Clinical Trial Results

AstraZeneca

Research Sponsor:	AstraZeneca AB
Drug Studied:	Benralizumab
National Clinical Trial #:	NCT02814643
EudraCT #:	2016-001717-24
Protocol #:	D3250C00033
Study Date:	July 2016 to January 2017
Short Study Title:	A study to see if benralizumab affects how the immune system reacts to a flu vaccine and if benralizumab is safe to use

Thank you!

As a clinical study participant, you belong to a large community of participants around the world. You help researchers answer important health questions and discover new medical treatments.

Thank you for taking part in the clinical study for the drug called benralizumab. This drug is being developed to treat asthma. You and all of the other participants helped researchers learn if benralizumab affects how the lungs and the immune system react to a flu vaccine, and if benralizumab is safe to use.

AstraZeneca AB, the sponsor of this study, thanks you for your help and thinks it is important for you to know the results of the study. An independent non-profit organization called CISCRP prepared this summary of the study results for you with the help of a medical writing organization. We hope it helps you understand and feel proud of your important role in medical research. If you have questions about the results, please speak with the study doctors or staff at your study site.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

What has happened since my study ended?

Your study started in July 2016 and ended in January 2017. The study included 103 participants at 30 study sites in the United States. When the study ended, the sponsor reviewed the data and created a report of the results. This is a summary of that report.

Why was the research needed?

Before a new drug can be approved, research must be done to show that it is safe and effective. The study drug, benralizumab, is being developed to treat asthma. Asthma can cause swelling in the lungs. This swelling can sometimes make breathing difficult. Benralizumab can reduce swelling in the lungs and make it easier to breathe.

In this study, researchers wanted to learn if benralizumab affects how the lungs and the immune system react to a flu vaccine in young adults. The vaccine used in this study was created to defend the body against 4 different types of the flu virus, also known as strains. All participants got the vaccine.

Researchers compared the results on how benralizumab affected all 4 strains of the flu vaccine. They also compared the results of participants who got a placebo. A placebo looks like the study drug but contains no real medicine. Researchers use a placebo so that they can compare the results of participants who get study drugs with the results of participants who get no medicine at all. Researchers wanted to know:

- Did benralizumab affect how the immune system reacted to the flu vaccine?
- Did benralizumab reduce participants' asthma symptoms?
- What medical problems did participants have during the study?

What kind of study was this?

Your study was a "double-blind" study. This means that none of the participants, researchers, or staff knew what treatment each participant got. Some studies are done this way because knowing what treatment each participant is taking can affect the results of the study. This way, the results are looked at fairly.

You and other participants got benralizumab or placebo. Which treatment participants got was decided by chance. For every participant who got benralizumab, 1 participant got a placebo.

Your study included 103 males and females with asthma who were between the ages of 12 and 21 years.

What happened during the study?

You and other participants were in the study for up to 24 weeks and visited your study site up to 7 times.

Visits 1 and 2 (2 to 4 weeks)
To see if you could join the study, study doctors did a physical examination and checked your height, weight, and temperature. Study doctors took blood and urine samples and checked your heart health using an electrocardiogram, or ECG. Study doctors also checked your lung function and asked about your medical history, how you were feeling, and what medicines you were taking.

If you are female, you had a blood test to make sure you were not pregnant.

Visits 3, 4, and 5 (8 weeks)
Each participant got 1 of 2 treatments in this study:

- 51 participants got a 30 milligram, or mg, injection of benralizumab during Visits 3, 4, and 5
- 52 participants got the placebo during Visits 3, 4, and 5

During Visit 5, you and all other participants got a flu vaccine injection. Researchers gave participants the vaccine because they wanted to learn how the immune system responded to benralizumab compared to the placebo, and if benralizumab lowered the effectiveness of the flu vaccine. Vaccines work by giving you a weak form of a virus that can make you sick. When your body fights this weak form of the virus, it makes cells called antibodies to protect you against it. If you get a stronger form of the virus later, your body will be ready to fight it.

