Clinical Study Results

Pearl™
A member of the AstraZeneca Group

Research Sponsor: Pearl Therapeutics, Inc.

Medicines Studied: Budesonide and Formoterol Fumarate

Study Title: A study to learn how different treatments of budesonide and formoterol fumarate affect the lung function of participants with moderate to very severe COPD

Thank you!

Thank you to the participants who took part in this clinical study for the study medicines budesonide and formoterol fumarate. You and all of the participants helped researchers learn more about treatments of budesonide and formoterol fumarate taken together to help people with moderate to very severe chronic obstructive pulmonary disease, also known as COPD.

Pearl Therapeutics, Inc. sponsored this study and thinks it is important to share the results of this 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 this study and have questions about the results, please speak with the doctor or staff at your study site.

What is happening with this study now?

Each participant was in this study for between 3 months and 1 year. But, the entire study took about 2 years to finish.

This study started in May 2016 and ended in April 2018. This study included 1,876 participants in 18 countries: Argentina, Austria, Belgium, Brazil, Canada, Chile, Denmark, Germany, Italy, Mexico, Norway, Peru, Russia, South Africa, Spain, Sweden, United Kingdom, and United States.

The sponsor reviewed the data collected when this study ended and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers are looking for a better way to treat COPD. COPD is a disease that can cause inflammation in the lungs, which can make it difficult to breathe. Before a treatment can be approved for patients to take, researchers do clinical studies to find out how it works and how safe it is.

At the time of this study, budesonide was available as a treatment for COPD when taken with formoterol fumarate through an inhaler. Formoterol fumarate was available as a treatment for COPD by itself through an inhaler.

The researchers compared 3 treatments:

- an inhaler that contained budesonide at a higher dose and formoterol fumarate together
- an inhaler that contained budesonide at a lower dose and formoterol fumarate together
- an inhaler that contained formoterol fumarate by itself

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

- How did the treatments affect how much air participants can exhale from the lungs in 1 second, also called lung function?
- Did the different treatments affect the participants in other ways?
- What medical problems did participants have during the study?

To answer the questions in this study, researchers asked for the help of men and women with moderate to very severe COPD. The participants in this study were 40 to 80 years of age when they enrolled in the study.

What kind of study was this?

This was a “double-blind” study. This means none of the participants, doctors, or other study staff knew what treatment each participant took. Some studies are done this way because knowing what treatment the participants are taking can affect the results of the study.

When the study ended, the research sponsor found out which treatment participants took so they could create a report of the study results.

The participants in the study took either 2 different doses of budesonide and formoterol fumarate together or formoterol fumarate by itself. Both treatments were taken through an inhaler.

A computer program was used to randomly choose the treatment each participant took. 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.

What happened during this study?

Before this study started, the participants visited their study site twice over the course of 4 weeks to make sure they could join the study. During this time, the doctors:

- did a physical examination of the participants
- checked the participants' lung function by having participants blow into a mouth piece connected to a meter that measures the amount of air they can force out of their lungs
- checked the participants' heart health by doing a test called an electrocardiogram, or ECG
- took blood samples
- asked about the participants' medical history
- asked the participants how they were feeling
- learned what medicines the participants were taking
- asked the participants to stop taking most of their own medicines to treat COPD

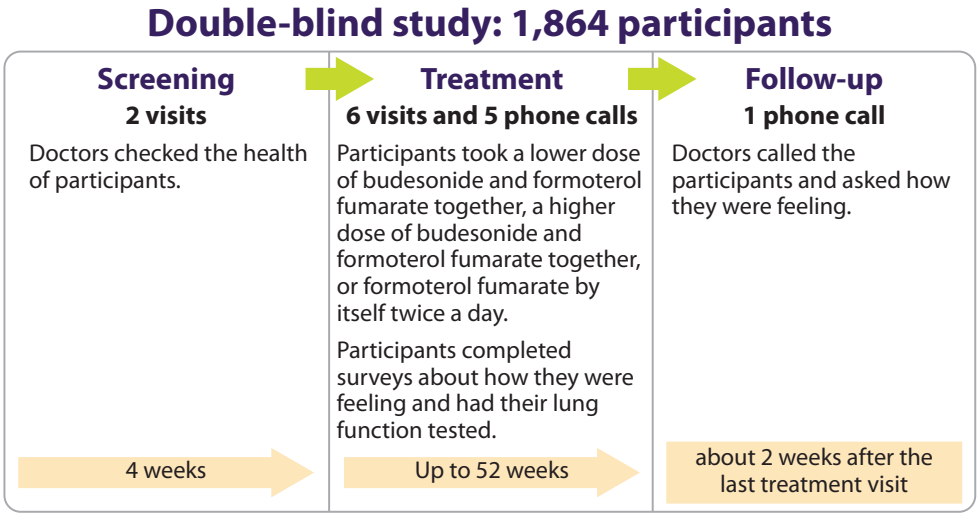
During this study, the participants visited their study site 6 times and had phone calls 5 times. During this time, the participants had their lung function tested and completed surveys. They took either 2 different doses of budesonide and formoterol fumarate together or formoterol fumarate by itself twice a day. Doses were measured in micrograms, or µg for short.

