Clinical Study Results

Pearl™
A member of the AstraZeneca Group

Research Sponsor: Pearl Therapeutics, Inc.

Treatments Studied: GP MDI and FF MDI

Study Title: A study to find out how GP MDI and FF MDI affect the lungs of participants with COPD

Thank you!

Thank you for taking part in the clinical study for the study treatments GP MDI, also called glycopyrronium metered dose inhaler, and FF MDI, also called formoterol fumarate metered dose inhaler.

You and all of the participants helped researchers learn more about how GP MDI and FF MDI may help people with chronic obstructive pulmonary disease, also called COPD.

Pearl Therapeutics, Inc. 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. 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 doctor or staff at your study site.

What is happening with the study now?

The participants were in the study for up to 12 weeks. But, the entire study took about 1.5 years to finish. The study started in December 2016 and ended in May 2018.

The study included 23 participants in Belgium. Some of the participants did not complete the study. One participant left the study after taking GP MDI only, and 3 participants left the study after taking FF MDI only. All 4 participants left the study because of worsening COPD.

The sponsor reviewed the data collected when the 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. Researchers do clinical studies to find out how a drug works and how safe it is.

In this study, the researchers wanted to find out how GP MDI and FF MDI work in participants with moderate to severe COPD. They also wanted to find out if the participants had any medical problems during the study.

COPD is a lung disease that blocks the airways and makes it hard for air to flow in and out of the lungs. It also causes shortness of breath. COPD gets worse over time. Most people who develop COPD are current or former smokers.

GP MDI and FF MDI work by expanding the airways in the lungs. This can help patients breathe better.

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

- Did GP MDI and FF MDI affect the participants' lung airways?
- What medical problems did the participants have during the study?

To answer the questions in this study, the researchers asked for the help of people with moderate to severe COPD. The men and women in this study were 41 to 78 years old.

All of the participants in the study had smoked for at least 10 "pack-years". This is about the same as smoking an average of at least 1 pack of cigarettes a day for 10 years.

What kind of study was this?

This was a "double-blind" study. This means none of the participants, doctors, other study staff, or the study sponsor 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 the participants took so they could create a report of the study results.

All the participants were asked to take both GP MDI and FF MDI at separate times during the study. Some participants took GP MDI first and some participants took FF MDI first.

A computer program was used to randomly choose the order of the treatments 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.

The participants took both treatments through a metered dose inhaler. A metered dose inhaler is a device that delivers a certain amount of medicine for the participant to inhale. The doses of the study treatments were measured in micrograms, also called µg.

Participants took:

- 14.4 µg of GP MDI 2 times a day for 2 weeks
- 9.6 µg of FF MDI 2 times a day for 2 weeks

The participants took a standard COPD maintenance medicine called Atrovent HFA for 7 to 21 days before taking the study treatments. This was done so that the participants would still get a COPD medicine when they stopped taking their usual COPD medicine. They also took Atrovent HFA between treatments.

If the participants had COPD symptoms that needed treatment right away, they took Ventolin HFA to relieve their COPD symptoms. This is another standard COPD maintenance medicine. In this study, it was used as a "rescue medicine" to treat sudden symptoms of COPD.

What happened during the study?

Before treatment, the doctors and nurses did tests to make sure the participants could join the study. The participants were asked to stop taking certain COPD medications. This was done so that the researchers could be sure that any effects seen during the study were due to the study treatment, and not due to other reasons.

