AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: Benralizumab

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

Protocol Number: D3250C00045

Thank you!

Thank you for taking part in the clinical study for the study drug benralizumab, also called MEDI-563.

You and all of the participants helped researchers learn more about benralizumab to help people with severe asthma that is not controlled well with treatments that are already available.

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 that is not controlled well with treatments that are already available. 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 get?

The participants in this study got benralizumab or a placebo. A placebo looks like a drug 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 benralizumab reduce the estimated number of asthma attacks that the participants would have experienced over 1 year?**

  Yes. Overall, the researchers found that benralizumab reduced the estimated number of asthma attacks that the participants would have experienced over 1 year compared with the placebo.

- **Did the participants feel that benralizumab helped their health-related quality of life and helped them control their asthma symptoms?**

  Yes. Overall, the researchers found that the participants who got benralizumab felt that it helped their health-related quality of life and helped them control their asthma symptoms compared with the participants who got the placebo.

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

  There were 14.0% of participants who had medical problems that the study doctors thought might be related to the study drug during the study. The most common medical problem was headache.

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 can also be found on those websites.

Who took part in this study?

The researchers asked for the help of men and women with severe asthma. The participants in this study were 18 to 74 years old when they joined. All of the participants had tried other treatments that are already available to treat asthma, but they were still having uncontrolled symptoms of asthma. This included a type of treatment called corticosteroids.

The study included 660 participants in Austria, Belgium, Canada, Denmark, Finland, France, Germany, Italy, the Netherlands, Norway, Spain, Sweden, 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 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 benralizumab worked in a large number of participants with severe asthma that is not controlled well with already available treatments. They also wanted to find out if the participants had any medical problems during the study.

Asthma is a long-term 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.

Inflammation in the lungs is linked to high levels of white blood cells called eosinophils in the lungs. Benralizumab works by reducing the number of eosinophils, which researchers believe can help control asthma symptoms.

In this study, the researchers wanted to find out if benralizumab affected the number of asthma attacks, also known as "exacerbations", that the participants would have experienced over 1 year.

What was the purpose of this study?

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

- Did benralizumab reduce the estimated number of asthma attacks that the participants would have experienced over 1 year?
- Did the participants feel that benralizumab helped their health-related quality of life and helped them control their asthma symptoms?
- 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 benralizumab helps improve the health of people with severe asthma.

What treatments did the participants get?

In this study, the participants got either benralizumab 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.

The participants got benralizumab or the placebo through a needle under the skin, also known as a "subcutaneous injection". The participants got the first 3 doses of their injections once every 4 weeks. They got their final dose 8 weeks later.

All of the participants also continued to take "standard of care" asthma treatments that they were using before joining the study. "Standard of care" means the treatment that the medical community thinks is the appropriate and widely accepted treatment for a condition.

This was a "double-blind" study. This means none of the participants, researchers, study doctors, or other study staff knew whether each participant was getting benralizumab or the placebo. 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 chart below shows the treatments the researchers planned to study.

