AstraZeneca

# Clinical Study Results

**Study Sponsor:** AstraZeneca AB

**Treatment Studied:** Benralizumab

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

**Protocol Number:** D3252C00001

## Thank you!

Thank you for taking part in the clinical study for the study treatment called benralizumab.

You and all of the participants helped researchers learn more about benralizumab to help people who have chronic rhinosinusitis with nasal polyposis. The participants in this study had inflammation of the sinuses, large nasal polyps inside the nose, and symptoms that lasted for more than 3 months. In this summary, we will refer to this condition as "nasal polyps". Nasal polyps are painless soft growths inside the nose and sinuses.

AstraZeneca 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

## Why was the research needed?

Researchers are looking for a better way to treat people who have nasal polyps. Before a treatment can be approved for people to take, 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 benralizumab or a placebo. A placebo looks like a treatment but does not have any medicine in it.

## What were the results of the study?

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

- **Did benralizumab shrink the participants' nasal polyps and reduce how blocked their nose was?**

  Yes. Overall, the researchers found that benralizumab reduced the size of the participants' nasal polyps and how blocked their nose was.

- **Did benralizumab help improve the participants' nasal polyp symptoms or their quality of life?**

  Yes. Overall, the researchers found that benralizumab helped improve the participants' nasal polyp symptoms and quality of life.

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

  There were 10.5% of participants who had medical problems that the study doctors thought might be related to the study treatments during the study. This was 43 out of 410 participants. The most common medical problems were having a fever and feeling tired. These medical problems happened in both the participants who got benralizumab and those who got the placebo.

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 severe nasal polyps in both nostrils that did not get better with standard treatment. Each participant also had symptoms caused by inflammation inside of the nose and sinuses that had lasted for more than 3 months. The participants were 18 to 75 years old when they joined the study.

The study included 413 participants in Austria, Belgium, Canada, Denmark, Germany, Hungary, Poland, and the United States.

# Why was the research needed?

Researchers are looking for a better way to treat severe nasal polyps. In this study, the researchers wanted to find out if benralizumab works in a large number of participants with severe nasal polyps. They also wanted to find out if the participants had any medical problems during the study.

Nasal polyps are soft growths inside the nose. They often develop in people who have long-lasting inflammation inside the nose and sinuses. The sinuses are the air spaces behind the cheek bones and forehead. They connect to the inside of the nose.

Common symptoms of nasal polyps include a blocked nose, a runny nose, a feeling of pressure in the face, and a reduced sense of smell.

Steroid pills or steroid nasal sprays are often used to treat nasal polyps. These help to reduce the long-lasting inflammation in the nose but do not always make the nasal polyps smaller. So, researchers are looking for other ways to treat nasal polyps.

Inflammation is caused by the immune system reacting to something the body does not recognize. In people with severe nasal polyps and long-lasting inflammation in the nose, two types of white blood cells in the body called "eosinophils" and "basophils" become too active. Eosinophils and basophils are involved in inflammation in the air passages in the nose. Researchers think that benralizumab can help the body reduce the number of these cells.

Benralizumab is currently available as a treatment for some patients with asthma. In this study, the researchers wanted to find out if benralizumab could help to shrink nasal polyps and help improve nasal polyp symptoms.

## What was the purpose of this study?

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

- Did benralizumab shrink the participants' nasal polyps and reduce how blocked their nose was?
- Did benralizumab help improve the participants' nasal polyp symptoms or their quality of life?
- 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 nasal polyps.

## What treatments did the participants get?

In this study, all of 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 take 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 their randomly chosen study treatment through a needle under the skin, also called a subcutaneous injection. The dose of benralizumab was measured in milligrams, also called mg.

All the participants also continued taking their normal nose spray during the study. This nose spray contained a steroid called mometasone furoate. The dose of mometasone furoate nasal spray was measured in micrograms, also called mcg.