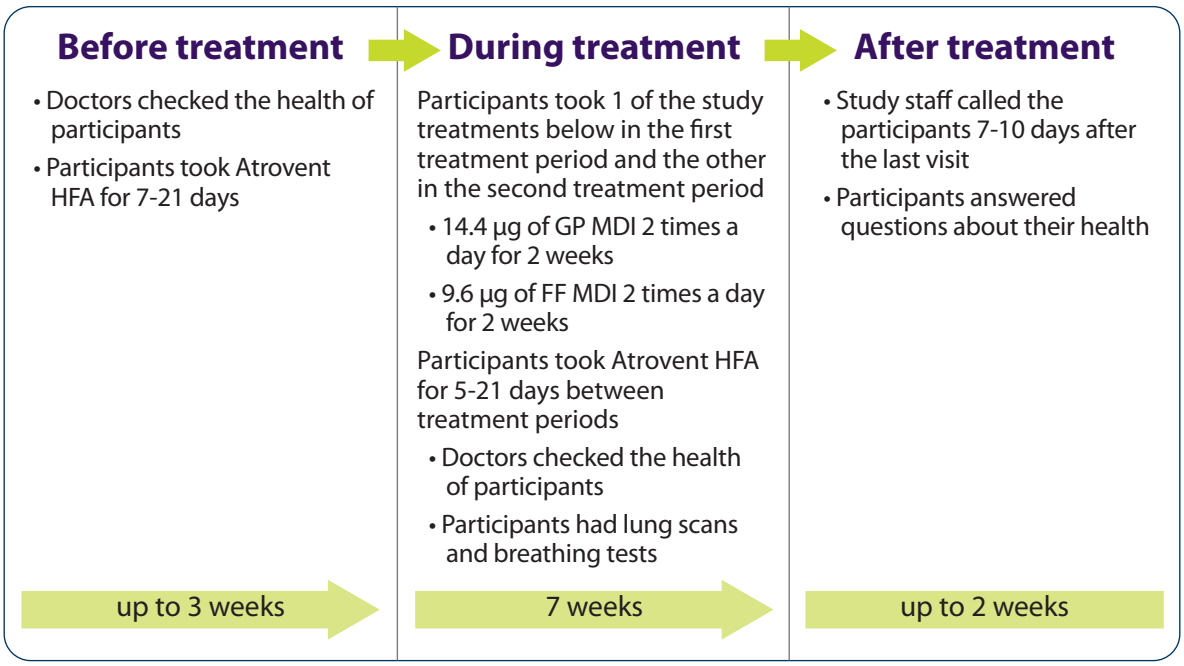
During treatment, each participant was asked to take GP MDI and FF MDI. First they took GP MDI or FF MDI 2 times a day for 2 weeks. After waiting 5 to 21 days, the participants took the other treatment 2 times a day for 2 weeks. This was done so that the first study treatment they took could leave the body before they started taking the other treatment. The participants took Atrovent HFA between the treatment periods to control their COPD.

The doctors and nurses did tests and scans of the lungs to check the participants' health, breathing, and lungs. They also took blood and urine samples. The participants answered questions about their smoking, how they were feeling, and what medicines they were taking.

Before treatment, the participants used a paper diary. They recorded when they took the study treatments, Atrovent HFA, and Ventolin HFA. They also recorded their COPD symptoms in the paper diary so the researchers could follow what happened to the participants during the study.

After treatment, the participants started taking their usual COPD medications again. The study staff called the participants 7 to 10 days after the last visit to ask them questions about their smoking, how they were feeling, and what medicines they were taking.

The figure below shows how the 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 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.

There were 4 participants who left the study during the first treatment period. All 4 participants left the study because of COPD that got worse.

- 1 participant left the study after taking GP MDI.
- 3 participants left the study after taking FF MDI.

Did GP MDI and FF MDI affect the participants' lung airways?

Yes. The participants had more airway volume in the lungs after taking GP MDI and after taking FF MDI. They also had less airway resistance after taking the 2 treatments. When there is more airway volume and less airway resistance in the lungs, it improves breathing.

To answer this question, the researchers used a new type of measurement called "functional respiratory imaging", also called FRI. FRI measurements were done after taking very detailed pictures of the lungs. The study staff took the pictures using a scan called "high-resolution computed tomography", also called HRCT. These scans help doctors look at the inside of the airways and the lungs.

Two measurements were done using FRI:

- airway volume, also called siVaw
- airway resistance, also called siRaw

The researchers took the FRI measurements before the patients took each study treatment and compared them to the measurements after the patients took the last dose of each study treatment. They calculated the difference in the results before and after treatment as a percentage.

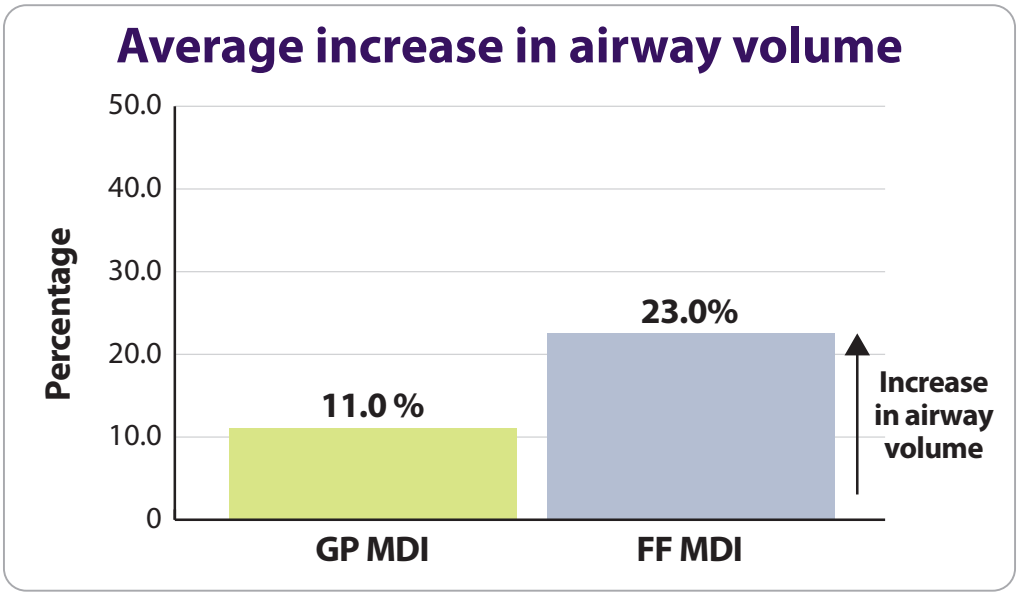
- An increase in airway volume means it might be easier to breathe.
- A decrease in airway resistance means it might be easier to breathe.

