Clinical Study Results

Pearl™
A member of the AstraZeneca Group

Research Sponsor: Pearl Therapeutics, Inc.

Drug Studied: Glycopyrronium inhalation aerosol, also called GP MDI or PT001

Study Title: A study to learn how different doses of GP MDI affected participants with asthma

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Thank you!

Thank you to the participants who took part in the clinical study for the study drug glycopyrronium inhalation aerosol, also called PT001 or GP MDI. All of the participants helped researchers learn more about GP MDI to help people who have asthma.

Pearl Therapeutics, Inc sponsored this study and thinks it is important to share the results of the study with the public. An independent non-profit organization called CISCRP helped prepare this summary of the study results.

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 7 months, but the entire study took 22 months to finish. The study started in December 2017 and ended in September 2019.

This study included a total of 1,077 participants in the United States.

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 people who have asthma. Before a drug can be approved for patients to take, researchers do clinical studies to find out how safe it is and how it works.

In this study, the researchers wanted to find out if GP MDI works in a large number of people with asthma. They also wanted to find out if the participants had any medical problems during the study.

Asthma is a condition that causes the airways to narrow. This makes it difficult to breathe. People with asthma can have wheezing, coughing, shortness of breath, and chest tightness. There are treatments that can help control asthma symptoms, but some people may still have uncontrolled asthma. This means that existing treatments do not fully control their asthma.

Asthma treatments are usually taken through an inhaler. GP MDI is taken through a "metered dose" inhaler that delivers a specific amount of the study drug to the lungs.

GP MDI is a "long-acting" study drug that works by relaxing muscles in the breathing tubes to allow more air into the lungs. This makes it easier to breathe.

In this study, the researchers wanted to find out how different doses of GP MDI affected the participants' asthma.

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

- Did GP MDI affect the amount of air the participants could breathe out?
- Did the participants' quality of life change after taking GP MDI?
- What medical problems did the participants have during the study?

To answer the questions in this study, the researchers asked for the help of men and women with asthma that had not been controlled by inhaler treatments. The participants in this study were 12 to 80 years old when they joined. The participants were not taking steroid tablets for their asthma, and were not current smokers.

What kind of study was this?

In this study, the researchers compared GP MDI to a common asthma treatment called Spiriva Respimat, and to 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 drug are actually caused by the drug.

There were 2 parts to this study, and they happened at the same time. There was 1 part that was “double-blind”. This means none of the participants, study 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.

In the double-blind part of the study, the participants took their regular asthma inhaler with either GP MDI or the placebo MDI. The doses of GP MDI were measured in micrograms, also known as µg. The participants took 2 puffs of their inhaler twice a day. There were 4 different treatment groups in this part:

- 237 participants were planned to take 28.8 µg of GP MDI
- 241 participants were planned to take 14.4 µg of GP MDI
- 241 participants were planned to take 7.2 µg of GP MDI
- 238 participants were planned to take the placebo MDI

There was also an “open-label” part of the study. This means the researchers and the participants knew what the participants in this part were taking. In this part of the study, 120 participants were planned to take Spiriva Respimat MDI as well as their regular asthma inhaler. They took 2 puffs of the Spiriva Respimat inhaler once a day. The dose of Spiriva Respimat was 2.5 µg.

A computer program was used to randomly choose the treatment or dose each participant took. This helps make sure the groups are chosen fairly. Researchers do this so that comparing the results of each treatment or dose is as accurate as possible.

What happened during the study?

Before the participants took study treatment, they visited their study site 3 times up to 4 weeks before they started the study. At these visits, the study doctors checked the overall health of the participants to make sure that they could join the study. The study doctors:

- did a physical exam and checked the participants' vital signs
- took blood and urine samples
- asked about the participants' medical history
- asked about the participants' asthma and any medications they were taking
- measured the participants' lung health by having them blow into a spirometer
- checked the participants' heart health using an electrocardiogram, also called an ECG
- gave the participants a questionnaire about their asthma