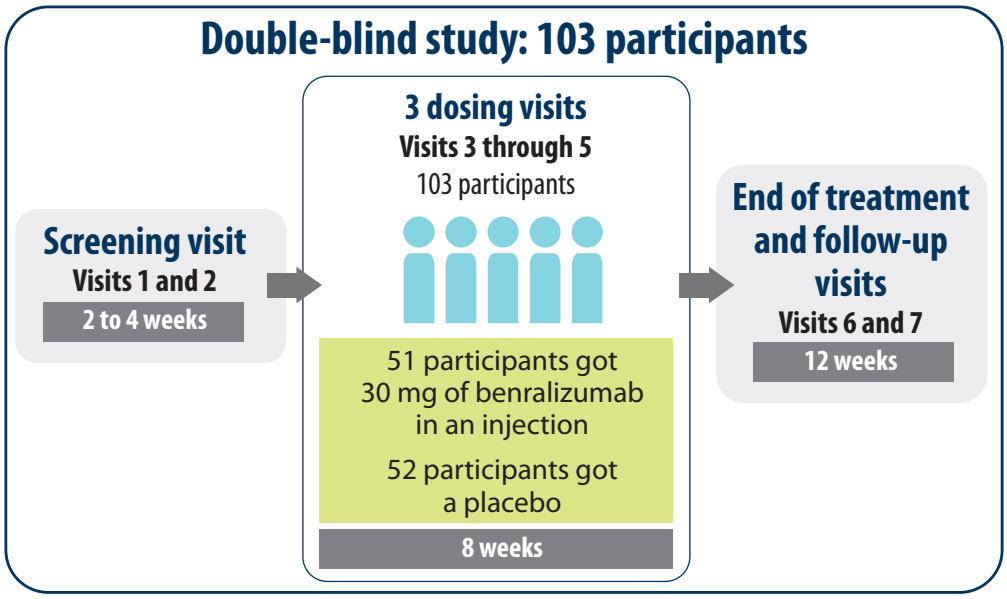
During the study, study doctors did a physical examination by checking your height, weight, and temperature. Study doctors also tested blood and urine samples to make sure that participants were still healthy, and asked participants how they were feeling. Finally, study doctors also checked your heart health and lung function.

At the end of the study, you and the other participants visited your study site 2 more times so that the study doctors could check your health again.

Visits 6 and 7 (12 weeks)
During Visit 6, which was the first follow-up visit, study doctors measured the amount of antibodies that your immune system made to protect you from the flu in the vaccine. During Visit 6, study doctors checked to see if you had any changes with your immune system or asthma symptoms.

During Visit 7, which was the second follow-up visit, study doctors checked your health again for the last time in the study.

The figure below shows how the study was done.



What were the study results?

Below is a summary of the results of some of the questions that researchers asked during this study. It is important to know that researchers look at the results of many studies to decide which medicines work best and are safest for patients.

In order to know how a medication works and in whom it works well, researchers ask questions that are answered in studies like this. Here are some of the questions that the researchers had and the results provided by the study in which you took part.

Further clinical studies with benralizumab are ongoing.

Did benralizumab affect how the immune system reacted to the flu vaccine?

Researchers wanted to learn how benralizumab affected the immune system. To do this, researchers gave all participants the 4-strain flu vaccine. Researchers compared the results for all 4 strains. They also compared the results for the participants who got benralizumab injections to the results for participants who got the placebo.

