Clinical Study Results

AstraZeneca

Research Sponsor: Pearl Therapeutics, Inc.

Drugs Studied: BGF MDI, GFF MDI, and BFF MDI

Study Title: A study to find out how BGF MDI affected flare-ups compared to GFF MDI and BFF MDI in participants with chronic obstructive pulmonary disorder

Thank you

Thank you for taking part in the clinical study for the study treatments BGF MDI, GFF MDI, and BFF MDI.

- BGF is also called budesonide glycopyrronium formoterol fumarate.
- GFF is also called glycopyrronium formoterol fumarate.
- BFF is also called budesonide formoterol fumarate.

You and all of the participants helped researchers learn more about BGF MDI, GFF MDI, and BFF MDI to help people with chronic obstructive pulmonary disorder.

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 organisation 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 of this study

Why was the research needed?

Researchers are looking for a better way to treat chronic obstructive pulmonary disorder, also called COPD. Before a treatment can be approved for participants 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 took 1 of 4 treatments through an inhaler:

- a “standard” dose of BGF MDI
- a “low” dose of BGF MDI
- GFF MDI
- BFF MDI

What were the results of the study?

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

- **Did the participants who took BGF MDI have COPD flare-ups less often?**
  Yes. Overall, the researchers found that the participants who took BGF MDI had COPD flare-ups less often than those who took GFF MDI or BFF MDI.
- **Did the participants feel their quality of life changed after taking BGF MDI?**
  Yes. Overall, the researchers found that the participants who took BGF MDI felt that it helped their quality of life compared to those who took GFF MDI or BFF MDI.
- **What medical problems did the participants have during the study?**
  There were 9.3% of participants who had medical problems during the study that the study doctors thought might be related to the study treatments. The most common medical problem was a yeast infection around the mouth.

Where can I learn more about this study?

You can find out more information about this study on the websites listed on the last page. When a full report of the study results is available, it can also be found on those websites.

Who took part in the study?

The researchers asked for the help of men and women with COPD. The participants in this study were 40 to 81 years old when they joined. 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.

The study included 8,588 participants in Argentina, Australia, Austria, Belgium, Canada, Chile, China, the Czech Republic, France, Germany, Hungary, Italy, Japan, Mexico, the Netherlands, New Zealand, Peru, Poland, Russia, Serbia, South Africa, Spain, Sweden, Taiwan, the United Kingdom, and the United States.

Why was the research needed?

Researchers are looking for a better way to treat COPD. 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.

COPD is a lung disease that causes blocked airways and inflammation, making 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. People with COPD often have periods of worse symptoms, also known as “flare-ups”.

BGF MDI, GFF MDI, and BFF MDI are inhalers that work by expanding the airways in the lungs and reducing inflammation. This can help people with COPD breathe more easily.

In this study, the researchers wanted to find out if BGF MDI works in a large number of participants with COPD to reduce flare-ups. They wanted to compare BGF MDI to GFF MDI and BFF MDI. They also wanted to find out if the participants had any medical problems during the study.

What was the purpose of this study?

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

- Did the participants who took BGF MDI have COPD flare-ups less often?
- Did the participants feel their quality of life changed after taking BGF MDI?
- 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 BGF MDI helps improve the health of people with COPD compared with GFF MDI and BFF MDI.

What treatments did the participants take?

In this study, the participants took their treatment through an MDI, also called a metered dose inhaler. An MDI is a device that delivers a specific amount of a treatment for the participant to breathe in. The participants took 2 puffs of their treatment twice a day.

The participants took either:

- a “standard” dose of BGF MDI
- a “low” dose of BGF MDI
- GFF MDI
- BFF MDI

The doses were measured in micrograms, also known as µg. These are shown in the chart below.

	Dose of budesonide	Dose of glycopyrronium	Dose of formoterol fumarate
Standard dose of BGF MDI	320 µg	14.4 µg	9.6 µg
Low dose of BGF MDI	160 µg	14.4 µg	9.6 µg
GFF MDI	None	14.4 µg	9.6 µg
BFF MDI	320 µg	None	9.6 µg

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 taking. 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.

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.

There were 4 different treatment groups in the study. The chart below shows the different treatments the participants took.

