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