AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: Tezepelumab

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

Protocol Number: D5180C00013

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.

AstraZeneca 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 drug 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 get?

The participants in this study got tezepelumab or a placebo. A placebo looks like a drug but does not have any medicine in it.

The participants in this study had been taking asthma treatments called inhaled corticosteroids before they joined the study. Inhaled corticosteroids are also known as "ICS".

What were the results of this study?

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

- **Did tezepelumab reduce the numbers of inflammatory cells in the participants' airways?**

  Overall, the researchers found that the number of 1 type of inflammatory cell called an eosinophil was much lower in the participants who got tezepelumab than in those who got the placebo. For all the other cell types, the researchers found that the changes in cell numbers were similar in both treatment groups. The results were too similar for the researchers to know if tezepelumab affected the numbers of these inflammation cells.

- **What medical problems did the participants have during this study?**

  There were 11.2% of participants who had medical problems that the study doctors thought might be related to the study drug during this study. This was 13 out of 116 participants. The most common medical problem was pain at the injection site.

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 this study?

The researchers asked for the help of men and women with moderate to severe asthma. The participants in this study were 18 to 74 years old when they joined.

Before the start of the study, the participants had taken a type of asthma treatment called inhaled corticosteroids for at least 12 months. Inhaled corticosteroids are also called "ICS". The participants had been on a steady dose of ICS for at least 3 months.

The study included 116 participants in Canada, Denmark, Germany, the United Kingdom, and the United States.

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 small 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 disease that causes the airways that carry air in and out of the lungs to become inflamed and narrow. This can make it difficult to breathe. People who have asthma may wheeze, cough, and have shortness of breath.

There are treatments that can help people with asthma to manage their symptoms. An example is ICS. Some people with severe asthma need many different treatments to help control their asthma.

The study drug, tezepelumab, was designed to help reduce inflammation in the airways in people with asthma. In this study, the researchers wanted to find out if tezepelumab could reduce the number of cells in the participants' airways that cause inflammation.

What was the purpose of this study?

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

- Did tezepelumab reduce the number of inflammatory cells in the participants' airways?
- 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 get?

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 get the study drug are actually caused by the study drug.

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, also known as an injection. The dose of tezepelumab was measured in milligrams, also known as mg.

The chart below shows the treatments the participants got.

	Tezepelumab	Placebo
	59 participants	57 participants
	Tezepelumab as an injection	Placebo as an injection
	Every 4 weeks for a total of up to 11 injections	

What happened during this study?

