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 about 7 months. But, the entire study took about 1.5 years to complete.

This study started in June 2016 and ended in November 2017. This study included 2,389 participants in Canada, the Czech Republic, Germany, Hungary, Poland, Russia, and the 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.

In this study, budesonide and formoterol fumarate were given in a type of inhaler called a metered dose inhaler, or MDI. These same medicines are also included in another MDI, which is approved in the US and other countries to treat COPD. These medicines are also approved in some countries in a different type of inhaler called a dry powder inhaler, or Turbuhaler, also known as TBH.

In this study, researchers wanted to find out if different treatments of budesonide and formoterol fumarate both used together and separately in a specific MDI work in a large number of participants with moderate to very severe COPD. They also wanted to find out if the participants had any medical problems during the study.

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.

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 from the participants
- 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

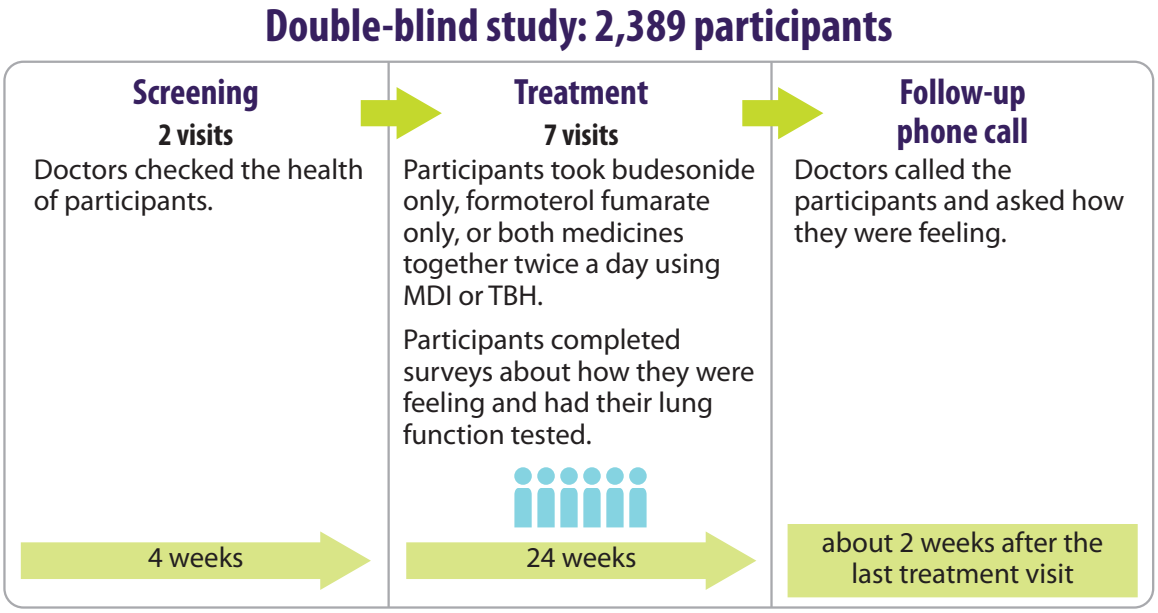
During this study, the participants were asked to visit their study site 7 more times over the next 24 weeks. During this time, the participants took 1 of the following treatments twice a day:

- 664 participants took 320 micrograms, or µg for short, of budesonide and 9.6 µg of formoterol fumarate together, using MDI
- 649 participants took 160 µg of budesonide and 9.6 µg of formoterol fumarate together, using MDI
- 648 participants took 9.6 µg of formoterol fumarate only, using MDI
- 209 participants took 320 µg of budesonide only, using MDI
- 219 participants took 400 µg of budesonide and 12 µg of formoterol fumarate together, using TBH

The participants could also use rescue medicines for COPD provided by the study doctor if they needed it.

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 treatment.

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?

In general, treatments of budesonide and formoterol fumarate together using MDI improved lung function of the participants more than the treatments with either budesonide or formoterol fumarate alone using MDI.

