AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Treatments Studied: Budesonide, glycopyrronium, and formoterol fumarate metered-dose inhalers

Study Purpose: This study was done to learn if inhalers with different propellants affected how much budesonide, glycopyrronium, and formoterol fumarate got into the blood of healthy male participants

Protocol Number: D5985C00001

Thank you!

Thank you for taking part in the clinical study for budesonide, glycopyrronium, and formoterol fumarate metered-dose inhalers, also called BGF MDIs. The BGF MDIs were delivered through 3 inhalers, each with a different propellant.

AstraZeneca AB sponsored this study and thinks it is important to share the results. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you.

If you participated in the study and have questions about the results, please speak with the study doctor or staff at your study site.

Who took part in this study?

The researchers asked for the help of healthy men. The participants in this study were healthy men who were 24 to 58 years old when they joined.

The study included 47 participants in the United States.

Why was the research needed?

Researchers are looking for more environmentally friendly ways to treat people who have chronic obstructive pulmonary disease, also called "COPD". Before a treatment can be approved for people to take, researchers do clinical studies to find out how safe it is and how it works.

COPD is a long-term condition caused by damage to the airways and narrowing of the airways. This can lead to symptoms such as feeling short of breath, coughing, and phlegm.

Budesonide, glycopyrronium, and formoterol fumarate are all inhaled drugs that doctors currently use to help people who have COPD manage their symptoms. Budesonide, glycopyrronium, and formoterol fumarate can be given in combination through different types of inhaler devices. The combination of these drugs is called "BGF". One type of inhaler device used to give BGF is a metered-dose inhaler, also called a "BGF MDI".

Drugs given through an MDI are carried to the lungs with the help of liquified gases called "propellants". These propellants are greenhouse gases that can contribute to global warming. Researchers are looking for propellants that can be used to deliver drugs to the lungs without contributing to global warming.

One way of taking budesonide, glycopyrronium, and formoterol fumarate is using an MDI containing a propellant called "HFA". In this study, the researchers wanted to compare how much budesonide, glycopyrronium, and formoterol fumarate got into the participants' blood when taken through BGF MDIs that have HFA or 2 new propellants called "HFC" and "HFO".

HFA is an approved propellant that is currently used by people with COPD, but it contributes to global warming. HFC and HFO do not contribute to global warming as much as HFA. These new propellants would allow people with COPD to continue taking inhaled treatments, while helping to reduce global warming.

What was the purpose of this study?

In this study, the researchers wanted to learn if BGF MDIs with different propellants affected how much budesonide, glycopyrronium, and formoterol fumarate got into the blood of healthy participants.

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

- Did BGF MDIs with different propellants affect how much of the study drugs got into the participants' blood?
- Did the participants notice any differences in taste when taking the study drugs?
- 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 so that researchers can learn the best and most environmentally friendly way for people who have COPD to take budesonide, glycopyrronium, and formoterol fumarate.

What treatments did the participants take?

In this study, all of the participants took a combination of budesonide, glycopyrronium, and formoterol fumarate.

The participants took 3 BGF MDIs, which each had a different propellant. Each participant took all 3 BGF MDIs in a different order. The propellants that were in each BGF MDI were:

- propellant **HFO**
- propellant **HFC**
- propellant **HFA**

This was a "single-blind" study. This means the researchers, study doctors, and other study staff knew what the participants were taking, but the participants did not.

There were 6 groups of participants. Each group took all of the study treatments, and each group took them in a different order. There were groups for all possible orders of taking the combined inhaled treatments. There were 7 or 8 participants in each of the groups.

A computer program was used to randomly choose the order in which each participant took the study treatments. 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 chart below shows the treatments the researchers planned to study.

	47 male participants in total
	BGF MDIs containing 3 different propellants
	• First BGF MDI 1 time, then • Second BGF MDI 1 time, 3 to 7 days later, then • Third BGF MDI 1 time, 3 to 7 days later

What happened during this study?

The study started in October 2020 and ended in May 2021.

Before the participants took study treatment, they visited their study site 1 time. This part of the study lasted for up to 4 weeks because the participants joined at different times. At this visit, the study doctors made sure the participants could join the study. They also:

- did physical exams and asked about the participants' medications and any medical problems they were having
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG

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

While the participants took study treatment, they visited their study site 3 times. During these visits, the participants stayed overnight for 2 nights.

After the participants took study treatment, they visited their study site 1 time, about 3 to 7 days later. At this visit, the study doctors checked the health of the participants.

What were the results of this 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.

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 websites listed at the end of this summary may have more information about the study results.

During the study, there were 23 participants who were given the study treatments by a nurse instead of taking the study treatments themselves. Because this was not how the study was supposed to be conducted, these results were not included. So, the results for how much of each study drug got into the participants' blood are for 24 of the 47 participants.

Did BGF MDIs with different propellants affect how much of the study drugs got into the participants' blood?