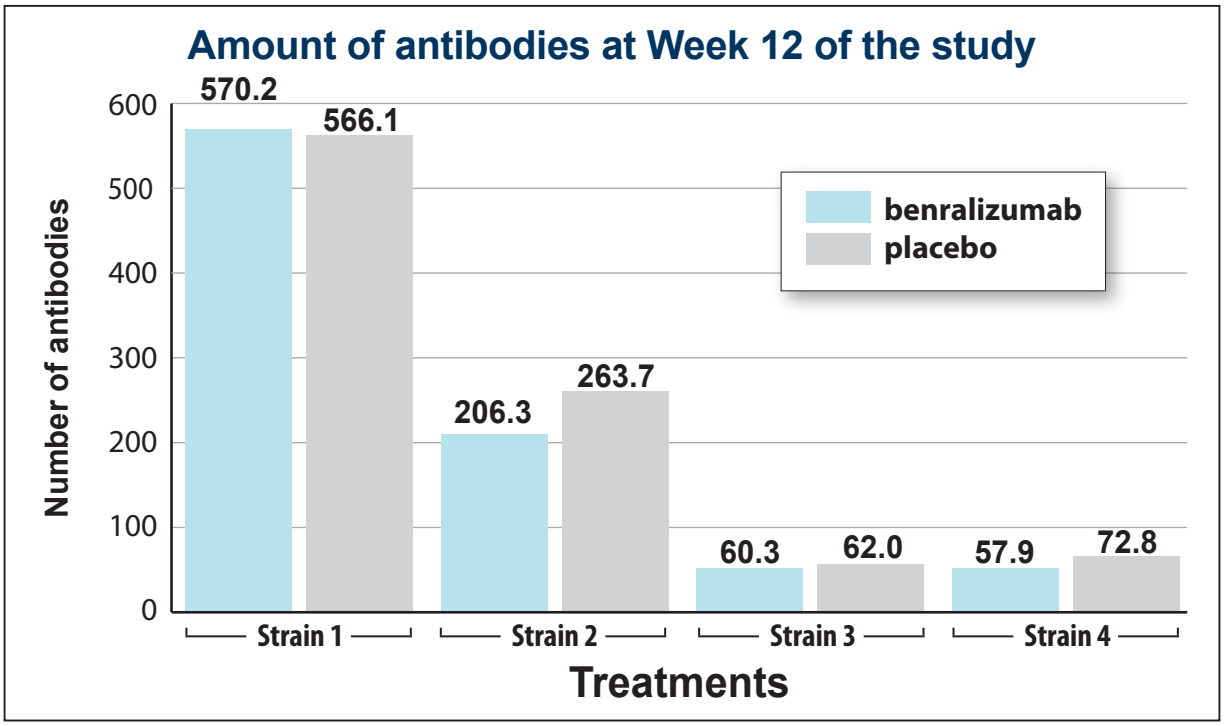
Researchers studied:

- The change in the amount of antibodies in the blood at week 12
- The amount of antibodies in the blood at Week 12
- The percentage of participants who had at least a 4 times increase in the amount of antibodies at Week 12 compared to Week 8
- The percentage of participants who had at least 40 antibodies at Week 12
- The percentage of participants who had at least 320 antibodies at Week 12

Change in the amount of antibodies in the blood at Week 12
Researchers measured the change in the amount of antibodies in the participants' blood. To do this, study doctors took blood samples throughout the study. At Week 12, researchers found that participants who got benralizumab and participants who got the placebo had a similar change in the amount of antibodies. This increase was similar across all 4 flu strains.

Amount of antibodies in the blood at Week 12
Researchers measured the amount of antibodies in the participants' blood at Week 12. They found that participants who got benralizumab and participants who got the placebo had similar amounts of antibodies. These amounts were similar across all 4 flu strains.

The figure below shows the amount of antibodies at Week 12 of the study across all 4 flu strains.



Percentage of participants who had at least a 4 times increase in the amount of antibodies at Week 12 compared to Week 8
Researchers measured the percentage of participants who had at least a 4 times increase in the amount of antibodies at Week 12 compared to Week 8. They found that the percentage of participants who had at least a 4 times increase in the amount of antibodies was similar between the benralizumab and placebo treatment groups. This percentage was similar across all 4 flu strains.

Percentage of participants who had an increase of at least 40 antibodies at Week 12
Researchers measured the percentage of participants who had at least 40 antibodies at Week 12. They found that the percentage of participants who had at least 40 antibodies was similar between the benralizumab and placebo treatment groups. This percentage was similar across all 4 flu strains.

