AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: Tezepelumab

Study Title: This study was done to learn how tezepelumab works and about its safety in participants with severe asthma

Protocol Number: D5180C00007

Thank you!

Thank you for taking part in the clinical study for the study drug tezepelumab.

You and all of the participants helped researchers learn more about tezepelumab to help people with severe asthma.

Astra Zeneca AB sponsored this study and believes it is important to share the results of the study with you and the public. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you. We hope it helps you understand and feel proud of your important role in medical research.

If you participated in the study and have questions about the results, please speak with the study doctor or staff at your study site.

Overview of this study

Why was the research needed?

Researchers are looking for a better way to treat severe asthma. Before a treatment can be approved for people to get, researchers do clinical studies to find out how it works and how safe it is.

What treatments did the participants take?

The participants in this study got tezepelumab or a placebo in addition to their usual asthma treatment. A placebo looks like a treatment but does not have any medicine in it.

What were the results of this study?

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

> **Did tezepelumab affect the number of asthma attacks over 1 year?**

Yes. Overall, the participants who got tezepelumab had fewer asthma attacks during 1 year compared to the participants who got the placebo.

> **Did the participants feel that tezepelumab helped their quality of life or helped them control their asthma?**

Yes. Overall, the participants who got tezepelumab felt that study treatment helped their quality of life and their asthma more than those who got the placebo.

> **What medical problems happened during the study?**

There were 8.4% of participants who had medical problems that the study doctors thought might be related to either study drug during the study. This was 89 out of 1,059 participants.

More details about the results of this study are included later in this summary.

Where can I learn more about this study?

You can find more information about this study on the websites listed on the last page. When a full report of the study results is available, it also can be found on these websites.

Who took part in the study?

The researchers asked for the help of male and female adults and adolescents with severe asthma. The participants in this study were 12 to 80 years old when they joined.

Before the start of the study, the participants:

- had 2 or more asthma attacks during the last 12 months
- had been taking at least a steroid inhaler plus another treatment to control their asthma for 3 months or more

The study included 1,061 participants in 17 countries: Argentina, Australia, Austria, Brazil, Canada, France, Germany, Israel, Japan, South Korea, Russia, Saudi Arabia, South Africa, Taiwan, Ukraine, the United States, and Vietnam.

Why was the research needed?

Researchers are looking for a better way to treat severe asthma. Before a treatment can be approved for people to get, researchers do clinical studies to find out how it works and how safe it is.

In this study, the researchers wanted to find out if tezepelumab works in a large number of participants with severe asthma. They also wanted to find out if the participants had any medical problems during the study.

Asthma is a lung disease that causes the airways to narrow and causes inflammation in the lungs. This can make it difficult to breathe. People who have asthma may wheeze, cough, and have shortness of breath. Researchers can check the blood of people with asthma for a certain type of white blood cells that are a sign of inflammation in the lungs. These white blood cells are known as eosinophils.

In people with asthma, high levels of eosinophils in the blood mean they are more likely to have asthma attacks.

There are treatments that can help people who have asthma to manage their symptoms. Some people who have severe asthma need several different treatments to help control their asthma. But, these treatments may not help some people control their symptoms.

The study drug, tezepelumab, is being developed as a treatment for asthma to help reduce inflammation in the lungs. In this study, the researchers wanted to find out if tezepelumab reduced the number of asthma attacks that the participants had over 1 year.

What was the purpose of this study?

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

- Did tezepelumab affect the number of asthma attacks over 1 year?
- Did the participants feel that tezepelumab helped their quality of life or helped them control their asthma?
- What medical problems did the participants have during the study?

The answers to these questions are important to know before other studies can be done to find out if tezepelumab helps improve the health of people with severe asthma.

What treatments did the participants take?

In this study, the participants got either tezepelumab or a placebo. A placebo looks like a drug but does not have any medicine in it. Researchers use a placebo to help make sure any of the effects they see in the participants who take the drug are actually caused by the drug. The participants also continued to take their usual asthma treatments.

This was a "double-blind" study. This means none of the participants, researchers, study doctors, or other study staff knew what treatment each participant was getting. Some studies are done this way because knowing what treatment the participants are getting can affect the results of the study. When the study ended, the research sponsor found out which treatment the participants got so they could create a report of the study results.

A computer program was used to randomly choose the treatment each participant got. This helps make sure the groups are chosen fairly. Researchers do this so that comparing the results of each treatment is as accurate as possible.

The participants got tezepelumab or the placebo through a needle under the skin. This is also known as an injection. The dose of tezepelumab was measured in milligrams, also known as mg.

The chart below shows the treatments the researchers planned to study.