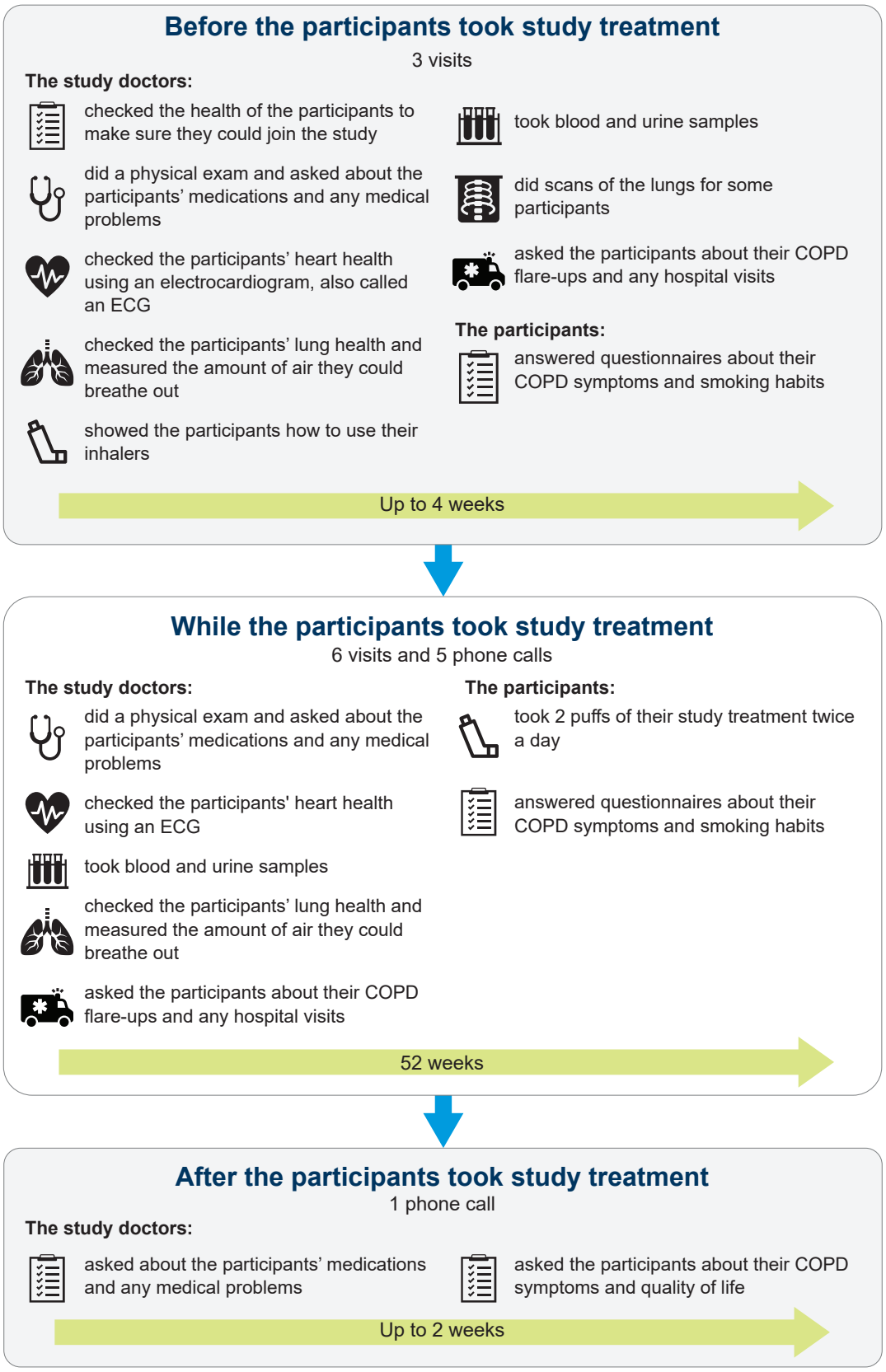
Standard dose of BGF MDI	2,157 participants 2 puffs a day through an MDI inhaler
Low dose of BGF MDI	2,137 participants 2 puffs a day through an MDI inhaler
GFF MDI	2,143 participants 2 puffs a day through an MDI inhaler
BFF MDI	2,151 participants 2 puffs a day through an MDI inhaler

What happened during the study?

The participants were in the study for up to 14 months. But, the entire study took 4 years to finish.

The study started in July 2015 and ended in July 2019.

The chart below shows what happened during the study.



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. 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.

The results below are for 8,509 out of 8,588 participants who took at least 1 dose of study treatment and had measurements taken.

Did the participants who took BGF MDI have COPD flare-ups less often?

Yes. Overall, the researchers found that the participants who took either dose of BGF MDI had COPD flare-ups less often compared with the participants who took GFF MDI or BFF MDI.

To answer this question, the researchers counted the number of times the participants had COPD flare-ups during the study that led to the participants needing additional treatment or hospitalization. Then, they calculated what the rate of COPD flare-ups per year would be for a participant in each of the BGF groups, compared to the other treatment groups. This comparison is known as the “risk reduction” and is measured as a percentage.

