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: D5180C00009

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 safe it is and how it works.

What treatments did the participants take?

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 oral corticosteroids before they joined the study. Oral corticosteroids are also known as "OCS".

What were the results of this study?

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

> **Did tezepelumab reduce the amount of OCS needed to control asthma symptoms?**

Overall, the researchers found that the percentage of participants who could reduce their OCS dose was similar in the tezepelumab group and in the placebo group. The difference between the groups was too small for the researchers to know if tezepelumab could reduce the amount of OCS needed to control asthma symptoms better than the placebo.

> **Did the participants feel that tezepelumab helped their quality of life or helped them to 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.

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

There were 4.7% of participants who had medical problems that the study doctors thought might be related to the study drug during the study. This was 7 out of 150 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 men and women with severe asthma. The participants in this study were 22 to 76 years old when they joined.

Before the start of the study, the participants:

- Had taken OCS during the last 6 months. They had to have been on a steady dose of OCS for 1 month or more.
- Had 1 or more asthma attacks during the last 12 months.
- Had been taking a high dose of steroid inhaler plus another treatment to control their asthma for 3 months or more.

The study included 150 participants in 7 countries: Argentina, Germany, South Korea, Poland, Turkey, Ukraine, and the United States.

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.

In this study, the researchers wanted to find out if tezepelumab works in participants with severe asthma who need OCS in addition to other treatments to control their 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.

There are treatments that can help people who have asthma to manage their symptoms. One example is oral corticosteroids, also known as "OCS". Some people who have severe asthma need several different treatments to help control their asthma.

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 could reduce the amount of OCS the participants needed to control asthma symptoms.

What was the purpose of this study?

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

- Did tezepelumab reduce the amount of OCS needed to control asthma symptoms?
- Did the participants feel that tezepelumab helped their quality of life or helped them to 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 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 treatment are actually caused by the treatment.

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
	74 participants	76 participants
	210 mg of tezepelumab through an injection under the skin	Placebo through an injection under the skin
	Every 4 weeks for a total of 12 injections	

What happened during the study?

The participants were in the study for up to 70 weeks. The entire study took just over 2.5 years to finish.

The study started in March 2018 and ended in September 2020.

The chart below shows what happened during the study.

Before the participants got study treatment

Up to 5 visits

The study doctors:

- checked the participants' health to make sure they could join the study
- did a physical exam and asked about the participants' medications and any medical problems
- checked the participants' heart health using an electrocardiogram, also called an ECG
- checked the participants' lung health and measured the amount of air they could breathe out
- took blood and urine samples
- based on the participant feedback, worked to find the best dose of oral corticosteroids to control asthma symptoms

The participants:

- answered questionnaires and completed a diary about their symptoms

Up to 10 weeks

While the participants got study treatment

13 visits

The study doctors:

- did a physical exam and asked about the participants' medications and any medical problems
- checked the participants' heart health using an electrocardiogram, also called an ECG
- checked the participants' lung health and measured the amount of air they could breathe out
- took blood and urine samples
- gave the participants study treatment at the study site
- if possible, reduced the participants' dose of oral corticosteroids during weeks 4 to 40. Then, the participants got the same dose during weeks 40 to 48

The participants:

- answered questionnaires and completed a diary about their symptoms

48 weeks

After the participants finished getting study treatment

2 visits

The study doctors:

- did a physical exam and asked about the participants' medications and any medical problems
- checked the participants' lung health and measured the amount of air they could breathe out
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG

The participants:

- could join another tezepelumab study

12 weeks

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.

Did tezepelumab reduce the amount of oral corticosteroids needed to control asthma symptoms?

Overall, the researchers found that the percentage of participants who could reduce their OCS dose was similar in the tezepelumab group and in the placebo group. The difference between the groups was too small for the researchers to know if tezepelumab could reduce the amount of OCS needed to control asthma symptoms better than the placebo.

To answer this question, the researchers calculated how many participants were able to reduce their dose of OCS after 48 weeks of getting study treatment. The researchers made categories based on how much participants were able to reduce their dose of OCS.

The researchers calculated the dose changes as a percentage change. Stopping OCS was the same as a 100.0% dose reduction. No change in OCS was the same as a 0.0% dose reduction.

At the end of the study, the participants' information was put into categories based on how much they had reduced their OCS dose by. The researchers also calculated the percentage of participants in each dose reduction group. The results are presented in the table below.

