NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of secukinumab in participants weighing at least 90 kg/198 lbs with moderate to severe plaque psoriasis

Protocol number: CAIN457A2324

Thank You!

Thank you for taking part in this trial for the drug AIN457, also known as secukinumab, and helping researchers learn more about how it works in people with psoriasis. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. As a participant, you belong to this large community and your valuable contributions are greatly appreciated.

Novartis sponsored this trial and believes it is important to share the results with the participants.

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 and 3 months. The trial started in June 2018 and ended in July 2020. The entire duration, from enrolling the first participant to the last participant completing the trial, was about 2 years and 1 month.

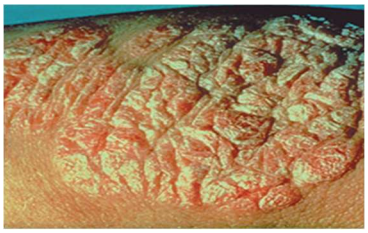
The researchers completed this trial as planned. When the trial ended, the researchers collected information on the trial treatments, secukinumab and placebo, and created a report of the trial results. This summary is based on that report.

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.

The most common symptoms of psoriasis include:

- Thickened, cracked, and scaly skin
- Skin rashes and dryness
- Inflammation and redness
- Itching or burning in affected areas



Source: National Psoriasis Foundation (psoriasis.org)

Current available treatments for psoriasis include medicines that are taken by mouth, creams and ointments that can be applied to the affected areas, and light therapy. However, these treatment options are not able to cure this skin condition completely. They usually just control the symptoms.

Secukinumab (pronounced as se-cu-KIN-umab) is the drug studied in this trial and is 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-17 A) is a protein, present in high levels in psoriasis patients, causing inflammation (swelling, redness, pain) and itch. Secukinumab binds to IL-17A and reduces its activity, thereby reducing swelling, redness, pain, and itch.

In this trial, researchers wanted to find out if taking secukinumab 300 mg every 2 weeks works better than the current recommended dose of secukinumab 300 mg every 4 weeks and is safe in psoriasis patients with higher body weight.

Trial drugs

The drugs given in this trial were:

Secukinumab

Secukinumab 1-mL pre-filled syringe is already available in the market for use. A pre-filled syringe is a disposable syringe that is supplied already loaded with the drug to be injected.

Placebo

It looks like the trial drug but has no medicine in it. It helps researchers better understand the effect of a trial drug by making sure that the changes were not happening by chance.

Throughout the trial, researchers advised participants to limit their exposure to ultraviolet (UV) light such as sunlight, to avoid any possible effect on their psoriatic plaques.

Trial purpose

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

After 16 weeks of treatment, how many participants had at least 90% improvement in their skin when they took secukinumab every 2 weeks compared to every 4 weeks?

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

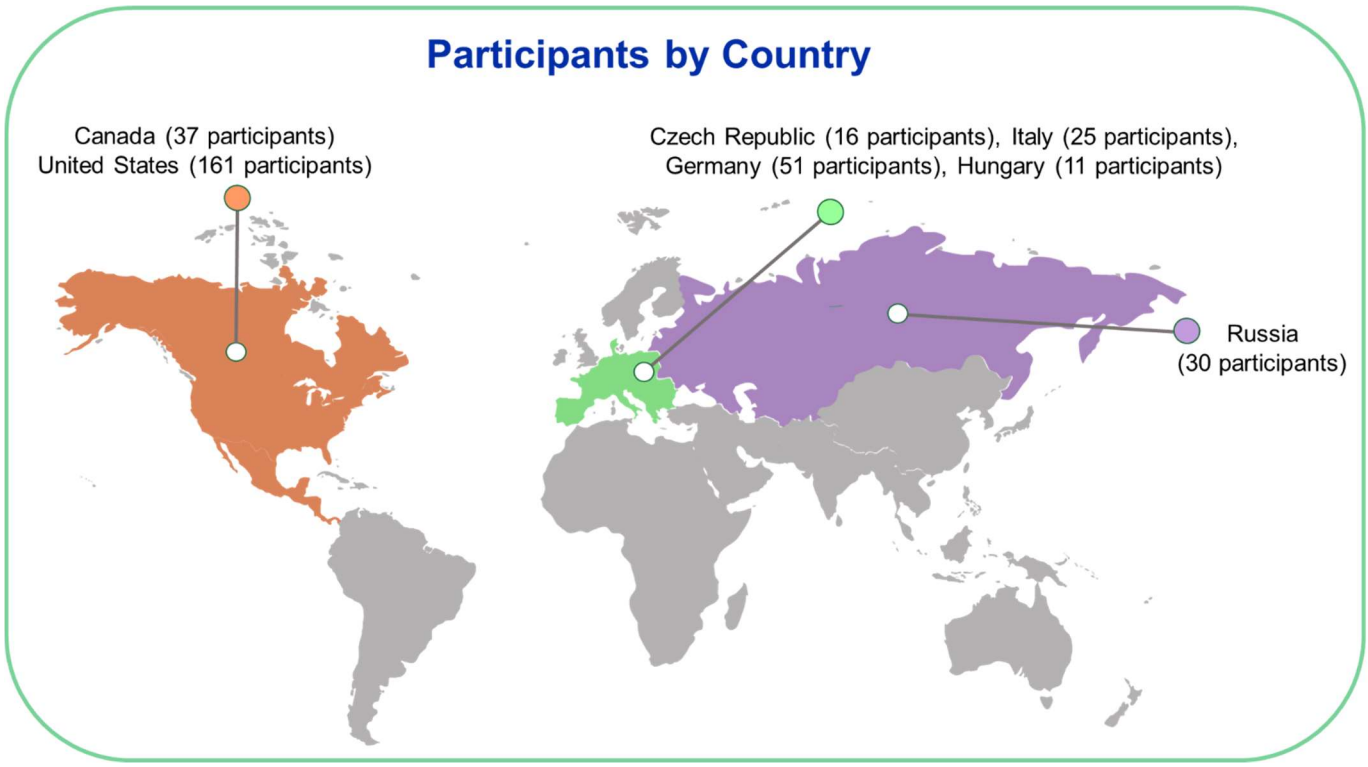
- After 16 weeks of treatment, how many participants had clear or almost clear skin when they took secukinumab every 2 weeks compared to every 4 weeks?