- 624 participants took 320 µg of budesonide and 9.6 µg of formoterol fumarate together
- 627 participants took 160 µg of budesonide and 9.6 µg of formoterol fumarate together
- 613 participants took 9.6 µg of formoterol fumarate only

The participants could also use rescue medicines provided by the study doctor if they needed it. A rescue medicine is a quick-acting medicine that could be used if COPD symptoms became severe.

At the end of this study, the doctors called the participants and asked how they were feeling and learned what medicines the participants were taking since their last dose of study medicine.

The figure below shows how this study was done.



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 the researchers wanted to answer can be found on the websites listed at the end of this summary. If 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.

How did the treatments affect lung function of the participants?

The researchers found that the participants who took either dose of budesonide and formoterol fumarate together had improved lung function compared with the participants who took formoterol fumarate by itself.

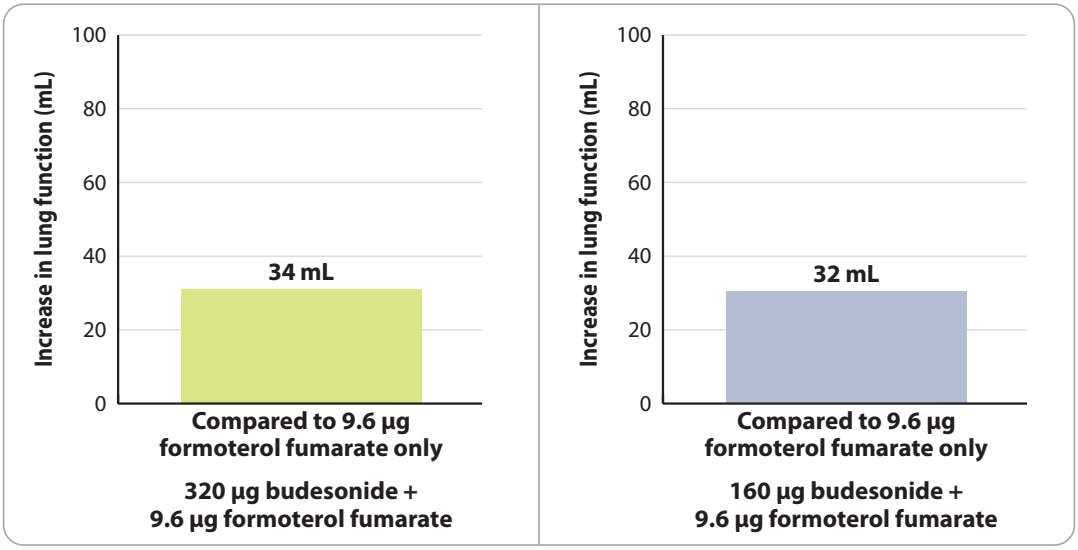
To answer this question, the researchers measured participants' lung function before and after they took the inhaler treatments. This was measured in milliliters, or mL for short.

Lung function at 12 weeks:

- The participants who took 320 µg of budesonide and 9.6 µg of formoterol fumarate together had increased lung function before taking a treatment dose than participants who took formoterol fumarate by itself. They were able to exhale an average of 34 mL more air than participants who took formoterol fumarate by itself.
- The participants who took 160 µg of budesonide and 9.6 µg of formoterol fumarate together had increased lung function before taking a treatment dose than participants who took formoterol fumarate by itself. They were able to exhale an average of 32 mL more air than participants who took formoterol fumarate by itself.

The figure below shows these results.

Increase in lung function at 12 weeks

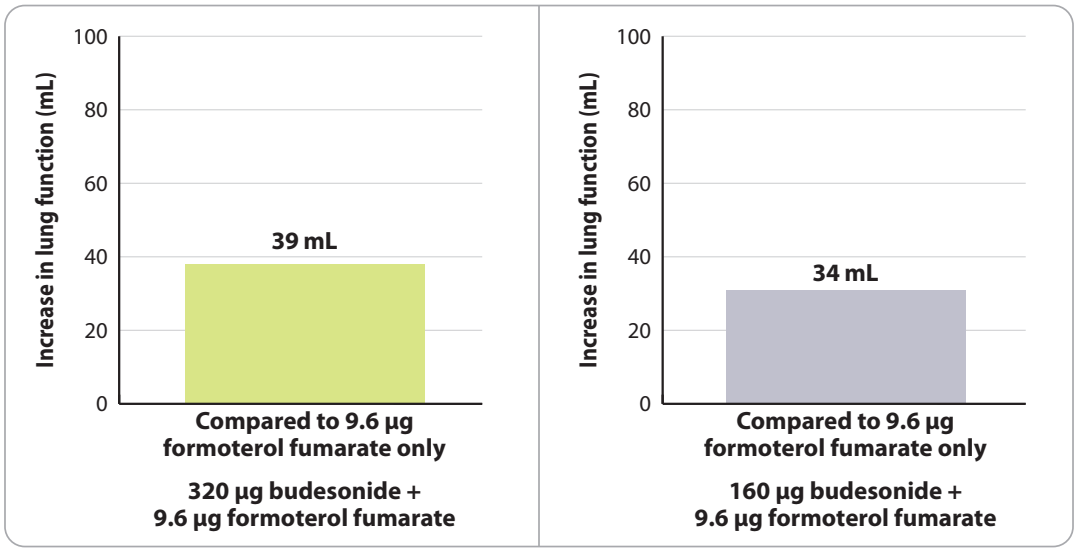


Lung function over 24 weeks:

- The participants who took 320 µg of budesonide and 9.6 µg of formoterol fumarate together had increased lung function before taking a treatment dose than participants who took formoterol fumarate by itself. They were able to exhale an average of 39 mL more air than participants who took formoterol fumarate by itself.
- The participants who took 160 µg of budesonide and 9.6 µg of formoterol fumarate together had increased lung function before taking a treatment dose than participants who took formoterol fumarate by itself. They were able to exhale an average of 34 mL more air than participants who took formoterol fumarate by itself.

The figure below shows these results.

Increase in lung function over 24 weeks



Did the different treatments affect the participants in other ways?

Researchers wanted to know if the study treatment helped participants' COPD symptoms and their ability to do daily activities. To find out, the doctors asked the participants to complete a survey at each of their study visits.

At 12 weeks of treatment, the doctors compared the participants' survey answers to the answers from the first week. The doctors did this again over 24 weeks of treatment.

At 12 weeks and over 24 weeks of treatment, the researchers found that both 320 µg budesonide plus 9.6 µg formoterol fumarate and 160 µg budesonide plus 9.6 µg formoterol fumarate treatments helped improve participants' COPD symptoms and their ability to do daily activities compared with formoterol fumarate by itself.

Researchers also wanted to know if the study treatment helped prevent exacerbations and decrease the need to use rescue medicines over 24 weeks of treatment. An exacerbation is a worsening of COPD symptoms that needs to be treated with corticosteroids and/or antibiotics for at least 3 days, requires hospitalization, or results in death. Doctors kept track of the number of exacerbations that each participant had in the study and of how much rescue medicine each participant used each day. Researchers found that budesonide plus formoterol fumarate helped prevent exacerbations and reduce how often rescue medicine was needed.

What medical problems did participants have during the study?

This section is a summary of the medical problems the participants had during this study that the study doctors thought might be related to the study medicines. 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 medicines. A lot of research is needed to know whether a medicine causes an adverse reaction. The websites listed at the end of this summary may have more information about the adverse reactions or other medical problems that happened during this study.

Some of the participants did not get any doses of study medicines or were not able to complete all study visits, so their information could not be used. Therefore, the researchers studied the medical problems for 1,843 of the 1,876 participants.

How many participants had serious adverse reactions?

There were 0.2% of participants who had serious adverse reactions during this study. This was 3 out of 1,843 participants. The only serious adverse reaction that happened to more than 1 participant was that their COPD symptoms got worse. This happened in 2 participants.

There were 1.2% of participants who died during this study. This was 22 out of 1,843 participants. The doctors did not think that any of these deaths were related to the study medicines.

How many participants had adverse reactions?

There were 4.4% of participants who had adverse reactions during this study. This was 81 out of 1,843 participants.

What adverse reactions did the participants have?

The most common adverse reaction was an infection of the mouth caused by yeast.

The adverse reactions shown in the table below happened in 1.0% or more of participants in any treatment group. There were other adverse reactions, but these happened in fewer participants.

Adverse reactions during this study

	320 µg budesonide + 9.6 µg formoterol fumarate (619 participants)	160 µg budesonide + 9.6 µg formoterol fumarate (617 participants)	9.6 µg formoterol fumarate (607 participants)	All participants (1,843 participants)
Infection of the mouth caused by yeast	1.0% (6)	0.8% (5)	0.8% (5)	0.9% (16)
Difficulty breathing	1.1% (7)	0.5% (3)	0.7% (4)	0.8% (14)

How has this study helped participants and researchers?

This study helped researchers learn how different treatments of budesonide and formoterol fumarate affect the lung function of patients with COPD.

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 in COPD with treatments of budesonide and formoterol fumarate together are not planned.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. If a full report of the study results is available, it can also be found here.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02727660"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home & Search"**. Then, type **"2016-000155-28"** in the search box and click **"Search"**.

Full study title: A Randomized, Double-Blind, Parallel Group, Multi-Center Study to Assess the Efficacy and Safety of PT009 Compared to PT005 in Subjects with Moderate to Very Severe COPD

Protocol number: PT009003

Pearl Therapeutics, Inc., a member of the AstraZeneca Group, sponsored this study and has its headquarters at 280 Headquarters Plaza, Morristown, NJ 07960.

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 participants.

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 patients for clinical studies, nor is it involved in conducting clinical studies.

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