To answer this question, the researchers measured participants' lung function before and after they took the inhaler treatments.

These amounts of air were measured in milliliters, or mL.

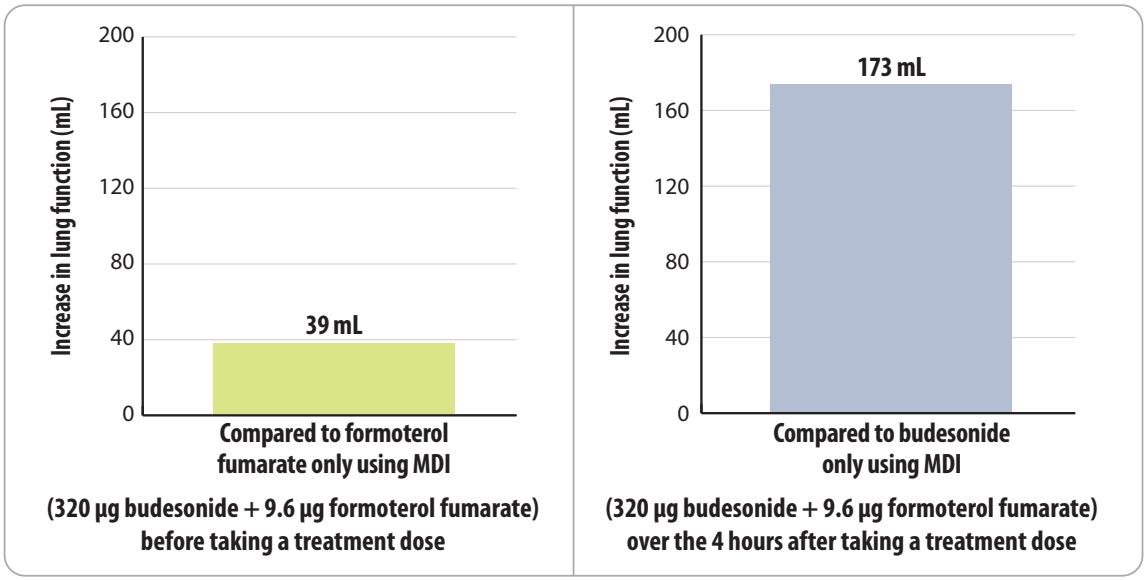
Lung function at 24 weeks:

Researchers measured the participants' lung function at the end of treatment.

- The participants who took 320 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI had more increased lung function before taking a treatment dose compared with participants who took formoterol fumarate by itself using MDI. They were able to exhale an average of 39 mL more air than participants who took formoterol fumarate by itself using MDI.
- The participants who took 320 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI had more increased lung function over the 4 hours after taking a treatment dose compared with participants who took budesonide by itself using MDI. They were able to exhale an average of 173 mL more air than participants who took budesonide by itself using MDI.

The figure below shows these results.