Who was in this trial?

The participants could take part in this trial if they:

- were at least 18 years of age,
- weighed at least 90 kg/198 lbs,
- had psoriasis lasting for at least 6 months before starting trial treatment,
- had moderate to severe psoriasis,
- had psoriasis that could not be effectively treated with creams and ointments, light therapy, or medicines that are taken by mouth.

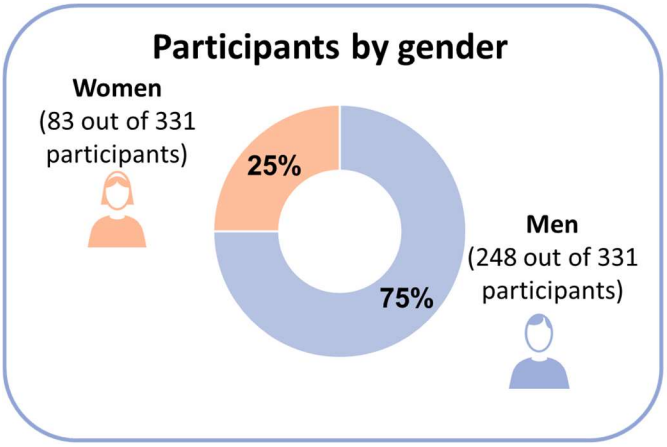
A total of 331 participants from 7 countries participated in this trial. The number of participants from each country is listed in the figure below.

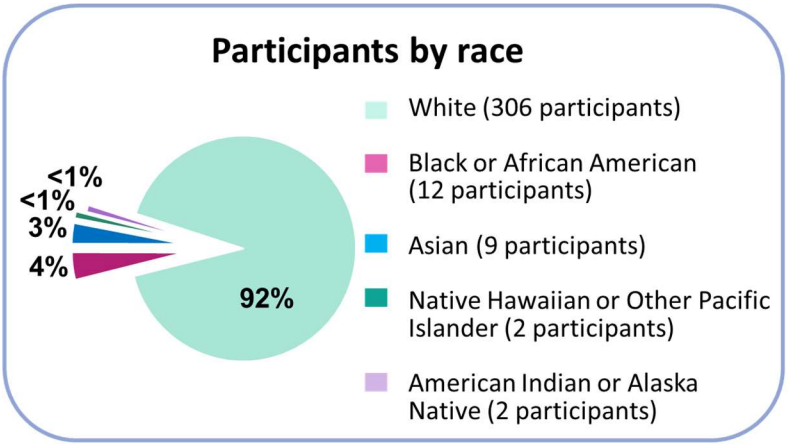


The average age of participants was 47 years. Participants' age ranged from 18 to 83 years. The majority of participants 75% (248 out of 331) were men and 92% (306 out of 331) were white. The average body weight of participants was 111 kg/245 lbs. Participants' weight ranged from 90 to 171 kg/198 to 377 lbs.