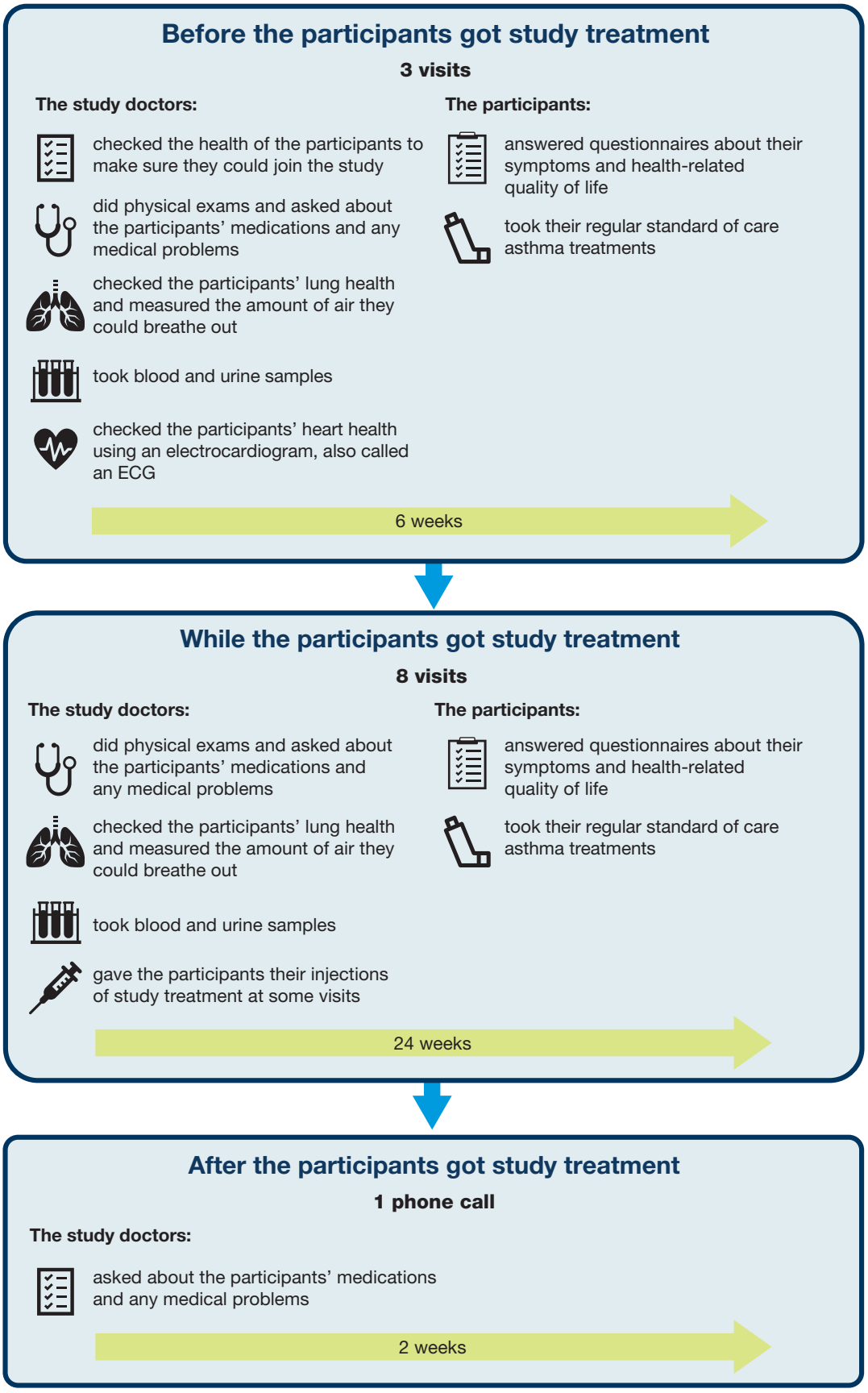
	Benralizumab	Placebo
	431 participants	229 participants
	Benralizumab as an injection	Placebo as an injection
	• 1 dose every 4 weeks for 3 doses • 1 dose 8 weeks later	
	All of the participants also continued taking their regular standard of care asthma treatments.	

What happened during this study?

The participants were in the study for just over 7 months, but the entire study took over 2 years to finish.

The study started in July 2017 and ended in September 2019.

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 that the 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 4 participants who did not get any doses of study treatment, so the results shown are for 656 out of 660 participants.

Did benralizumab reduce the estimated number of asthma attacks that the participants would have experienced over 1 year?

Yes. Overall, the researchers found that benralizumab reduced the estimated number of asthma attacks that the participants would have had over 1 year compared with the placebo.

To answer this question, the researchers counted the number of asthma attacks that the participants had during the 24 weeks that they got study treatment. The participants had an asthma attack if they had worsening symptoms of asthma and needed any of the following:

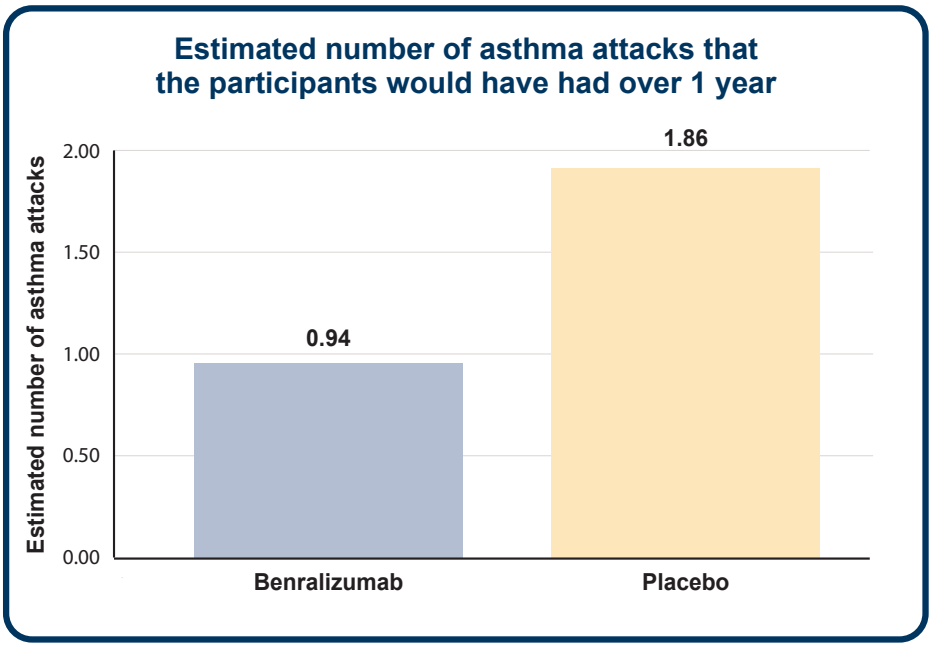
- a higher dose of their regular asthma treatment for at least 3 days
- additional medication
- to see a doctor
- to go to the hospital

Then, the researchers calculated the average number of asthma attacks that the participants had in each treatment group. Finally, the researchers used a math equation to estimate how many asthma attacks the participants would have had if they stayed in the study for 1 year.