The chart below shows the number of participants in the study and what treatments they were given.

| | Benralizumab | Placebo |
|---|---|---|
|  | • 207 participants | • 206 participants |
|  | • 30 mg of benralizumab as an injection<br>• 400 mcg of mometasone furoate nose spray | • Placebo as an injection<br>• 400 mcg of mometasone furoate nose spray |
|  | • benralizumab or placebo: 3 doses once every 4 weeks, then 5 doses once every 8 weeks, for a total of 56 weeks<br>• mometasone furoate: 2 sprays in each nostril twice a day, for the entire study | |

## What happened during this study?

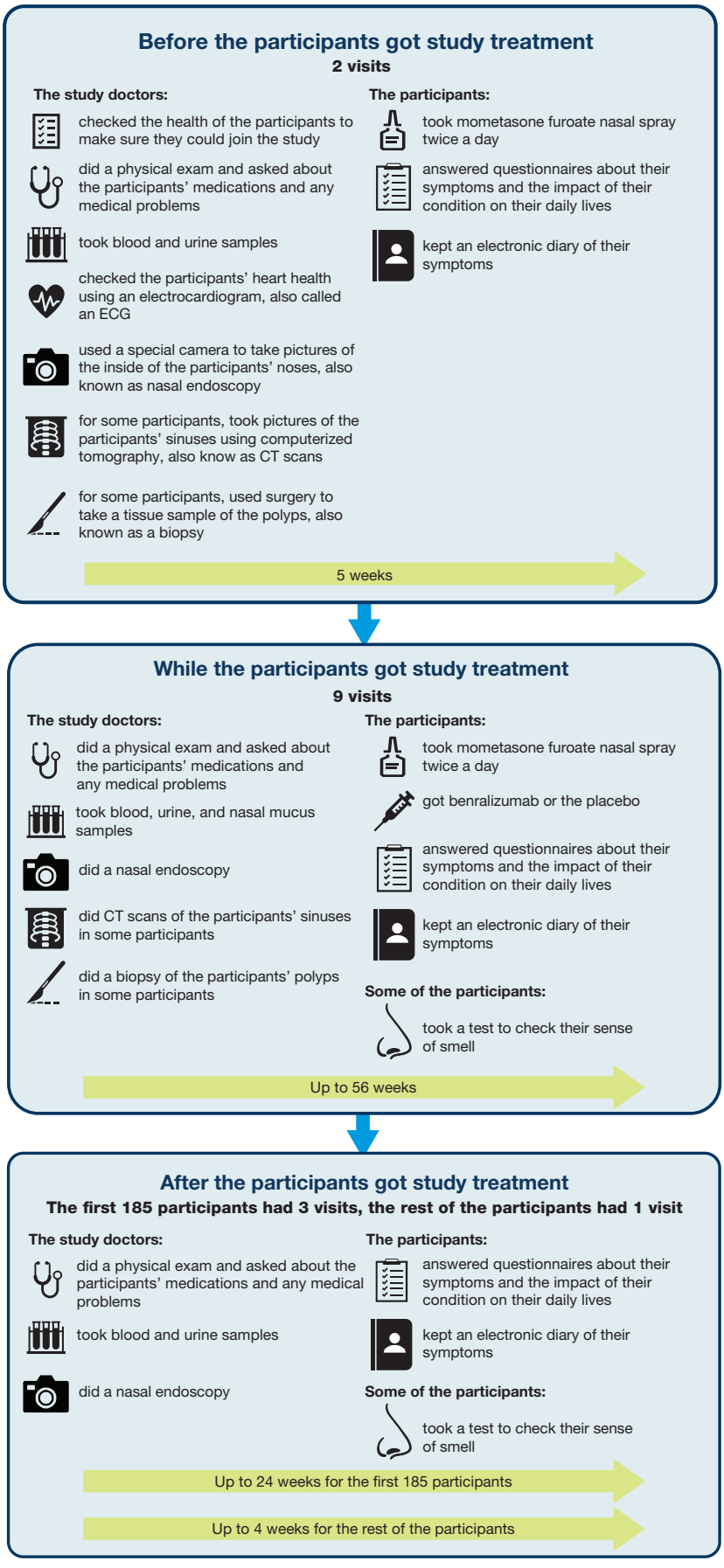
Half of the participants were in the study for up to 65 weeks. The other half of the participants had additional visits to the study site after they stopped taking the study treatment. These participants were in the study for up to 85 weeks. The entire study took 2.5 years to finish.