What kind of trial was this?

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

The trial had 2 parts:

Treatment Period 1 (Week 1 to Week 16).

At the start of the trial, researchers randomly assigned (like tossing a coin) participants into 1 of 2 treatment groups in a ratio of 1:1:

- Secukinumab 300 mg every 2 weeks:
  Participants received 2 injections of secukinumab 150 mg under the skin, once weekly for 4 weeks and thereafter every 2 weeks until Week 16.
- Secukinumab 300 mg every 4 weeks:

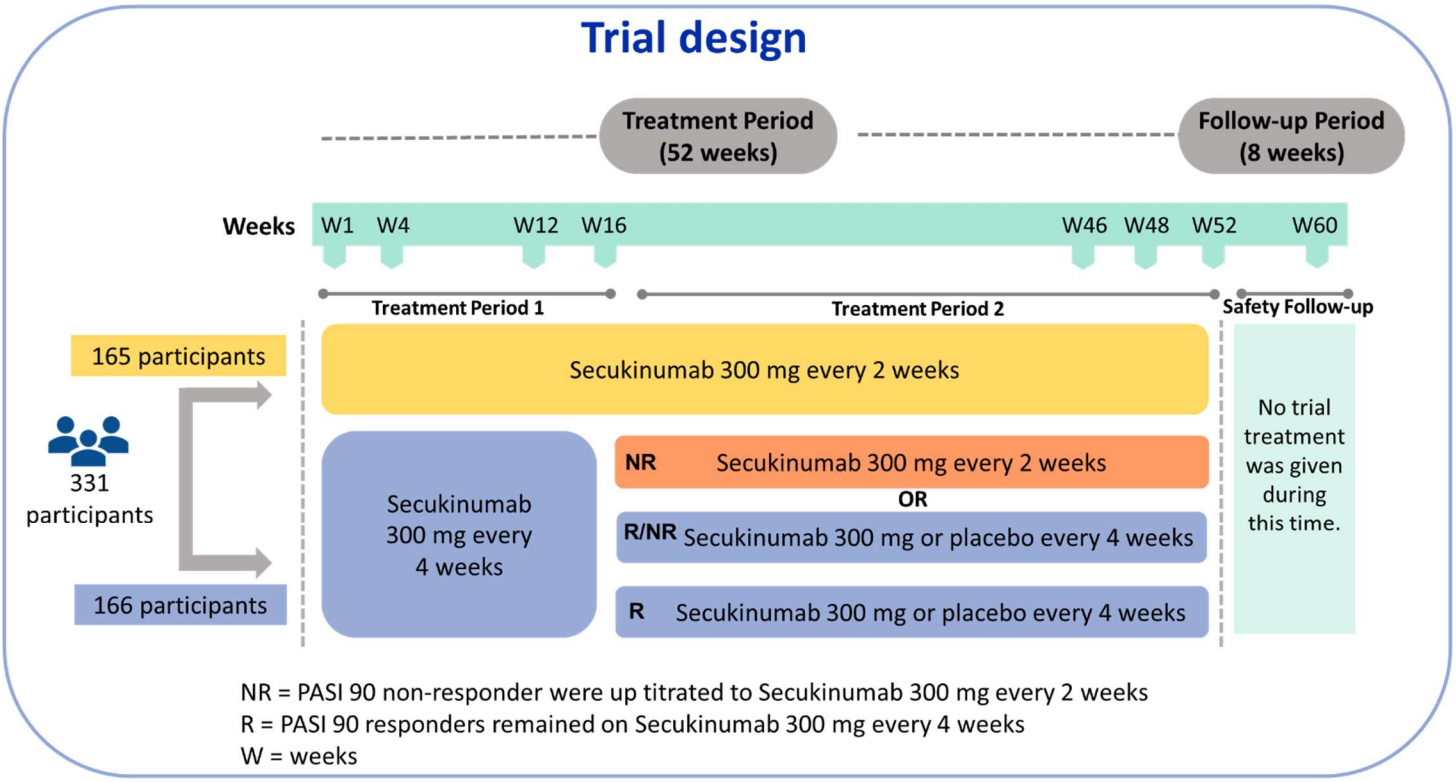
Participants received 2 injections of secukinumab 150 mg under the skin, once weekly for 4 weeks and thereafter alternating doses of secukinumab and placebo every 2 weeks until Week 16. This was to ensure they did not know which treatment they were receiving.