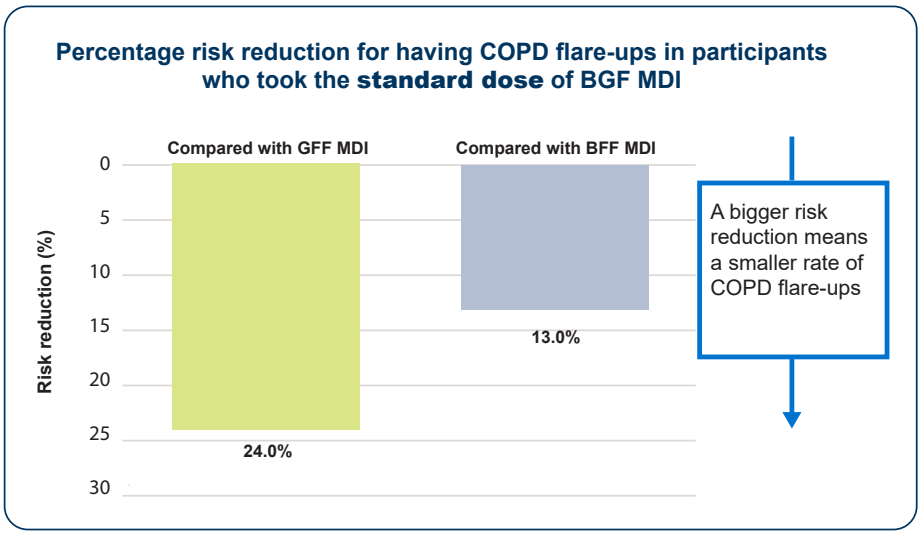
The researchers found that the participants taking the standard dose of BGF MDI had:

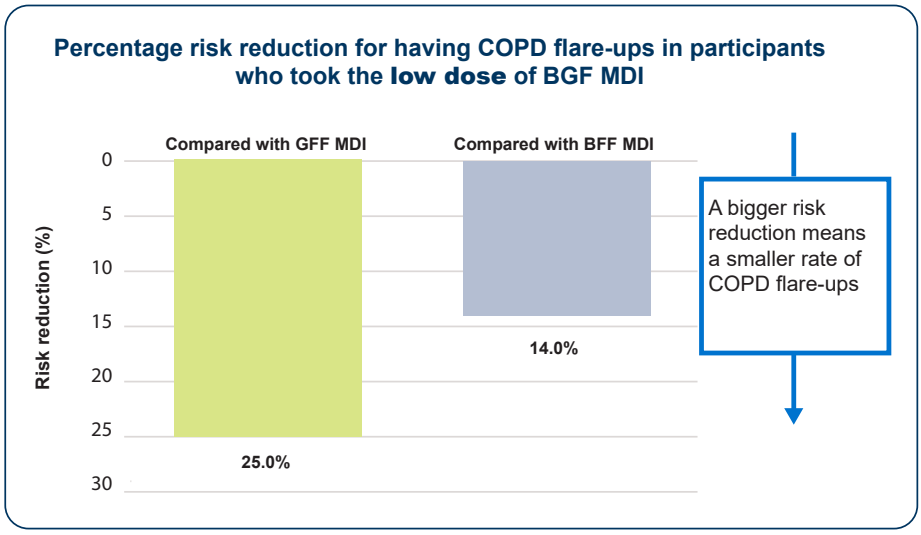
- 24.0% less COPD flare-ups than the participants taking GFF MDI
- 13.0% less COPD flare-ups than the participants taking BFF MDI

The researchers found that the participants taking the low dose of BGF MDI had:

- 25.0% less COPD flare-ups than the participants taking GFF MDI
- 14.0% less COPD flare-ups than the participants taking BFF MDI

These results are shown in the graphs below.





Did the participants feel their quality of life changed after taking BGF MDI?

Yes. Overall, the researchers found that the participants who took either dose of BGF MDI felt that it helped their quality of life compared to those who took GFF MDI or BFF MDI.

To answer this question, the study doctors asked the participants to answer 2 questionnaires about their COPD symptoms and quality of life:

- St. George's Respiratory Questionnaire, also called SGRQ
- Exacerbations of Chronic Pulmonary Disease Tool, also called EXACT

For each questionnaire, the study doctors calculated scores from 0 to 100 based on the participants' responses. The higher the score, the more a participant's COPD symptoms were affecting their quality of life.

For each questionnaire, the researchers calculated the average score for the participants in each group. For SGRQ, they compared the average score over the first 24 weeks of treatment with the average score before the participants started taking treatment. For EXACT, they compared the average score over 52 weeks of treatment with the average score before the participants started taking treatment.

Over 24 weeks of treatment, the researchers found that the participants' SGRQ scores decreased by an average of:

- 6.5 points for the participants taking the standard dose of BGF MDI
- 6.2 points for the participants taking the low dose of BGF MDI
- 4.9 points for the participants taking GFF MDI
- 5.1 points for the participants taking BFF MDI

Over 52 weeks of treatment, the researchers found that the participants' EXACT scores decreased by an average of:

- 1.8 points for the participants taking the standard dose of BGF MDI
- 1.6 points for the participants taking the low dose of BGF MDI
- 0.7 points for the participants taking GFF MDI
- 0.8 points for the participants taking BFF MDI

What medical problems happened 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 treatment. 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 the 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.