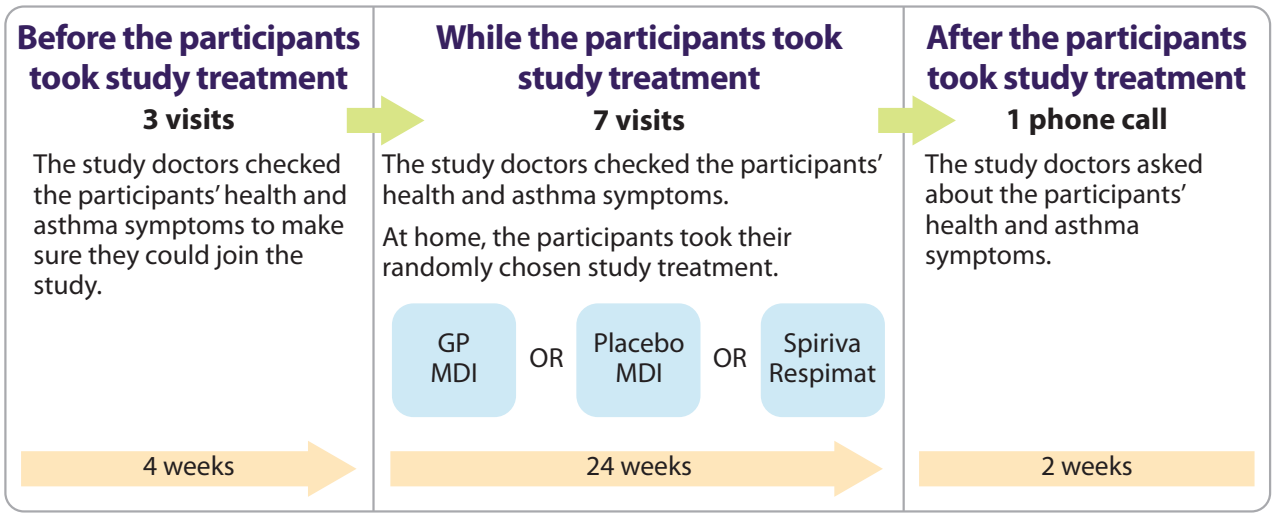
The doctors also did these tests and measurements throughout the study.

While the participants took study treatment as well as their regular asthma inhaler, they visited their study site 7 times over 24 weeks. At each site visit, the study doctors checked the health of participants.

At some visits, the study doctors checked the participants' heart health using an ECG.

On the days when participants did not visit the study site, they took their treatment by MDI inhaler every day at home.

About 2 weeks after the participants finished taking study treatment, the study doctors called them to ask about their asthma and any medications they were taking.



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 11 participants who did not finish taking all of their study treatments. So, the results below include information for 1,066 out of 1,077 participants.

Did GP MDI affect the amount of air the participants could breathe out?

To answer this question, the study doctors measured the amount of air the participants breathed out in 1 second. They did this 15 minutes after the participants took their treatment as well as their regular asthma inhaler. The study doctors repeated this measurement 4 times during the first 4 hours after the participants took their treatment. The researchers then calculated the average amount of air that was breathed out. This was measured in liters, also called L. They compared the amount breathed out after 24 weeks of treatment to the amount breathed out before the participants started treatment.

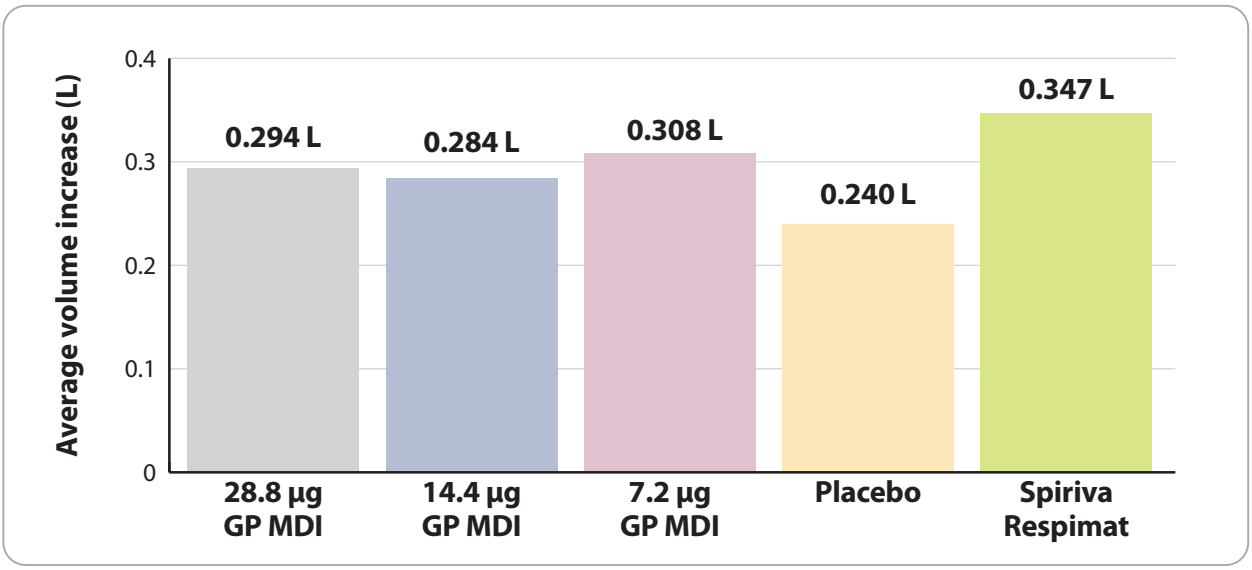
The researchers found that in each treatment group, the participants could breathe out more air after 24 weeks of treatment. This amount increased more in the participants who took 7.2 µg of GP MDI compared to the participants who took the placebo. But, the differences between the other GP MDI treatment groups and the placebo were too small for the researchers to know for sure if GP MDI affected the participants' breathing.