Participants' psoriasis symptoms were measured using a standard scoring system called the **Psoriasis Area and Severity Index** (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 to be a Responder (R) if they had a reduction of 90% or more in their PASI score (PASI 90) compared to the start of the trial. A participant was considered to be a Non-Responder (NR) if they did not have a reduction of 90% or more in their PASI score compared to the start of the trial.

Treatment Period 2 (Week 16 to Week 52).

At Week 16, approximately half of the Non-Responders (NR) in the secukinumab every 4 weeks group were randomly assigned to change to the secukinumab every 2 weeks and the other half remained on secukinumab every 4 weeks. Those Responders (R) in the secukinumab every 2 weeks group remained on secukinumab every 4 weeks until Week 52.

Safety follow-up period - participants' health was monitored, but they were not given any trial drug. All participants attended an end of treatment visit to the trial site at Week 52. Participants' health was monitored throughout the trial.



What were the key results of this trial?

This section is a summary of the average results for all participants in the 2 treatment groups up to Week 16 or Treatment period 1. 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.

After 16 weeks of treatment, how many participants had at least 90% improvement in their skin when they took secukinumab every 2 weeks compared to every 4 weeks?

More participants in the secukinumab every 2 weeks group had improvement in their skin compared to participants in the secukinumab every 4 weeks group.

How were these results measured?

Researchers used the PASI scoring system to measure the improvement in participants' skin.

What were the other results of this trial?

After 16 weeks of treatment, how many participants had clear or almost clear skin when they took secukinumab every 2 weeks compared to every 4 weeks?

To answer this question, the researchers rated the participants' overall psoriatic symptoms using Investigator Global Assessment, or IGA. IGA measures psoriasis symptoms on a scale of 0 to 4, where 0 is no sign of psoriasis (clear skin) and 1 is no thickening and very little scaling (almost clear skin).

After 16 weeks of treatment, 74% (122 out of 165) of participants in the secukinumab every 2 weeks group had clear or almost clear skin compared to 66% (109 out of 166) of participants in the secukinumab every 4 weeks group. However, the difference was not large enough to confirm that taking secukinumab every 2 weeks was better than every 4 weeks at improving the signs of psoriasis on participants' skin.

What medical problems did the participants have during the entire trial, up to Week 60?

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 the entire trial, up to Week 60. This includes Non-Responders (31 participants) who started on secukinumab every 4 weeks and changed to secukinumab every 2 weeks at Week 16.

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.

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

How many participants had adverse events?

The participants were assigned to 2 different groups: secukinumab every 2 weeks and secukinumab every 4 weeks until Week 16. At Week 16, approximately half of the Non-Responders (NR) in the secukinumab every 4 weeks group were randomly assigned to change to secukinumab every 2 weeks and the other half remained on secukinumab every 4 weeks. Responders (R) in the secukinumab every 2 weeks group remained on secukinumab every 4 weeks until Week 52.

248 out of 330 participants (75%) had 1 or more adverse events. During the trial, 15 out of 330 participants (5%) stopped the trial treatment because of adverse events. Serious adverse events happened in 36 out of 330 participants (11%) in the trial. One participant died during this trial due to a heart attack (acute myocardial infarction) but this was not related to the trial treatment.

The safety analysis excluded one participant who quit the trial before receiving any trial treatment.

Number of Participants (%) With Adverse Events			
	Secukinumab every 2 weeks (Out of 165 participants)	**Secukinumab every 4 weeks (Out of 134 participants)**	**Secukinumab every 4 weeks / Secukinumab every 2 weeks NR* (Out of 31 participants)**
At least 1 adverse event	127 (77%)	97 (72%)	24 (77%)
At least 1 serious adverse event	14 (9%)	17 (13%)	4 (13%)
Stopped trial treatment due to adverse events	4 (2%)	9 (7%)	2 (6%)
Death	0	1 (1%)	0

** Non-Responders (NR) in the secukinumab every 4 weeks group who were randomly assigned to change to secukinumab every 2 weeks at Week 16.*

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 in any group are presented below.