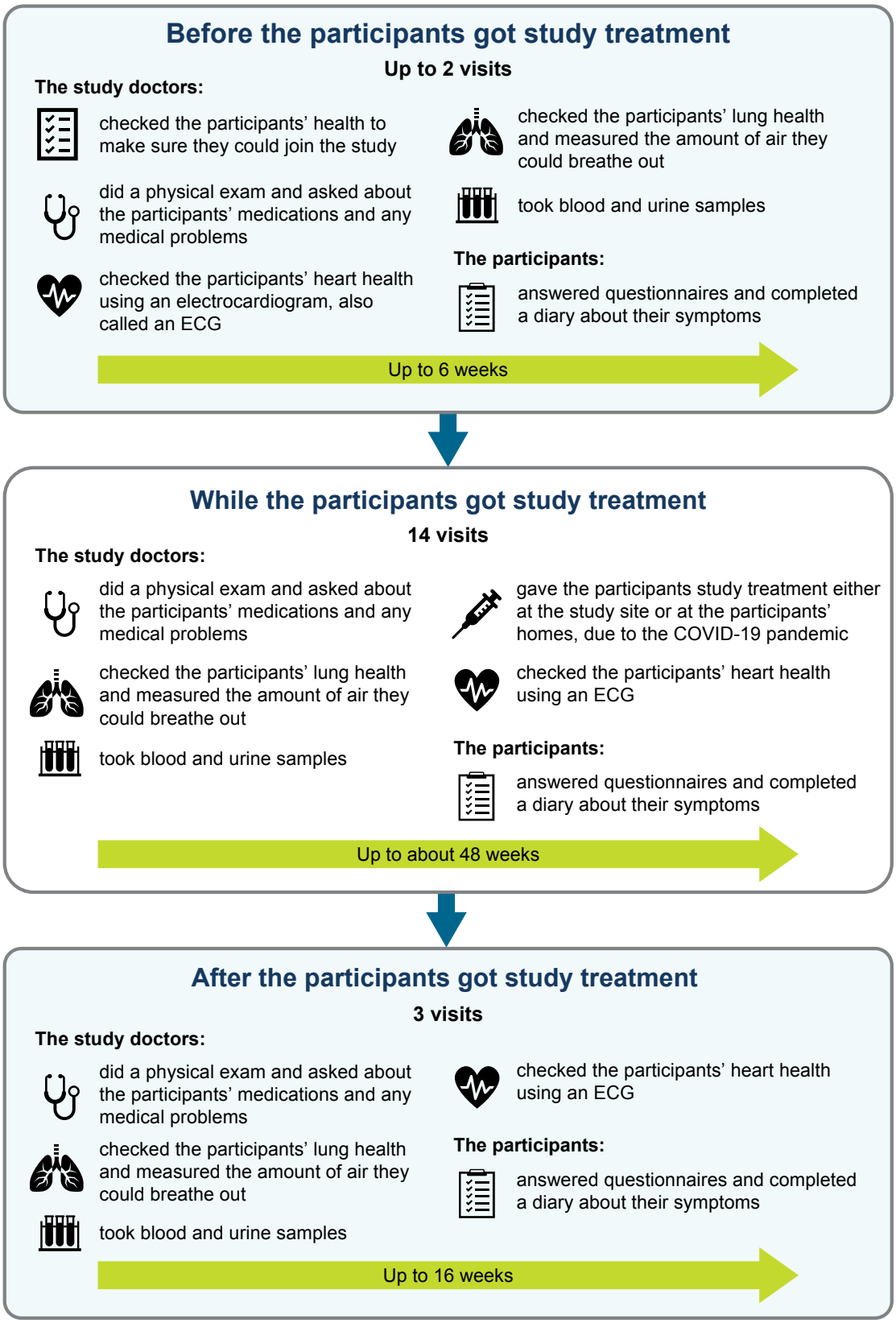
	Tezepelumab	Placebo
	529 participants	532 participants
	210 mg of tezepelumab through an injection under the skin	Placebo through an injection under the skin
	Once every 4 weeks for a total of 13 injections	

What happened during the study?

The participants were in the study for just over 17 months. But, the entire study took nearly 3 years to finish.

The study started in November 2017 and ended in September 2020.

The chart below shows what happened during the study. Due to the COVID-19 pandemic, some changes were made to the study as of March 2020.



What were the results of the study?

This is a summary of the main results from this study overall. The results each participant had might be different and are not in this summary. A full list of the questions researchers wanted to answer can be found on the websites listed at the end of this summary. When a full report of the study results is available, it can also be found on these websites.