The results below are for 8,529 out of 8,588 participants who took at least 1 dose of study treatment and had measurements taken.

Did any adverse reactions happen during this study?

	Standard dose of BGF MDI (out of 2,144 participants)	Low dose of BFF MDI (out of 2,124 participants)	GFF MDI (out of 2,125 participants)	BFF MDI (out of 2,136 participants)
How many participants had adverse reactions?	10.4% (222)	9.4% (200)	7.1% (151)	10.3% (220)
How many participants had serious adverse reactions?	1.3% (27)	1.7% (37)	0.9% (19)	1.3% (27)
How many participants stopped taking study treatment because of adverse reactions?	1.5% (33)	1.1% (24)	1.3% (28)	1.8% (38)

What serious adverse reactions happened during this study?

The most common serious adverse reaction was worsening of COPD symptoms.

The table below shows the serious adverse reactions that happened in more than 1 participant. There were other serious adverse reactions, but these happened in fewer participants.

Most common serious adverse reactions during the study

Serious adverse reaction	Standard dose of BGF MDI (out of 2,144 participants)	Low dose of BGF MDI (out of 2,124 participants)	GFF MDI (out of 2,125 participants)	BFF MDI (out of 2,136 participants)
Worsening of COPD symptoms	0.7% (15)	0.9% (20)	0.5% (10)	0.7% (16)
Pneumonia	0.4% (8)	0.1% (3)	0.1% (3)	0.2% (4)
Irregular heartbeat	0.0% (0)	0.1% (3)	0.0% (0)	0.0% (0)
Heart attack	0.0% (0)	0.0% (0)	0.1% (2)	0.0% (0)
Heart suddenly stops beating, also known as cardiac arrest	0.1% (1)	0.0% (0)	0.1% (1)	0.0% (0)
Clogging or narrowing of the blood vessels	0.1% (2)	0.0% (0)	0.0% (0)	0.0% (0)

There were less than 0.1% of participants who died from serious adverse reactions during the study. This was 6 out of 8,529 participants.

- Less than 0.1% of the participants who took the standard dose of BGF MDI died from serious adverse reactions. This was 3 out of 2,144 participants.
- None of the 2,124 participants who took the low dose of BGF MDI died from serious adverse reactions.

- Less than 0.1% of the participants who took GFF MDI died from serious adverse reactions. This was 2 out of 2,125 participants.
- Less than 0.1% of the participants who took BFF MDI died from serious adverse reactions. This was 1 out of 2,136 participants.

What adverse reactions happened during this study?

The most common adverse reaction was a yeast infection around the mouth.

The table below shows the adverse reactions that happened in 0.5% or more of participants. This means they happened in at least 1 out of every 200 participants. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions during the study

Adverse reaction	Standard dose of BGF MDI (out of 2,144 participants)	Low dose of BGF MDI (out of 2,124 participants)	GFF MDI (out of 2,125 participants)	BFF MDI (out of 2,136 participants)
Yeast infection around the mouth	2.4% (51)	1.3% (27)	0.7% (14)	1.4% (29)
Worsening of COPD symptoms	0.7% (15)	0.9% (20)	0.5% (10)	0.8% (17)
Loss of voice	1.3% (28)	0.6% (13)	0.2% (4)	0.8% (17)
Shortness of breath	0.7% (14)	0.4% (9)	0.6% (12)	1.0% (21)
Cough	0.5% (10)	0.6% (12)	0.4% (8)	0.4% (9)
Muscle spasms	0.6% (13)	0.4% (9)	0.1% (3)	0.6% (12)
Pneumonia	0.5% (11)	0.2% (5)	0.2% (5)	0.4% (8)

How has this study helped patients and researchers?

This study helped researchers learn more about how BGF MDI affected symptoms compared to GFF MDI and BFF MDI in participants 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 with BGF MDI, GFF MDI, and BFF MDI 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 **"NCT02465567"** into the search box, and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2014-005671-92"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"PT010005"** into the search box, and click **"Find a Study"**.

Full Study Title: A Randomized, Double-Blind, Multi-Center, Parallel-Group Study to Assess the Efficacy and Safety of PT010 Relative to PT003 and PT009 on COPD Exacerbations over a 52-Week Treatment Period in Subjects With Moderate to Very Severe COPD

AstraZeneca Protocol Number: PT010005

National Clinical Trials number: NCT02465567

EudraCT number: 2014-005671-92

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

The phone number for the AstraZeneca Information Centre 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 organisation 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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