Number (%) of participants with most common non-serious adverse events

	Secukinumab every 2 weeks (N=165)	Secukinumab every 4 weeks (N=134)	Secukinumab every 4 weeks / Secukinumab every 2 weeks NR* (N=31)
Back pain	3 (2%)	6 (4%)	2 (6%)
Common cold (Upper respiratory tract infection)	12 (7%)	9 (7%)	3 (10%)
Cough	7 (4%)	2 (1%)	2 (6%)
Decrease in neutrophil count (Neutrophil count decreased)	1 (1%)	3 (2%)	3 (10%)
Diabetes (Diabetes mellitus)	3 (2%)	0 (0%)	2 (6%)
Diarrhea	10 (6%)	6 (4%)	2 (6%)
Feeling like you want to be sick (Nausea)	1 (1%)	4 (3%)	2 (6%)
Feeling tired (Fatigue)	4 (2%)	3 (2%)	2 (6%)
Fever (Pyrexia)	2 (1%)	2 (1%)	2 (6%)
Headache	11 (7%)	6 (4%)	1 (3%)
Infection in the urinary system (Urinary tract infection)	1 (1%)	5 (4%)	2 (6%)
Insect bite (Arthropod bite)	0 (0%)	1 (1%)	2 (6%)
Joint pain (Arthralgia)	7 (4%)	6 (4%)	2 (6%)
Nose and throat infection (Nasopharyngitis)	32 (19%)	22 (16%)	5 (16%)
Pus within a tooth cavity (Tooth abscess)	1 (1%)	0 (0%)	2 (6%)
Skin rash (Intertrigo)	4 (2%)	0 (0%)	3 (10%)
Throat pain (Oropharyngeal pain)	3 (2%)	7 (5%)	2 (6%)

** Non-Responders (NR) in the secukinumab every 4 weeks group who were randomly assigned to change to secukinumab every 2 weeks dose at Week 16.*

What were the most common serious adverse events?

The most common serious adverse events that happened in at least 1% (1 out of 100) of participants in any group are shown below.

Number (%) of participants with most common serious adverse events

	Secukinumab every 2 weeks (N=165)	Secukinumab every 4 weeks (N=134)	Secukinumab every 4 weeks / Secukinumab every 2 weeks NR* (N=31)
Body's extreme response to an infection (Sepsis)	0 (0%)	2 (1%)	0 (0%)
Chest pain not caused by heart disease (Non-cardiac chest pain)	2 (1%)	0 (0%)	0 (0%)
Fall (Fall)	1 (1%)	0 (0%)	1 (3%)
Irregular heartbeat (Atrial Fibrillation)	0 (0%)	1 (1%)	1 (3%)
Inflammation of the gall bladder (Cholecystitis chronic)	0 (0%)	0 (0%)	1 (3%)
Part of intestine bulging through the lower abdomen (Inguinal hernia)	0 (0%)	0 (0%)	1 (3%)
Lung infection (Pneumonia)	0 (0%)	0 (0%)	1 (3%)
Rapid heart rate (Tachycardia)	0 (0%)	1 (1%)	1 (3%)
Pus within a tooth cavity (Tooth abscess)	0 (0%)	0 (0%)	1 (3%)

** Non-Responders (NR) in the secukinumab every 4 weeks group who were randomly assigned to change to secukinumab every 2 weeks at Week 16.*

How many participants stopped trial drug due to adverse events?

During the trial, 5% (15 out of 330) of participants stopped secukinumab early due to adverse events. The most common adverse events that caused participants to stop the trial drug were increase of liver proteins* called gamma-glutamyltransferase in the blood (gamma-glutamyltransferase increased) and worsening of psoriasis (psoriasis).

*An increase in the level of gamma-glutamyltransferase in the blood may indicate that the liver may be inflamed or injured. Elevations are also seen after ingestion of alcoholic beverages.

How was this trial useful?

This trial was important, as the data has been submitted to the health authorities in the United States and Europe to support the use of flexible dosing of secukinumab in people who are at least 90 kg/198 lbs with psoriasis and who do not respond well when given the current approved dose. Also, the higher dose was included in this trial because previous trials have shown that secukinumab is cleared more quickly from the bodies of people with a higher body weight. Researchers also found that the adverse events that happened during this trial were similar to those found in previous trials with secukinumab in people with moderate to severe plaque psoriasis. Results from this trial may be used in other clinical trials for people with moderate to severe plaque psoriasis.

Please remember, this summary only shows the results of this 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 are available in the scientific summary of the results on the Novartis Clinical Trial Results website (www.novctrd.com). Use the study identifier CAIN457A2324 in the search field.

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

- www.clinicaltrials.gov In the search field, use the NCT identifier NCT03504852.
- https://www.clinicaltrialsregister.eu/ctr-search/search In the search field, use the EudraCT identifier 2015-004620-60.

Full clinical trial title:

A randomized, double blind, multicenter study assessing short (16 weeks) and long term efficacy (up to 1 year), safety, and tolerability of sub cutaneous secukinumab in subjects of body weight 90 kg or higher with moderate to severe chronic plaque type psoriasis.

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 a new dose for treating psoriasis patients.

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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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