Researchers look at the results of many studies to decide which treatments work best and are safest. Other studies may provide new information or different results. Always talk to a doctor before making any treatment changes.

There was 1 participant in the tezepelumab group and 1 participant in the placebo group who did not get any study treatment. So, the results in this summary are from the 1,059 participants who got study treatment.

Did tezepelumab affect the number of asthma attacks over 1 year?

Yes. Overall, the researchers found that tezepelumab reduced the participants' number of asthma attacks over 1 year.

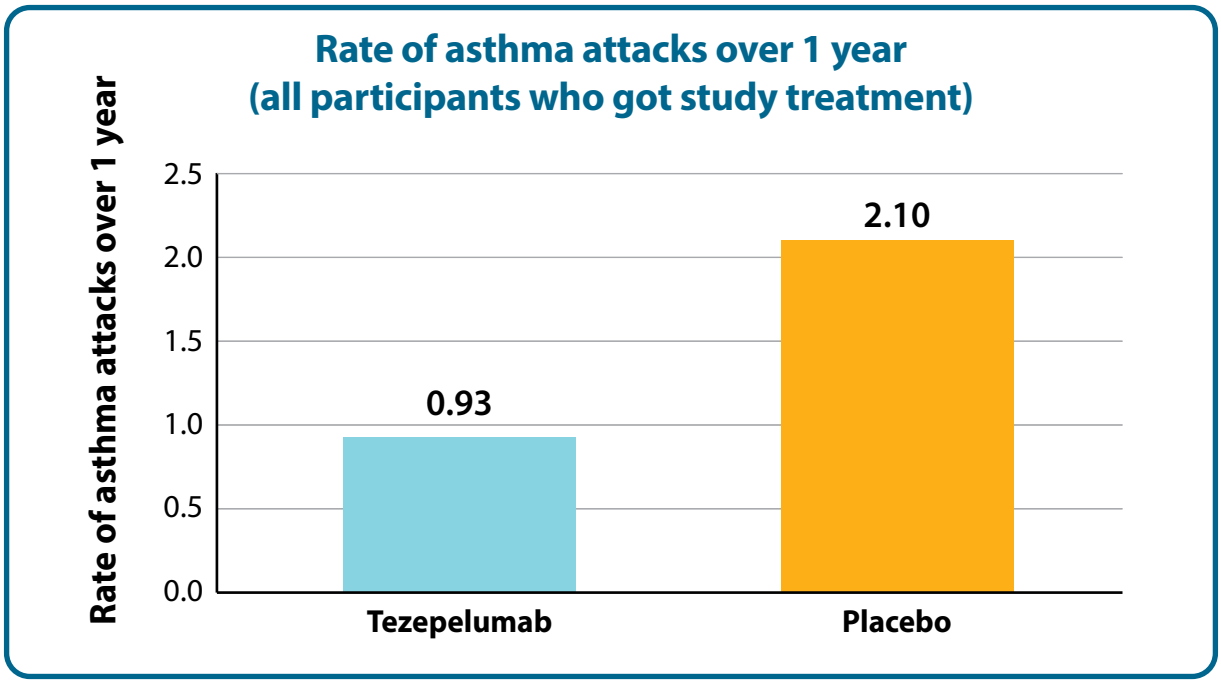
To answer this question, the researchers calculated the number of asthma attacks the participants had during the 1 year of study treatment. This is known as the "annual rate". Then, they compared the annual rate of asthma attacks between the participants who got tezepelumab with those who got the placebo.

The researchers found that the annual rate of asthma attacks was:

- 0.93 for the 528 participants who got tezepelumab
- 2.10 for the 531 participants who got the placebo

This was a reduction in annual rate of 56.0% for the participants who got tezepelumab compared to those who got the placebo.

The chart below shows these results.