The researchers found that the estimated number of asthma attacks that the participants would have had over 1 year was:

- 0.94 for the participants who got benralizumab
- 1.86 for the participants who got the placebo

These results are shown in the chart below.



Did the participants feel that benralizumab helped their health-related quality of life and helped them control their asthma symptoms?

Yes. Overall, the researchers found that the participants who got benralizumab felt that it helped their health-related quality of life and helped them control their asthma symptoms compared with the participants who got the placebo.

To answer this question, the researchers asked the participants to complete several different questionnaires throughout the study. Then, the researchers compared the participants' answers after 24 weeks of getting study treatment with their answers before getting any study treatment.

The chart below shows the questionnaires the participants answered. These questionnaires were completed by all of the participants, except for the "Sino-Nasal Outcome Test Item 22", which was only completed by the participants who had inflammation of the sinuses with soft growths inside their noses, also known as "nasal polyps".

Questionnaire	**Did the participants who got benralizumab feel that it helped with the symptoms and aspects of health-related quality of life that each questionnaire asked about, compared with the participants who got the placebo?**
Saint George's Respiratory Questionnaire	Yes
Asthma Control Questionnaire 6	Yes
Social Functioning Short Form 36-Item Health Survey, Version 2 – physical health summary	Yes
Social Functioning Short Form 36-Item Health Survey, Version 2 – mental health summary	No
Patient Global Impression of Severity	Yes
Patient Global Impression of Change	Yes
Predominant Symptom and Impairment Assessment	Yes
Sino-Nasal Outcome Test Item 22	Yes

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 drug. 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 drug. A lot of research is needed to know whether a drug causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for benralizumab.

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?

	Benralizumab (out of 427 participants)	Placebo (out of 229 participants)
How many participants had adverse reactions?	16.9% (72)	8.7% (20)
How many participants had serious adverse reactions?	0.9% (4)	0.0% (0)
How many participants stopped taking study treatment due to adverse reactions?	0.9% (4)	0.0% (0)

What serious adverse reactions happened during this study?

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

Serious adverse reactions

Serious adverse reaction	Benralizumab (out of 427 participants)	Placebo (out of 229 participants)
A type of severe inflammatory immune system reaction called "cytokine release syndrome"	0.2% (1)	0.0% (0)
Dilated eyes	0.2% (1)	0.0% (0)
Pneumonia	0.2% (1)	0.0% (0)
Raised itchy rash, also known as "hives" or "welts"	0.2% (1)	0.0% (0)

None of the participants died because of serious adverse reactions.

What adverse reactions happened during this study?

The most common adverse reaction was headache.

The table below shows the adverse reactions that happened in 3 or more of the participants during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions

Adverse reaction	Benralizumab (out of 427 participants)	Placebo (out of 229 participants)
Headache	4.0% (17)	1.7% (4)
Fever	4.0% (17)	0.9% (2)
General weakness	1.6% (7)	1.3% (3)
Fatigue	1.6% (7)	1.3% (3)
Nausea	1.4% (6)	1.3% (3)
Chills	0.7% (3)	0.4% (1)
Dizziness	0.7% (3)	0.4% (1)
Diarrhea	0.5% (2)	0.4% (1)
Muscle pain	0.5% (2)	0.4% (1)
Vomiting	0.2% (1)	0.9% (2)

How has this study helped patients and researchers?

This study helped researchers learn more about benralizumab for people 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 studies with benralizumab may be 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 **"NCT03170271"** into the search box and click **"Search"**.
- http://www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search",** then type **"2017-001040-35"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D3250C00045"** into the search box, and click **"Find a Study"**.

Full Study Title: A Multicenter, Randomized, Double-blind, Parallel Group, Placebo-controlled, Phase IIIb Study to Evaluate the Safety and Efficacy of Benralizumab 30 mg sc in Patients with Severe Asthma Uncontrolled on Standard of Care Treatment (ANDHI)

AstraZeneca Protocol Number: D3250C00045

National Clinical Trials Number: NCT03170271

EudraCT Number: 2017-001040-35

AstraZeneca sponsored this study and has its headquarters in 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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