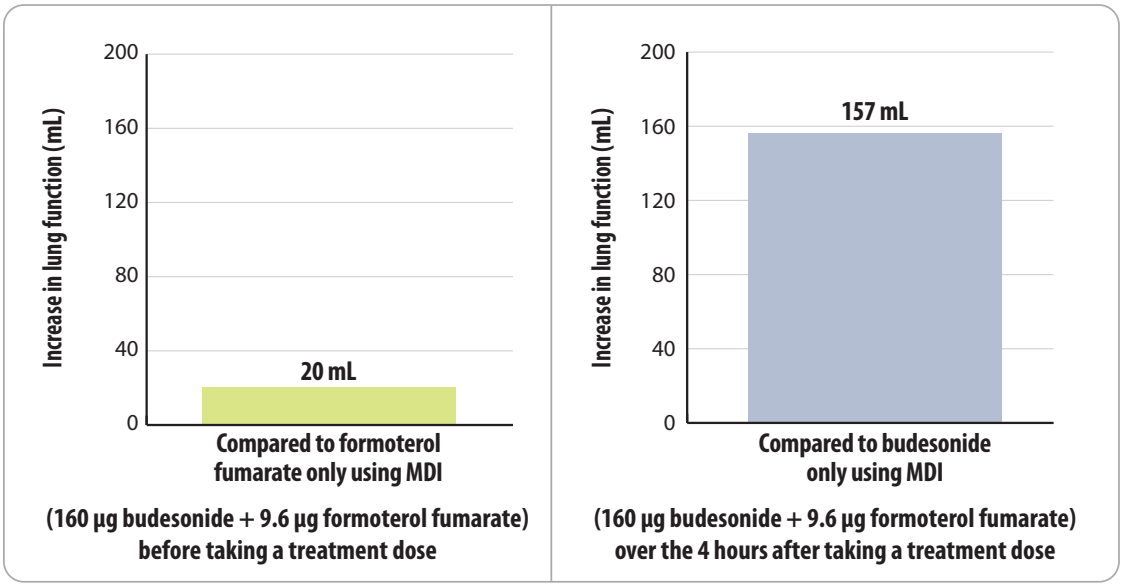
Change in lung function at 24 weeks for participants who took 320 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI



The participants who took 160 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI had more increased lung function over the 4 hours after taking a treatment dose compared with participants who took budesonide by itself using MDI. They were able to exhale an average of 157 mL more air than participants who took budesonide by itself.

The difference in the study medicines was too small for the researchers to know if participants who took 160 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI had more increased lung function before taking a treatment dose compared with participants who took formoterol fumarate by itself using MDI.

Change in lung function at 24 weeks for participants who took 160 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI



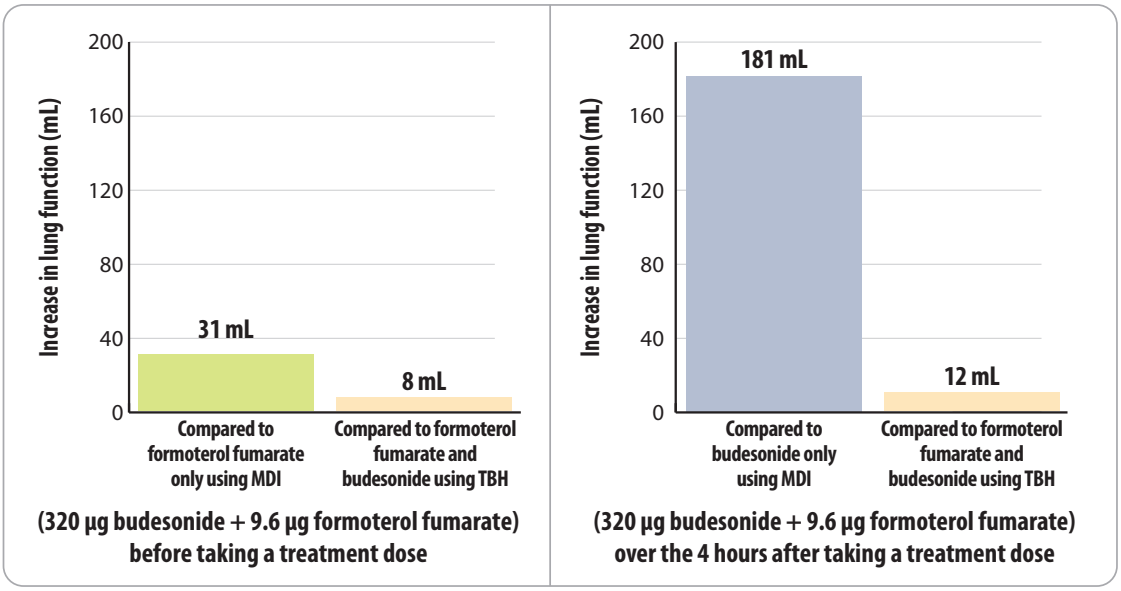
Lung function over 24 weeks

Researchers measured the participants' average lung function over the course of treatment.