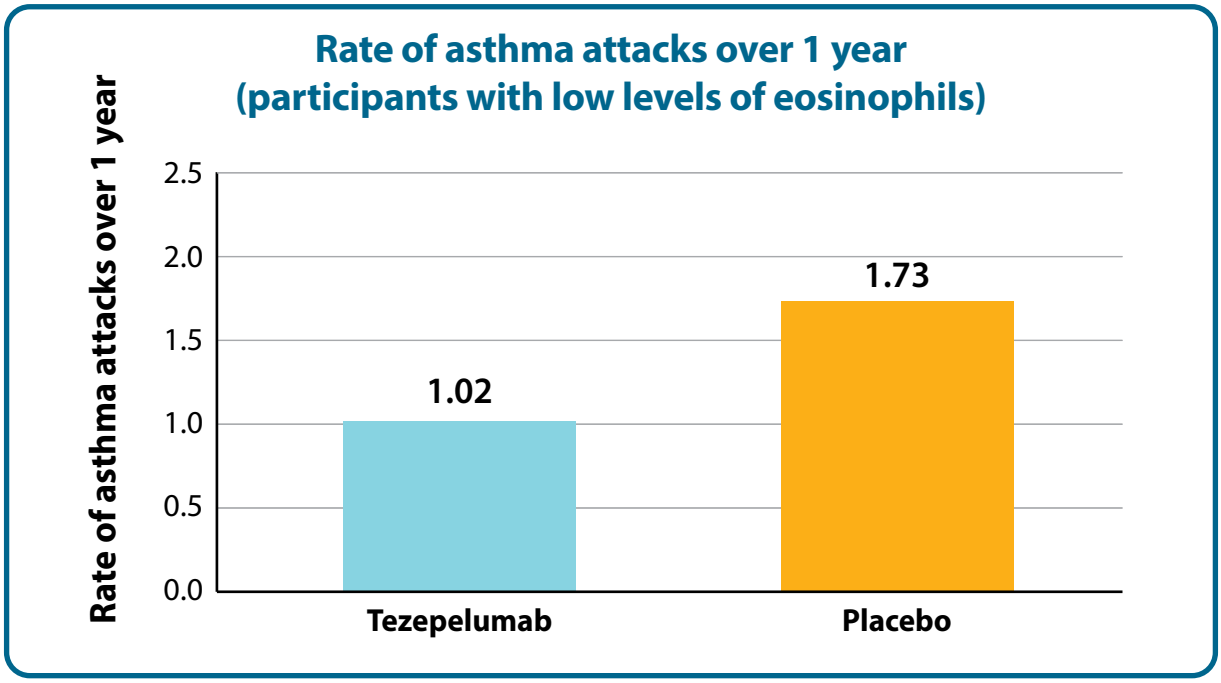
The researchers also calculated the annual rate of asthma attacks for the participants who had low levels of eosinophils in their blood.

The researchers found that the annual rate of asthma attacks was:

- 1.02 for the 309 participants who had low levels of eosinophils in their blood and got tezepelumab
- 1.73 for the 309 participants who had low levels of eosinophils in their blood and got the placebo

This was a reduction in annual rate of 41.0% for the participants who got tezepelumab compared to those who got the placebo.

The chart below shows these results.



Did the participants feel that tezepelumab helped their quality of life or helped them control their asthma?

Yes. Overall, the researchers found that the participants who got tezepelumab felt that study treatment helped their quality of life and their asthma more than those who got the placebo.

To answer this question, the study doctors asked the participants to answer some questionnaires about their quality of life and their asthma symptoms. The participants answered these questionnaires at the beginning of the study and after they got study treatment. These questionnaires were:

- Standardised Asthma Quality of Life Questionnaire for 12 Years and Older, also called AQLQ(S)+12
- Asthma Control Questionnaire-6, also called ACQ-6
- Asthma Symptom Diary, also called the ASD

AQLQ(S)+12

The participants gave responses to each question on the AQLQ(S)+12 on a scale from 1 to 7, which then gave a score. The researchers then calculated average AQLQ(S)+12 scores. A high average score meant that the participant's asthma was not affecting their quality of life. A low average score meant that asthma was severely affecting their quality of life.

The researchers compared the change in scores before and after 1 year of treatment. They compared the results for the participants who got tezepelumab to those for the participants who got the placebo. An increase in average AQLQ(S)+12 score meant that the participants felt that study treatment helped their quality of life.

Overall, the researchers found that the change in average AQLQ(S)+12 score was:

- an increase of 1.48 for the participants who got tezepelumab
- an increase of 1.14 for the participants who got the placebo

ACQ-6

The participants received scores from 0 to 6 on each question based on their responses to the ACQ-6. From the responses to the ACQ-6, the researchers calculated average ACQ-6 scores. A high average ACQ-6 score meant that the participant's asthma was not well controlled, and a low average ACQ-6 score meant that the participant's asthma was well controlled.

The researchers compared the average ACQ-6 scores before and after 1 year of treatment. They compared the results for the participants who got tezepelumab to those for the participants who got the placebo. A decrease in average ACQ-6 score meant that the participants felt that study treatment helped control their asthma.

Overall, the researchers found that the change in average ACQ-6 score was:

- a decrease of 1.53 for the participants who got tezepelumab
- a decrease of 1.20 for the participants who got the placebo

ASD

The participants completed the ASD twice a day. The ASD asks about 5 main asthma symptoms in the morning and 5 main asthma symptoms at night. The participants received scores from 0 to 4 for each main symptom based on their responses. A low score on the ASD meant that the participant's asthma symptoms were minor. A high score meant that the participant's asthma symptoms were severe.