The study started in January 2018 and ended in July 2020.

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

- Some of their site visits may have been delayed or canceled.
- Some of the tests that had been planned were not done.
- Some site visits may have been replaced with phone calls.
- They may have completed some questionnaires remotely.

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 3 participants in the placebo group who did not get any study treatment. So, the results below are for the 410 participants who got at least 1 dose of study treatment.

## Did benralizumab shrink the participants' nasal polyps and reduce how blocked their nose was?

Yes. Overall, the researchers found that benralizumab reduced the size of the participants' nasal polyps and how blocked their nose was.

To find out if the participants' nasal polyps shrank during the study, the study doctors used a special camera to take pictures of the participants' nasal polyps. Then they gave the participants a "score" from 0 to 4 for each nostril. A score of 0 meant no polyps and a score of 4 meant large polyps that were completely blocking the nostril. Because the participants had a score for each nostril, their total score could range from 0 to 8. This was the participants' "nasal polyp score", also called NPS. A higher NPS meant more nasal polyps or larger nasal polyps.

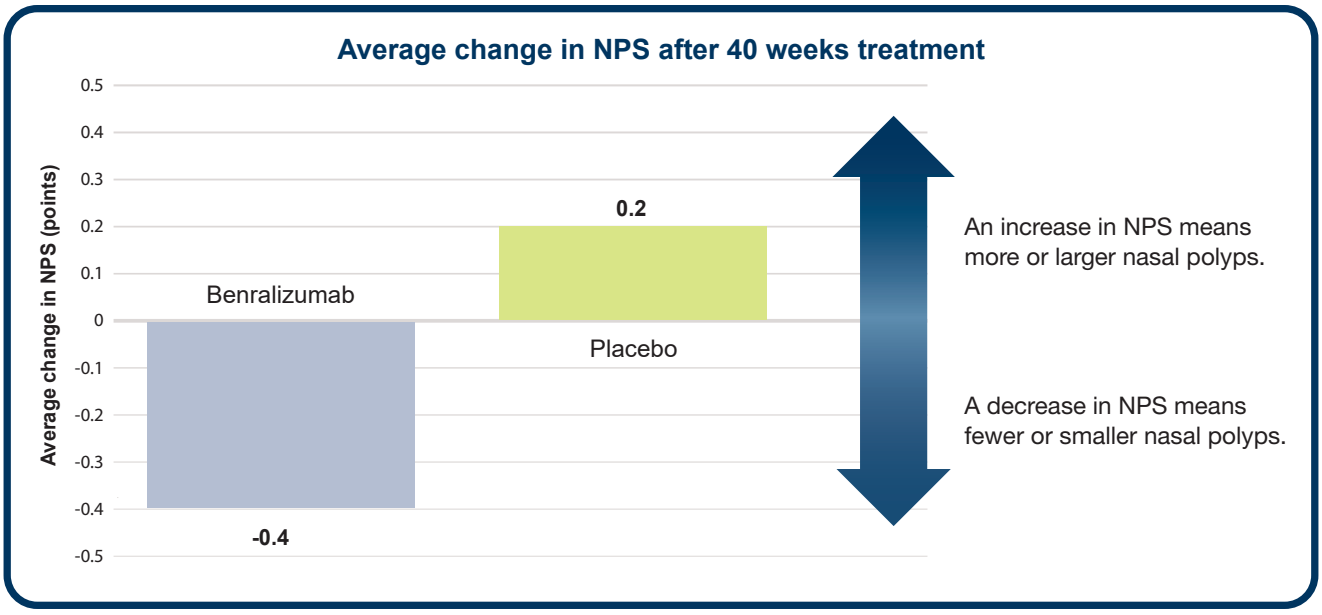
The researchers compared the participants' NPS at the start of the study to their NPS after 40 weeks of treatment. The researchers then calculated the average change in NPS in the participants who took benralizumab and in the participants who took the placebo.