The researchers found that after 24 weeks of taking study treatment:

- The participants taking 28.8 µg of GP MDI breathed out an average of 0.294 L more air than they did at the start of the study.
- The participants taking 14.4 µg of GP MDI breathed out an average of 0.284 L more air than they did at the start of the study.
- The participants taking 7.2 µg of GP MDI breathed out an average of 0.308 L more air than they did at the start of the study.
- The participants taking the placebo breathed out an average of 0.240 L more air than they did at the start of the study.
- The participants taking 2.5 µg of Spiriva Respimat breathed out an average of 0.347 L more air than they did at the start of the study.

The chart below shows these results.

Average increase in the amount of air the participants could breathe out after 24 weeks



Did the participants' quality of life change after getting GP MDI?

Overall, the researchers could not conclude that GP MDI changed the participants' quality of life.

To answer this question, the doctors asked the participants to answer 3 different questionnaires before and after they took study treatment. These questionnaires were the Asthma Control Questionnaire 5 and 7, also called ACQ-5 and ACQ-7, and the Asthma Quality of Life Questionnaire, also called AQLQ.

The questionnaires asked how the participants felt about their asthma symptoms and about their quality of life. The doctors gave the participants a score based on their answers.

The researchers compared the participants' scores before and after they took study treatment. Overall, the differences between the GP MDI groups and the placebo and Spiriva Respimat groups were too small for the researchers to know if GP MDI changed the participants' quality of life.

What medical problems did participants have during the 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 treatments. 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 treatments cause 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.

There were 6 participants who joined the study, but never took any study treatment. So, the results below include information for 1,071 out of the 1,077 participants.

How many participants had serious adverse reactions?

Less than 0.1% of participants had serious adverse reactions during the study. This was 1 out of the 1,071 participants. This participant was in the placebo group and had the serious adverse reaction of an asthma attack.

None of the participants died due to serious adverse reactions in this study.

How many participants had adverse reactions?

There were 2.6% of participants who had adverse reactions during the study. This was 28 out of the 1,071 participants.

There were 0.8% of participants who stopped taking study treatment because of adverse reactions they had during the study. This was 9 out of the 1,071 participants.

The table below shows which treatment groups these participants were in.

	28.8 µg GP MDI (out of 235 participants)	14.4 µg GP MDI (out of 240 participants)	7.2 µg GP MDI (out of 240 participants)	Placebo (out of 237 participants)	Spiriva Respimat (out of 119 participants)
How many participants had adverse reactions?	2.1% (5)	2.5% (6)	3.8% (9)	2.5% (6)	1.7% (2)
How many participants stopped taking study treatment because of adverse reactions?	0.4% (1)	0.8% (2)	2.1% (5)	0.4% (1)	0.0% (0)

What adverse reactions did the participants have?

The most common adverse reaction was having a dry mouth.

The table below shows the most common adverse reactions that happened in 2 or more participants during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions during the study

Adverse Reactions	28.8 µg GP MDI (out of 235 participants)	14.4 µg GP MDI (out of 240 participants)	7.2 µg GP MDI (out of 240 participants)	Placebo (out of 237 participants)	Spiriva Respimat (out of 119 participants)
Dry mouth	0.9% (2)	0.0% (0)	0.0% (0)	0.4% (1)	1.7% (2)
Headache	0.9% (2)	0.0% (0)	0.4% (1)	0.0% (0)	0.0% (0)
Loss of voice	0.4% (1)	0.4% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Infection of the main airways of the lungs	0.0% (0)	0.0% (0)	0.4% (1)	0.4% (1)	0.0% (0)
Sore throat	0.0% (0)	0.0% (0)	0.8% (2)	0.0% (0)	0.0% (0)
Chest discomfort	0.0% (0)	0.4% (1)	0.4% (1)	0.0% (0)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn more about how GP MDI affects breathing in participants with asthma that had not been controlled by their usual asthma treatments.

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 with GP MDI are not planned.

Where can I learn more about the 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 **"NCT03358147"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"PT001102-04"** into the search box and click **"Find a Study"**.

Full study title: A Randomized, Double-Blind, Parallel Group, Multi-Center 24-Week Study Comparing the Efficacy and Safety of Three Doses of PT001 to Placebo and Open-label Spiriva® Respimat® in Subjects With Persistent Asthma

National Clinical Trial number: NCT03358147

Pearl Therapeutics, Inc Protocol Number: PT001102-04

Pearl Therapeutics, Inc., sponsored this study and has its headquarters in Redwood City, CA, USA

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 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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