The researchers calculated the average ASD scores before and after 1 year of treatment. They compared the results for the participants who got tezepelumab to those for the participants who got the placebo. A decrease in average ASD score meant that the participants felt that study treatment helped their asthma symptoms.

Overall, the researchers found that the change in average ASD score were:

- a decrease of 0.70 for the participants who got tezepelumab
- a decrease of 0.59 for the participants who got the placebo

What medical problems happened during this study?

This section is a summary of the medical problems the participants had during the study that the study doctors thought might be related to the study treatment. These medical problems are called "adverse reactions". An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or requires hospital care.

These adverse reactions may or may not be caused by the study treatment. A lot of research is needed to know whether a treatment causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for tezepelumab.

The websites listed at the end of this summary may have other information about adverse reactions or other medical problems that happened during this study.

Did any adverse reactions happen during this study?

Overall, there were 8.4% of participants who had medical problems that the study doctors thought might be related to either study drug during the study. This was 89 out of 1,059 participants. Some participants had more than 1 adverse reaction.

	Tezepelumab (out of 528 participants)	**Placebo** (out of 531 participants)
How many participants had adverse reactions?	8.7% (46)	8.1% (43)
How many participants had serious adverse reactions?	0.9% (5)	0.9% (5)
How many participants stopped getting study treatment due to adverse reactions?	0.9% (5)	1.5% (8)

None of the participants died due to serious adverse reactions.

What serious adverse reactions happened during this study?

The most common serious adverse reaction was asthma worsening leading to hospitalization.

The table below shows the serious adverse reactions that happened during this study. Some participants had more than 1 serious adverse reaction.

Serious adverse reactions

Serious adverse reaction	**Tezepelumab** (out of 528 participants)	**Placebo** (out of 531 participants)
Asthma worsening leading to hospitalization	0.4% (2)	0.0% (0)
Early stage of malignant melanoma (a type of skin cancer)	0.2% (1)	0.0% (0)
Infection of the nasal passages and the throat	0.2% (1)	0.0% (0)
Inflammation in the muscles	0.2% (1)	0.0% (0)
Migraine	0.2% (1)	0.0% (0)
Death of lung tissue caused by an infection	0.0% (0)	0.2% (1)
Death of muscle tissue	0.0% (0)	0.2% (1)
Increased levels of a protein in the blood called creatinine kinase	0.0% (0)	0.2% (1)
Multiple joints affected by joint pain	0.0% (0)	0.2% (1)
Seizure	0.0% (0)	0.2% (1)

What adverse reactions happened during this study?

The most common adverse reaction was redness at the site of the injection.

The table below shows the adverse reactions that happened in 0.5% or more of participants during the study. There were other adverse reactions but these happened in fewer participants.

Most common adverse reactions

Adverse reaction	**Tezepelumab** (out of 528 participants)	**Placebo** (out of 531 participants)
Injection site redness	1.5% (8)	1.9% (10)
Headache	1.5% (8)	0.9% (5)
Fatigue	0.9% (5)	0.8% (4)
Injection site pain	0.9% (5)	0.8% (4)
Injection site swelling	0.8% (4)	0.2% (1)
Pain in a joint	0.8% (4)	0.2% (1)
Lack of energy	0.6% (3)	0.4% (2)
Rash	0.0% (0)	0.6% (3)

How has this study helped patients and researchers?

This study helped researchers learn more about how tezepelumab works and about its safety in participants with severe asthma.

Researchers look at the results of many studies to decide which treatments work best and are safest. This summary shows only the main results from this 1 study. Other studies may provide new information or different results.

Further clinical studies with tezepelumab are planned.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. If more information about the study results is available, it can also be found here.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT03347279"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2017-003078-15"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5180C00007"** into the search box, and click **"Find a Study"**.

Full Study Title: A Multicentre, Randomised, Double-Blind, Placebo Controlled, Parallel Group, Phase 3 Study to Evaluate the Efficacy and Safety of Tezepelumab in Adults and Adolescents with Severe Uncontrolled Asthma (NAVIGATOR)

AstraZeneca Protocol number: D5180C00007

National Clinical Trials number: NCT03347279

EudraCT number: 2017-003078-15

AstraZeneca AB sponsored this study and has its headquarters at Södertälje, Sweden.

The phone number for the AstraZeneca Information Center is +1-877-240-9479.

Thank you!

Clinical study participants and their families belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP is not involved in recruiting participants for clinical studies, nor is it involved in conducting clinical studies.

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