Due to the COVID-19 pandemic, some participants could not get to all of their study treatment, and the researchers were not able to collect complete information after Week 40. Because of this, the researchers used the information from Week 40, even though the participants were meant to take the study treatment for 56 weeks.

The researchers found that after 40 weeks of treatment, the participants' average NPS:

- decreased by 0.4 points in the participants who got benralizumab
- increased by 0.2 points in the participants who got the placebo

The graph below shows these results.

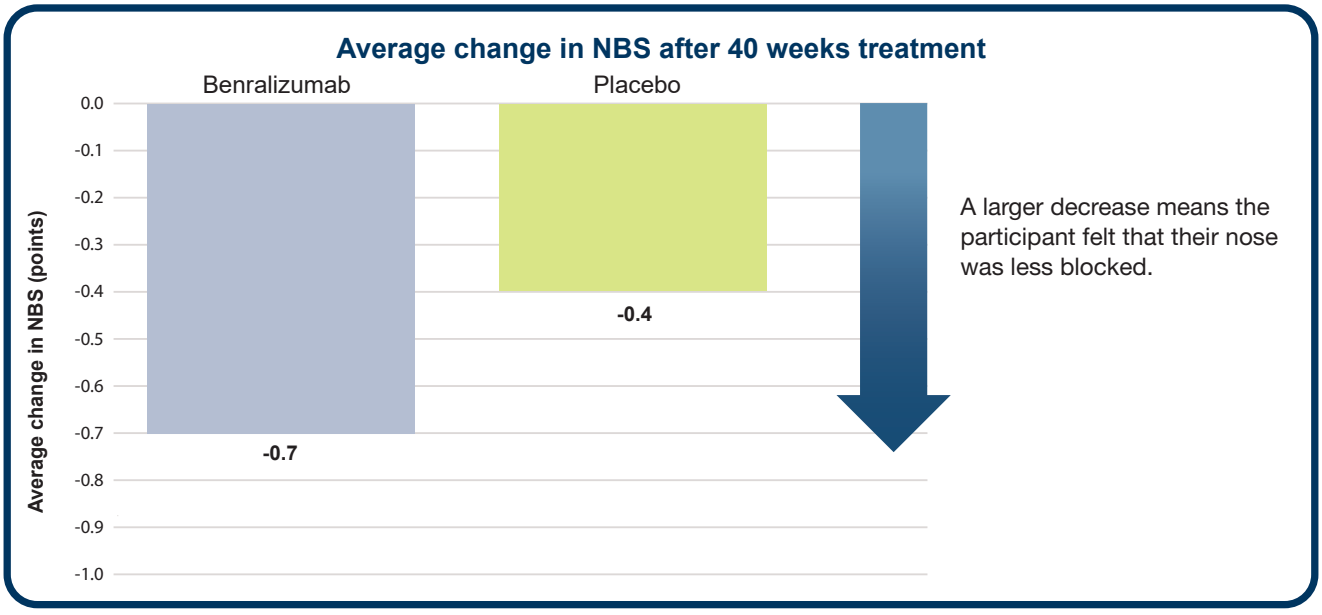


The participants also answered a question about their daily nasal polyp symptoms and how they impacted their quality of life. They kept track of their answers in an electronic diary. The participants rated how blocked their nose had been in the last 24 hours with a score of 0 to 3. A score of 0 meant no blockage and a score of 3 meant severe blockage. This is called the "nasal blockage score", also known as NBS.