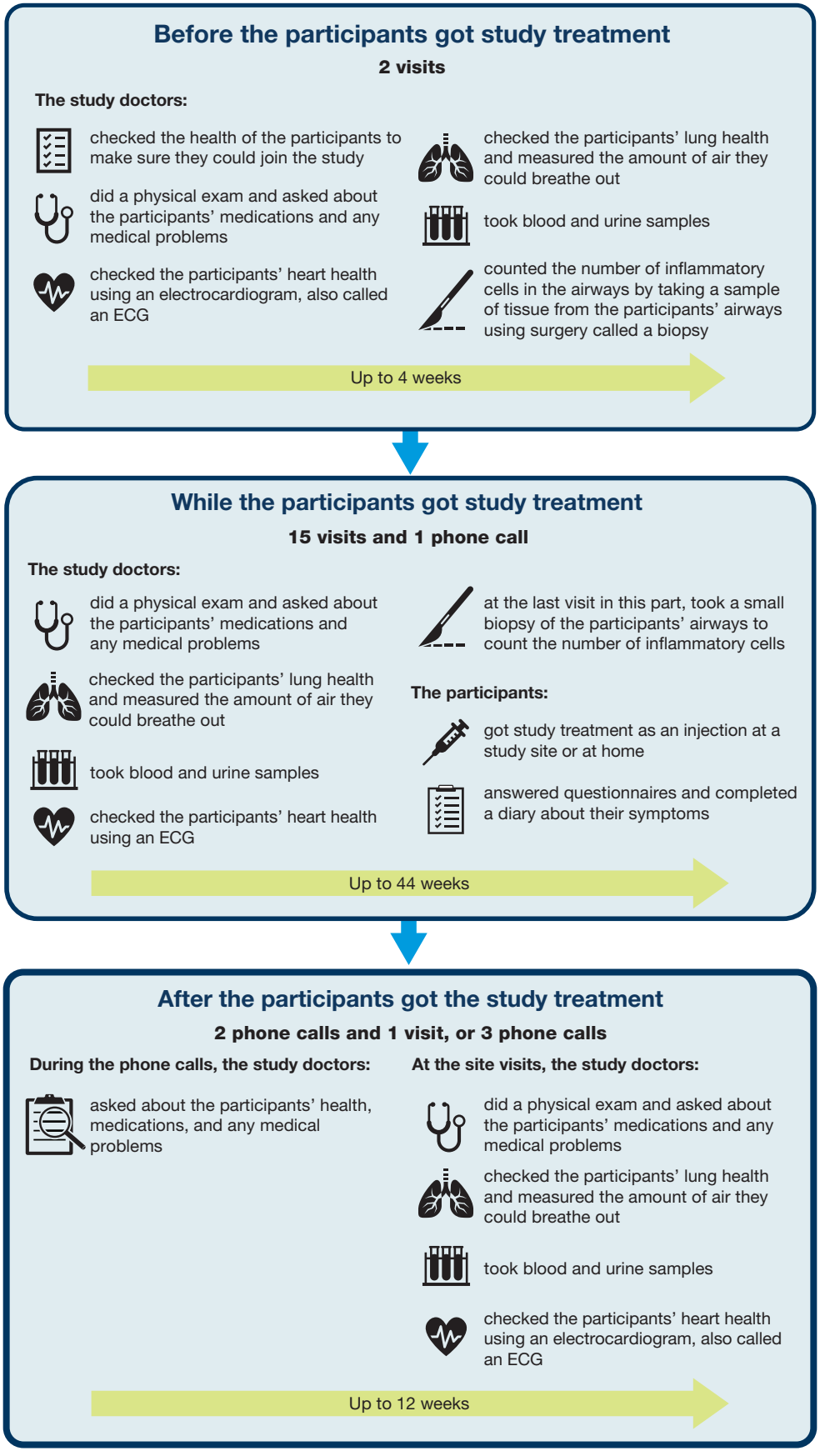
The researchers originally planned for the participants to be in the study for up to 44 weeks. But, because of delays due to the COVID-19 pandemic, the participants were in the study for up to 60 weeks. The entire study took 2 years to finish.

The study started in November 2018 and ended in November 2020.

The participants who were still in the study when the COVID-19 pandemic started:

- could get their injections done at home by a healthcare provider so they did not have to visit their study site
- got study treatment for 44 weeks instead of 28 weeks
- could have a phone call instead of visiting the study site for the final visit

The chart below shows what happened during the study.



What were the results of this 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 were 116 participants in this study. But, the results below are only for the 99 participants who got at least 20 weeks of study treatment, had biopsies of their airways before and after they took the study treatment and went to an end of treatment site visit within 8 weeks.

Did tezepelumab reduce the number of inflammatory cells in the participants' airways?

To answer this question, the study doctors used surgery to take samples of the tissue in the participants' airways. This is called a biopsy. The study doctors used a microscope to see the different types of inflammation cells in the biopsy samples. They then counted the number of cells per square millimeter. The researchers compared the number of cells per square millimeter at the start of the study and at the end of the study. Then, they calculated the average change in the number of cells in the participants.

The researchers compared the results between the participants who got tezepelumab and the participants who got the placebo. They measured this difference as a ratio. A ratio shows how similar 2 numbers are to each other. The closer the ratio is to 1.00, the more similar the numbers are.

The researchers looked at 6 types of inflammatory cells. All of these cells are part of the immune system that helps to protect the body from infections. The 6 types of cells that the researchers looked at are called:

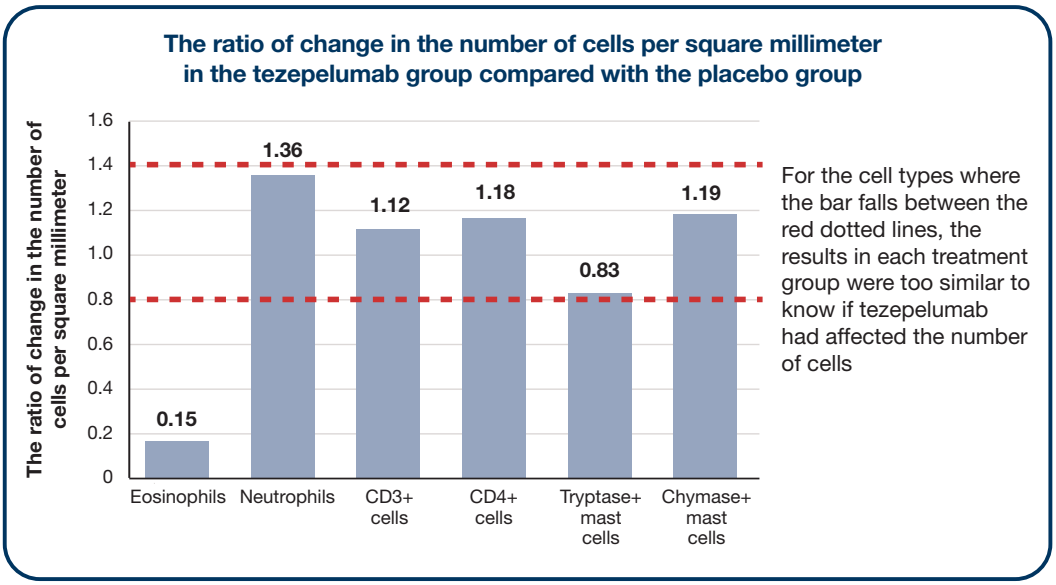
- eosinophils
- neutrophils
- CD3+ cells
- CD4+ cells
- tryptase+ mast cells
- chymase+ mast cells

Overall, the researchers found that the number of eosinophils per square millimeter decreased more in the participants who got tezepelumab than in those who got the placebo. For all the other cell types, the researchers found that the changes in cell numbers were similar in both treatment groups. The results were too similar for the researchers to know if tezepelumab affected the numbers of these inflammation cells.

The list below shows the results. A ratio lower than 1.00 means that the average number of cells decreased more or increased less in the participants who got tezepelumab. A ratio higher than 1.00 means that the average number of cells decreased less or increased more in the participants who got tezepelumab. The researchers found that the ratios of cells per square millimeter in the tezepelumab group compared to the placebo group were:

- 0.15 for eosinophils
- 1.36 for neutrophils
- 1.12 for CD3+ cells
- 1.18 for CD4+ cells
- 0.83 for tryptase+ mast cells
- 1.19 for chymase+ mast cells

These results are shown in the graph below.



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 treatments. 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 treatments. 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?

There were 15.3% of participants who got tezepelumab who had adverse reactions during this study. This was 9 out of 59 participants.

There were 7.0% of participants who got the placebo who had adverse reactions during this study. This was 4 out of 57 participants.

None of the participants had serious adverse reactions during this study. None of the participants stopped getting study treatment due to adverse reactions.

What serious adverse reactions happened during this study?

None of the participants had serious adverse reactions during this study.

What adverse reactions happened during this study?

There were 11.2% of participants who had adverse reactions during this study. This was 13 out of 116 participants.

The most common adverse reaction was a rash at the injection site.

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

Adverse reactions

Adverse reaction	Tezepelumab (out of 59 participants)	Placebo (out of 57 participants)
Rash at the injection site	8.5% (5)	3.5% (2)
Itching at the injection site	6.8% (4)	1.8% (1)
Inflammation at the injection site	3.4% (2)	0.0% (0)
Headache	1.7% (1)	3.5% (2)
Too much fat in the liver	1.7% (1)	0.0% (0)
Fungal skin infection	1.7% (1)	0.0% (0)
Suddenly developing hives	1.7% (1)	0.0% (0)
Pain at the injection site	1.7% (1)	0.0% (0)
Skin bump at the injection site	1.7% (1)	0.0% (0)
Swelling at the injection site	1.7% (1)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn more about tezepelumab 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 one 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. When a full report of the study results is available, it also can be found here.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT03688074"** into the search box and click **"Search"**.
- http://www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search",** then type **"2018-002069-21"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5180C00013"** into the search box, and click **"Find a Study"**.

Full Study Title: A Phase 2, Randomized, Double-blind, Parallel Group, Placebo Controlled Study to Evaluate the Effect of Tezepelumab on Airway Inflammation in Adults with Inadequately Controlled Asthma on Inhaled Corticosteroids and at Least one Additional Asthma Controller (CASCADE)

AstraZeneca Protocol Number: D5180C00013

National Clinical Trials Number: NCT03688074

EudraCT Number: 2018-002069-21

AstraZeneca sponsored this study and has its headquarters at Cambridge, UK.

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

Thank you!

Clinical study participants 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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Version 1.0 2021_10_29