Overall, the researchers found that using BGF MDIs with different propellants did not affect how much budesonide, glycopyrronium, and formoterol fumarate got into the participants' blood.

To answer this question, the study doctors took blood samples throughout the study. In these samples, they measured:

- the highest amounts of budesonide, glycopyrronium, and formoterol fumarate in the participants' blood
- the total amounts of budesonide, glycopyrronium, and formoterol fumarate in the participants' blood until the amounts could no longer be measured
- the total amounts of budesonide, glycopyrronium, and formoterol fumarate in the participants' blood

The researchers then calculated an average for each of these measurements. The researchers compared the results for each of the study drugs when the participants used the BGF MDIs with the 3 different propellants.

Overall, the researchers found that the average highest amounts of budesonide, glycopyrronium, and formoterol fumarate that got into the participants' blood were similar when the study drugs were taken using BGF MDIs with different propellants.

Additionally, the researchers found that the average total amounts of budesonide, glycopyrronium, and formoterol fumarate in the participants' blood until the amounts could no longer be measured were similar when the study drugs were taken using BGF MDIs with different propellants.

Finally, the researchers found that the average total amounts of budesonide and formoterol fumarate in the participants' blood were similar when the study drugs were taken using BGF MDIs with different propellants. There were not enough results collected for the researchers to know for sure if the average total amount of glycopyrronium in the participants' blood over time was different when the study drugs were taken using BGF MDIs with different propellants.

Did the participants notice any differences in taste when taking the study drugs?

Overall, the participants did not notice any differences in taste when taking the study drugs using BGF MDIs with different propellants.

To answer this question, the study doctors asked the participants to complete a survey about how the study drugs tasted when taken using BGF MDIs with different propellants.

What medical problems happened during this 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 drugs. 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 drugs. A lot of research is needed to know whether a drug causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for budesonide, glycopyrronium, and formoterol fumarate.

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 for medical problems were not affected by the study drugs being given by a nurse instead of being taken by the participants themselves. So, the results below are for all 47 participants in the study.

Did any adverse reactions happen during this study?

A summary of the adverse reactions thought to be related to the propellants in the different BGF MDIs is shown below.

- Propellant **HFO:** there were 6.4% of participants who had adverse reactions. This was 3 out of 47 participants.
- Propellant **HFC:** there were 12.8% of participants who had adverse reactions. This was 6 out of 47 participants.
- Propellant **HFA:** there were 10.6% of participants who had adverse reactions. This was 5 out of 47 participants.

What serious adverse reactions happened during this study?

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

What adverse reactions happened during this study?

The most common adverse reactions were cough, headache, and having a dry mouth.

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

Adverse Reactions

Adverse reaction	Propellant HFO (out of 47 participants)	Propellant HFC (out of 47 participants)	Propellant HFA (out of 47 participants)
Cough	2.1% (1)	0.0% (0)	2.1% (1)
Headache	0.0% (0)	2.1% (1)	2.1% (1)
Dry mouth	0.0% (0)	2.1% (1)	2.1% (1)
Feeling dizzy	2.1% (1)	0.0% (0)	0.0% (0)
Feeling bloated	2.1% (1)	0.0% (0)	0.0% (0)
Chest discomfort	2.1% (1)	0.0% (0)	0.0% (0)
Constipation	2.1% (1)	0.0% (0)	0.0% (0)
Dry throat	0.0% (0)	2.1% (1)	0.0% (0)
Strange dreams	0.0% (0)	2.1% (1)	0.0% (0)
Diarrhea	0.0% (0)	2.1% (1)	0.0% (0)
Feeling short of breath	0.0% (0)	2.1% (1)	0.0% (0)
Feeling anxious	0.0% (0)	0.0% (0)	2.1% (1)
Stuffy nose	0.0% (0)	0.0% (0)	2.1% (1)
Wet cough	0.0% (0)	0.0% (0)	2.1% (1)
Sore throat	0.0% (0)	0.0% (0)	2.1% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about how much budesonide, glycopyrronium, and formoterol fumarate got into the blood of healthy male participants when taken using BGF MDIs containing different propellants.

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 looking for the propellant that works best in BGF MDIs 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 **"NCT04600505"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D5985C00001"** into the search box, and click **"Find a Study"**.

Full Study Title: A Randomized, Single blind, 3-Period, 3-Treatment, Single dose, Crossover Study to Assess the Relative Bioavailability of BGF MDI HFO and BGF MDI HFC Compared with BGF MDI HFA in Healthy Subjects

AstraZeneca AB Protocol Number: D5985C00001

National Clinical Trials Number: NCT04600505

AstraZeneca AB sponsored this study and has its headquarters in Södertälje, Sweden.

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.

CISCRP | One Liberty Square, Suite 1100 • Boston, MA 02109 | 1-877-MED-HERO | www.ciscrp.org

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