The researchers compared the participants' NBS at the start of the study to their NBS after 40 weeks of treatment. The researchers then calculated the average change in NBS in the participants who got benralizumab and in those who got the placebo.

- decreased by 0.7 points in the participants who got benralizumab
- decreased by 0.4 points in the participants who got the placebo

The graph below shows these results.



## Did benralizumab help improve the participants' nasal polyp symptoms or their quality of life?

To answer this question, the researchers checked the participants' nasal polyp symptoms using 6 different questionnaires. Many of the measurements checked the participants' nasal symptoms and sense of smell. Nasal polyps can also affect quality of life because they can be very painful. So, the researchers also checked the participants' physical and mental health. The table below shows these tests and the results.

| What was the measurement? | What did it measure? | After how many weeks of treatment? | Did benralizumab help improve the participants' symptoms or quality of life? |
|---|---|---|---|
| Sino-Nasal Outcome Test-22 | How severe the sinus and nasal symptoms were and impact on daily life | 40 weeks | No |
| Difficulty with sense of smell | Difficulty with sense of smell | 40 weeks | Yes |
| University of Pennsylvania Smell Identification Test | If the participant can identify different smells | 40 weeks | No |
| Nasal symptom scores | Nasal polyp symptoms | 40 weeks | Yes |
| Short Form (36) Health Survey, Version 2: physical component summary | Physical health | 56 weeks | Yes |
| Short Form (36) Health Survey, Version 2: mental component summary | Mental health | 56 weeks | No |

# 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 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 benralizumab.

There were 3 participants in the placebo group who did not get any study treatment. So, the results below are for the 410 participants who got at least 1 dose of study treatment.

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 207 participants) | Placebo (out of 203 participants) |
|---|---|---|
| How many participants had adverse reactions? | 15.0% (31) | 5.9% (12) |
| How many participants had serious adverse reactions? | 1.4% (3) | 0.0% (0) |
| How many participants stopped taking study treatment due to adverse reactions? | 1.9% (4) | 1.0% (2) |

## 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 207 participants) | Placebo (out of 203 participants) |
|---|---|---|
| Immune system destroys red blood cells, leading to low levels of red blood cells | 0.5% (1) | 0.0% (0) |
| Cancer of the salivary gland | 0.5% (1) | 0.0% (0) |
| Sudden inflammation of the pancreas | 0.5% (1) | 0.0% (0) |

None of the participants died due to any serious adverse reactions during the study.

## What adverse reactions happened during this study?

There were 10.5% of participants who had medical problems that the study doctors thought might be related to the study treatments during the study. This was 43 out of 410 participants. The most common adverse reactions were fever and tiredness.

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

### Most common adverse reactions

| Adverse reaction | Benralizumab (out of 207 participants) | Placebo (out of 203 participants) |
|---|---|---|
| Fever | 1.4% (3) | 0.5% (1) |
| Tiredness | 1.0% (2) | 1.0% (2) |
| Headache | 1.4% (3) | 0.0% (0) |
| Joint pain | 1.4% (3) | 0.0% (0) |
| Dizziness | 1.4% (3) | 0.0% (0) |
| Inflammation of the breathing tubes, also called asthma | 0.5% (1) | 1.0% (2) |

# How has this study helped patients and researchers?

This study helped researchers learn more about how benralizumab works in participants with severe nasal polyps.

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 benralizumab 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 **"NCT03401229"** into the search box and click **"Search"**.
- http://www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search",** then type **"017-003675-61"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D3252C00001"** into the search box, and click **"Find a Study"**.

**Full Study Title:** A Multicenter, Randomised, Double-Blind, Parallel-Group, Placebo-Controlled Phase 3 Efficacy and Safety Study of Benralizumab in Patients with Severe Nasal Polyposis (OSTRO)

**AstraZeneca AB Protocol Number:** D3252C00001

**National Clinical Trials Number:** NCT03401229

**EudraCT Number: 2017-003675-61**

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

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

# Thank you!

Participants in clinical studies 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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