	Tezepelumab (out of 74 participants)	Placebo (out of 76 participants)
90% or more dose reduction	54.1% (40)	46.1% (35)
Between 75% and less than 90% dose reduction	6.8% (5)	5.3% (4)
Between 50% and less than 75% dose reduction	13.5% (10)	18.4% (14)
Dose reduction less than 50%	6.8% (5)	11.8% (9)
No change or an increase in dose	18.9% (14)	18.4% (14)

Did the participants feel that tezepelumab helped their quality of life or helped them to 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 while they got the study treatment. Some of these questionnaires were:

- Standardized Asthma Quality of Life Questionnaire for 12 Years and Older, also called AQLQ(S)+12
- Asthma Control Questionnaire-6, also called ACQ-6
- European Quality of Life – 5 Dimensions 5 Levels Questionnaire, also called EQ-5D-5L
- Asthma Symptom Diary, also called the ASD
- Average number of nighttime awakenings per week reported by participants

AQLQ(S)+12

The participants responded to each question on the AQLQ(S)+12 on a scale from 1 to 7. Then, the researchers calculated average 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 treatment to after 48 weeks of treatment. They compared the average change in score for the participants who got tezepelumab to those who got the placebo. An increase in average score meant that the participants felt that the study treatment helped their quality of life.

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

- an increase of 0.94 for the participants who got tezepelumab
- an increase of 0.58 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. Then, the researchers calculated average scores. A high average score meant that the participant's asthma was not well controlled. A low average score meant that the participant's asthma was well controlled.

The researchers compared the average scores before treatment to after 48 weeks of treatment. They compared the results for the participants who got tezepelumab to those who got the placebo. A decrease in average score meant that the participants felt that study treatment helped control their asthma.

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

- a decrease of 0.87 for the participants who got tezepelumab
- a decrease of 0.51 for the participants who got the placebo

EQ-5D-5L

In the EQ-5D-5L questionnaire, participants reported their health in a visual way. They marked a point on a line between 'The best health you can imagine' and 'The worst health you can imagine', also called a visual analogue scale. The placement of each point was turned into a score. The higher the score, the better the participant felt about their quality of life.

The researchers compared the average EQ-5D-5L visual analogue scale scores before treatment to after 48 weeks of treatment. They compared the results for the participants who got tezepelumab to those who got the placebo. An increase in average EQ-5D-5L visual analogue scale score meant that the participants felt that the study treatment helped their quality of life.

Overall, the researchers found that the change in average EQ-5D-5L score was:

- an increase of 9.21 for the participants who got tezepelumab
- an increase of 2.00 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 treatment to after 48 weeks of treatment. They compared the results for the participants who got tezepelumab to those who got the placebo. The difference between the groups was too small for the researchers to know if tezepelumab had helped the participants' asthma symptoms.

Nighttime awakenings

The participants kept a record of how often they were awoken by their asthma symptoms and required additional medication each week. The researchers calculated the average number of nights that participants were woken up by their asthma symptoms before treatment to after 48 weeks of treatment. They compared the results for the participants who got tezepelumab to those who got the placebo. The difference between the groups was too small for the researchers to know if tezepelumab had helped control nighttime awakenings.

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?

	Tezepelumab (out of 74 participants)	Placebo (out of 76 participants)
How many participants had adverse reactions?	4.1% (3)	5.3% (4)
How many participants had serious adverse reactions?	0.0% (0)	1.3% (1)
How many participants stopped getting study treatment due to adverse reactions?	0.0% (0)	1.3% (1)

What serious adverse reactions happened during this study?

There were 1.3% of participants who got the placebo who had a serious adverse reaction. This was 1 out of 76 participants. The serious adverse reaction was a headache. None of the participants who got tezepelumab had a serious adverse reaction.

None of the participants died due to a serious adverse reaction.

What adverse reactions happened during this study?

The table below shows the adverse reactions that happened during the study.

Adverse reactions		
Adverse reaction	**Tezepelumab (out of 74 participants)**	**Placebo (out of 76 participants)**
Muscle pain	1.4% (1)	0.0% (0)
Skin redness	1.4% (1)	0.0% (0)
High temperature	1.4% (1)	0.0% (0)
Headache	0.0% (0)	1.3% (1)
Pain in a joint	0.0% (0)	1.3% (1)
Mouth ulcer	0.0% (0)	1.3% (1)
Dizziness	0.0% (0)	1.3% (1)
Altered sense of taste	0.0% (0)	1.3% (1)
Fatigue	0.0% (0)	1.3% (1)
Injection site redness	0.0% (0)	1.3% (1)
Injection site swelling	0.0% (0)	1.3% (1)
Injection site itching	0.0% (0)	1.3% (1)
Difficulty seeing	0.0% (0)	1.3% (1)

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 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. 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 **"NCT03406078"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2017-003079-69"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5180C00009"** into the search box, and click **"Find a Study"**.

Full Study Title: A Multicentre, Randomized, Double-Blind, Placebo Controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Tezepelumab in Reducing Oral Corticosteroid Use in Adults with Oral Corticosteroid Dependent Asthma (SOURCE)

AstraZeneca Protocol number: D5180C00009

National Clinical Trials number: NCT03406078

EudraCT number: 2017-003079-69

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 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.

CISCRP | One Liberty Square, Suite 1100 • Boston, MA 02109 | 1-877-MED-HERO | www.ciscrp.org

Version 1.0 2021_07_23