Percentage of participants who had an increase of at least 320 antibodies at Week 12
Researchers measured the percentage of participants who had at least 320 antibodies in Week 12. They found that the percentage of participants who had at least 320 antibodies was higher when participants got Strains 1 and 2 compared to Strains 3 and 4 for both treatment groups.

Did benralizumab reduce participants' asthma symptoms?

Researchers also wanted to learn if benralizumab reduced asthma symptoms. To do this, researchers gave participants a survey about their asthma symptoms at different times throughout the study. They compared these survey scores with the scores that participants reported at the beginning of the study.

Overall, participants who got benralizumab and participants who got the placebo both reported reduced asthma symptoms at Week 4. This reduction was still consistent at Week 8 and Week 12 for both treatment groups. At Week 12, participants who got benralizumab reported a slightly higher reduction in asthma symptoms compared to the placebo group.

What medical problems did participants have during the study?

A lot of research is needed to know whether a drug causes a medical problem. Researchers keep track of all medical problems that participants had have during the study. These medical problems are called "adverse events". They may or may not be caused by the study drug.

How many participants had medical problems during the study?

A similar number of participants in each treatment group had medical problems. No participants stopped study treatment because of medical problems. The table below shows how many participants in the study had medical problems.

How many participants had medical problems?

	30 mg Benralizumab (Out of 51 participants)	Placebo (Out of 52 participants)	Total (Out of 103 participants)
How many participants had medical problems?	43.1% (22)	44.2% (23)	43.7% (45)
How many participants had serious medical problems?	0.0% (0)	3.8% (2)	1.9% (2)

How many participants had serious medical problems?

A medical problem is considered serious when it is life-threatening, causes lasting problems, or needs hospital care. In this study, no participants died. A total of 2 of the 103 participants (1.9%) in this study had a serious medical problem. Both of these participants got the placebo:

- Suicidal thoughts in 1 participant who got the placebo
- Severe asthma in 1 participant who got the placebo

Both serious medical problems happened after treatment was over. Study doctors did not think either of the serious medical problems were related to treatment.

What were the most common medical problems in the study?

Overall, researchers found that participants who got benralizumab and participants who got the placebo had a similar number of common medical problems. Asthma, which was not severe, was the most common medical problem in the study.

The table below shows the most common medical problems that happened in at least 3% of participants during the study.

What were the most common non-serious medical problems?

Medical problem	30 mg Benralizumab (Out of 51 participants)	Placebo (Out of 52 participants)	Total (Out of 103 participants)
Non-severe asthma	5.9% (3)	7.7% (4)	6.8% (7)
Headache	3.9% (2)	7.7% (4)	5.8% (6)
Common cold	3.9% (2)	7.7% (4)	5.8% (6)
Pain in the mouth or throat	5.9% (3)	3.8% (2)	4.9% (5)
Viral stomach bug	5.9% (3)	1.9% (1)	3.9% (4)
Infection of the nose, throat, and airways	5.9% (3)	1.9% (1)	3.9% (4)

Where can I learn more about the study?

If you have questions about the results, please speak with the study doctor or staff at your study site. You can find more information about your study online at the below websites:

- www.clinicaltrials.gov/show/results/NCT02814643
- https://www.trialsummaries.com

Official study title: A Multicentre, Randomised, Double-blind, Parallel Group, Placebo-controlled, Phase 3b Study to Evaluate the Potential Effect of Benralizumab on the Humoral Immune Response to the Seasonal Influenza Vaccination in Adolescent and Young Adult Patients with Severe Asthma (ALIZE)

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

The results presented here are for a single study. Other studies may provide new information or different results. You should not make changes to your therapy based on the results of a single study without first consulting your healthcare professional.

Thank you

It is said that the greatest gift is one which is given anonymously, giving when you do not know whether you will get direct personal benefit.

This is the gift that you have given by taking part in a clinical trial. It is a brave and selfless act, one that advances medical knowledge and benefits public health.

Thank you for the gift of your participation in clinical research.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

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 trials, nor is it involved in conducting clinical studies.

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