- The participants who took 320 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI had more increased lung function before taking a treatment dose compared with participants who took formoterol fumarate by itself using MDI. They were able to exhale an average of 31 mL more air than participants who took formoterol fumarate by itself using MDI.
- The participants who took 320 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI had more increased lung function over the 4 hours after taking a treatment dose compared with participants who took budesonide by itself using MDI. They were able to exhale an average of 181 mL more air than participants who took budesonide by itself using MDI.
- The participants who took 320 µg of budesonide and 9.6 µg of formoterol fumarate together had a similar increase in lung function before taking a treatment dose and at 4 hours after taking a treatment dose compared with participants who took 400 µg of budesonide and 12 µg of formoterol fumarate together using TBH.

The figure below shows these results.

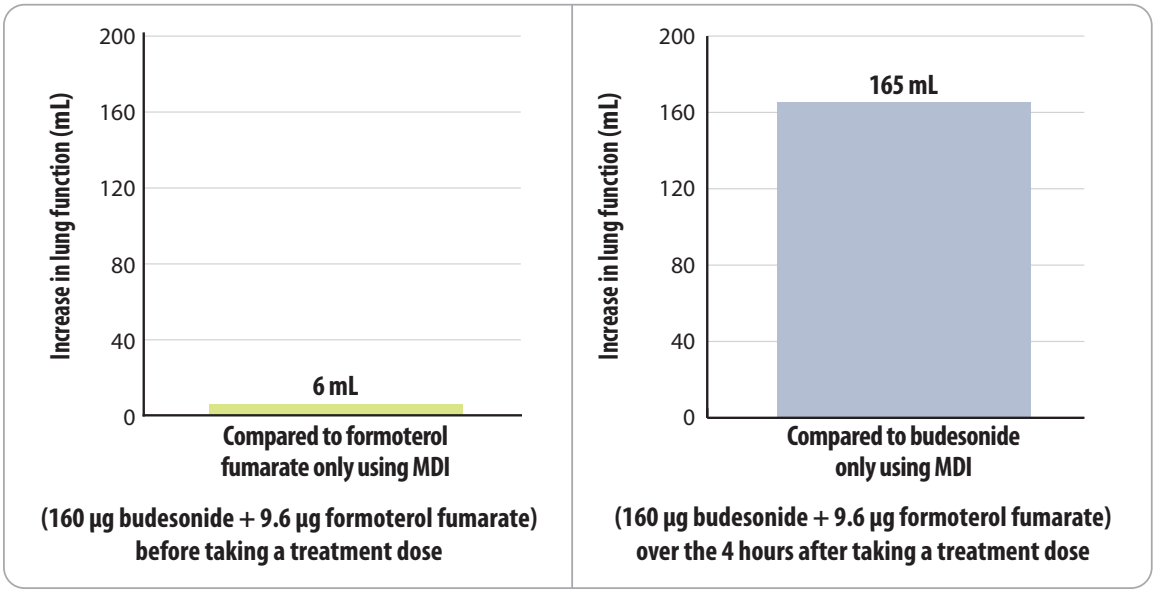
Change in lung function over 24 weeks for participants who took 320 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI



The participants who took 160 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI had more increased lung function over the 4 hours after taking a treatment dose compared with participants who took budesonide by itself using MDI. They were able to exhale an average of 165 mL more air than participants who took budesonide by itself using MDI.

The difference in the study medicines was too small for the researchers to know if participants who took 160 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI had more increased lung function before taking a treatment dose than participants who took formoterol fumarate by itself using MDI.

Change in lung function over 24 weeks for participants who took 160 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI



Did the different treatments affect the participants in other ways?

Researchers wanted to know if the study treatment helped participants' COPD symptoms and ability to do daily activities. To find out, the doctors asked the participants to complete a survey each time they came to the doctor for a study visit.