Airway volume

The researchers found that:

- When participants took GP MDI, the airway volume increased by 11.0%.
- When participants took FF MDI, the airway volume increased by 23.0%.

These results are shown in the figure below.

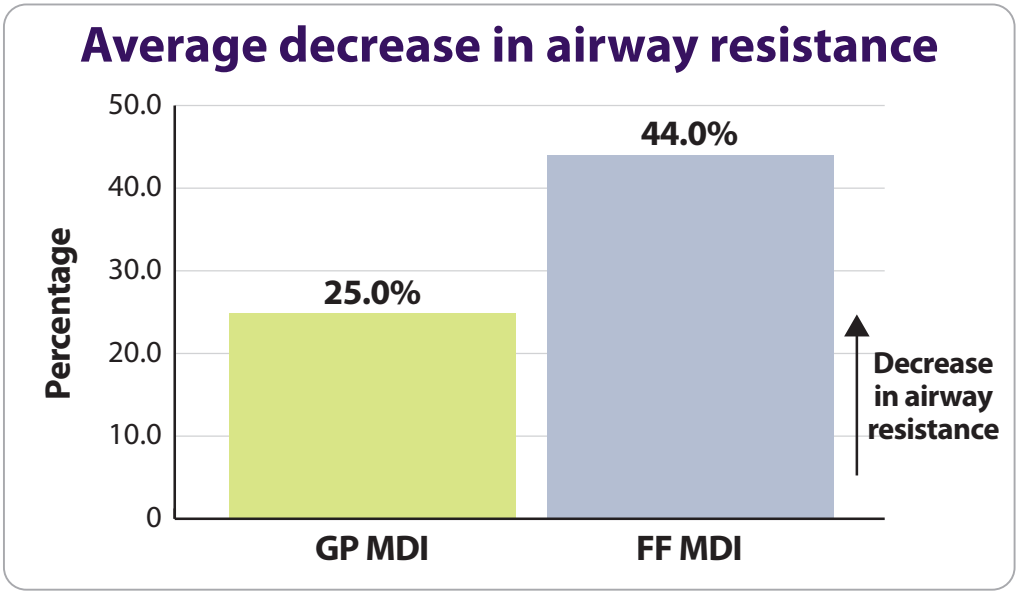


Airway resistance

The researchers found that:

- When participants took GP MDI, the airway resistance decreased by 25.0%.
- When participants took FF MDI, the airway resistance decreased by 44.0%.

These results are shown in the figure below.



What medical problems did the participants have?

The medical problems that participants have during clinical studies that the doctors think might be related to the study treatments are called “adverse reactions”. An adverse reaction is considered “serious” when it is life threatening, causes lasting problems, or requires hospital care.

The adverse reactions that happen in a study may or may not be caused by the study treatments. A lot of research is needed to know whether a drug causes an adverse reaction.

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.

How many participants had serious adverse reactions?

None of the participants had serious adverse reactions in this study. None of the participants died during the study.

How many participants had adverse reactions?

There were 8.7% of participants who had adverse reactions during the study. This was 2 out of 23 participants.

- 1 participant had 2 adverse reactions while taking GP MDI. These were problems breathing when moving the body and an increase of mucus in the lungs.
- 1 participant had an adverse reaction of worsening COPD while taking FF MDI.

There were 4.3% of participants who left the study early because of an adverse reaction they had during the study. This was 1 out of 23 participants. The adverse reaction happened while the participant was taking FF MDI.

How has this study helped patients and researchers?

This study helped researchers learn more about how GP MDI and FF MDI work to treat participants with COPD. It also helped them learn more about using the FRI to look at airway volume and airway resistance.

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 clinical studies comparing GP MDI and FF MDI are not planned at this time.

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 **"NCT02937584"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search"**, then type **"2015-001744-11"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"PT003019"** into the search box, and click **"Find a Study"**.

Full study title: A Randomized, Double-Blind, Two Treatment, Two Period, Chronic Dosing (2 Weeks), Cross-Over, Multi-Center Study to Evaluate the Effects of PT001 and PT005 on Specific Image Based Airway Volumes and Resistance in Subjects With Moderate to Severe COPD.

AstraZeneca protocol number: PT003019

Pearl Therapeutics, Inc., a member of the AstraZeneca Group, sponsored this study and has its headquarters at
Pearl Therapeutics, Inc. 200 Cardinal Way, 2nd Floor Redwood City, CA 94063

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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