At 24 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 24 weeks:

- Participants who took 320 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI had more improved COPD symptoms and ability to do daily activities compared with participants who took formoterol fumarate by itself using MDI.
- The difference in the study medicines was too small for the researchers to know if participants who took 320 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI had more improved COPD symptoms and ability to do daily activities compared with participants who took:
  - budesonide by itself using MDI
  - 160 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI
  - 400 µg of budesonide and 12 µg of formoterol fumarate together using TBH
- The difference in the study medicines was too small for the researchers to know if participants who took 160 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI had more improved COPD symptoms and ability to do daily activities compared with participants who took either budesonide or formoterol fumarate by itself using MDI.

Over 24 weeks:

- The difference in the study medicines was too small for the researchers to know if participants who took 320 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI had improved COPD symptoms and ability to do daily activities compared with participants who took either budesonide or formoterol fumarate by itself using MDI.
- Participants who took 320 µg of budesonide and 9.6 µg of formoterol fumarate together using MDI had similar improvement in COPD symptoms and ability to do daily activities compared with participants who took 400 µg of budesonide and 12 µg of formoterol fumarate together using TBH.
- The difference in the study medicines was too small for the researchers to know if participants who took 160 µg of budesonide and 9.6 µg of formoterol fumarate together had more improved COPD symptoms and ability to do daily activities compared with participants who took either budesonide or formoterol fumarate by itself using MDI.

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, and some participated in other studies, so their information could not be used. Therefore, the researchers studied the medical problems for 2,361 of the 2,389 participants.

How many participants had serious adverse reactions?

There were 0.2% of participants who had serious adverse reactions during this study. This was 5 out of 2,361 participants.

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

Serious adverse reactions during this study

	320 µg budesonide + 9.6 µg formoterol fumarate (655 participants)	160 µg budesonide + 9.6 µg formoterol fumarate (637 participants)	9.6 µg formoterol fumarate (644 participants)	320 µg budesonide (206 participants)	400 µg budesonide + 12 µg formoterol fumarate (219 participants)
Lung infection	0.3% (2)	0.2% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Sudden lung failure	0.2% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Chest pain due to lack of oxygen and blood flow to the heart	0.0% (0)	0.2% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Life-threatening high blood pressure	0.0% (0)	0.2% (1)	0.0% (0)	0.0% (0)	0.0% (0)

There were 0.5% of participants who died during this study. This was 12 out of 2,361 participants. The researchers did not think that any of these deaths were related to the study medicines.

How many participants had adverse reactions?

There were 7.0% of participants who had adverse reactions during this study. This was 165 out of 2,361 participants.

There were 1.5% of participants who stopped taking treatment because of adverse reactions that they had during this study. This was 36 out of 2,361 participants.

What adverse reactions did the participants have?

The most common adverse reactions were hoarse voice and infection of the mouth caused by yeast.

The adverse reactions below happened in 2.0% 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 (655 participants)	160 µg budesonide + 9.6 µg formoterol fumarate (637 participants)	9.6 µg formoterol fumarate (644 participants)	320 µg budesonide (206 participants)	400 µg budesonide + 12 µg formoterol fumarate (219 participants)
Hoarse voice	2.1% (14)	1.7% (11)	0.2% (1)	1.0% (2)	0.5% (1)
Infection of the mouth caused by yeast	2.0% (13)	1.6% (10)	0.3% (2)	0.5% (1)	1.4% (3)
Difficulty breathing	0.5% (3)	0.5% (3)	0.5% (3)	2.4% (5)	0.0% (0)

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 **"NCT02766608"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu . Once you are on the website, click **"Home & Search"**. Then type **"2016-000154-34"** 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, PT008, and Open-label Symbicort® Turbuhaler®, as an Active Control, on Lung Function over a 24-Week Treatment Period in Subjects With Moderate to Very Severe COPD

Protocol number: PT009002

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

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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