Clinical Study Results

AstraZeneca

Research Sponsor: AstraZeneca AB

Drug Studied: Glycopyrronium / formoterol fumarate

Study Title: This study was done to learn how glycopyrronium / formoterol fumarate worked compared with umeclidinium / vilanterol and how safe it was in people with chronic obstructive pulmonary disease.

Thank you!

Thank you to the participants who took part in the clinical study for the study drug glycopyrronium / formoterol fumarate, also called GFF. You and all the participants helped researchers learn more about using GFF to help people with chronic obstructive pulmonary disease, also called COPD.

AstraZeneca AB sponsored this study and thinks 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 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 doctor or staff at your study site.

What is happening with the study now?

The participants were in the study for up to about 30 weeks. The study started in May 2017 and ended in May 2018. The study included 1,119 participants in Bulgaria, Canada, France, Hungary, Russia, Ukraine and 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 with moderate to very severe COPD. Researchers do clinical studies to find out how a treatment works and how safe it is. In this study, researchers wanted to find out if GFF works at least as well as umeclidinium / vilanterol, also called UV, in a large number of participants with moderate to very severe COPD. They also wanted to find out if the participants taking GFF had any different medical problems during the study compared with those taking UV.

COPD is a long-term condition that causes the airways to narrow. This makes it difficult to breathe. There are treatments for COPD to help people breathe more easily, but these treatments do not work well for everyone with moderate to very severe COPD.

GFF is used to treat COPD. It works by relaxing muscles in the airways to allow more air into the lungs. This makes it easier to breathe. GFF is taken through an inhaler that delivers a specific amount of GFF to the lungs. The inhaler is known as a metered dose inhaler, also called MDI.

UV is also used to treat COPD. But, UV is taken through a different type of inhaler called a dry powder inhaler, also called DPI.

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

- Did GFF affect the amount of air participants could breathe out at least as much as UV did?
- Compared with participants taking UV, how breathless were participants taking GFF during common daily activities?
- Did GFF affect the early morning symptoms of COPD at least as much as UV did?
- 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 between 40 and 86 years old
- did not have any other lung condition or infection
- had COPD symptoms for more than one year before the study
- had smoked at least 10 pack-years, which means they had smoked an average of at least one 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 or other study staff knew what treatment each participant received. 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.

The participants in this study took either an active GFF inhaler or an active UV inhaler.

- GFF inhaler: this was made up of 7.2 micrograms, also called µg, of a drug called glycopyrronium combined with 4.8 µg of a drug called formoterol fumarate. The participants took two puffs twice a day of this inhaler.
- UV inhaler: this was made up of 62.5 µg of a drug called umeclidinium combined with 25 µg of a drug called vilanterol. The participants took one puff once a day of this inhaler.

All participants also used a placebo inhaler for the alternative treatment, which did not have any medicine in it. The placebo inhaler was designed to look like either the GFF or the UV inhaler, so participants could not tell which one had the medicine in it. Researchers use a placebo to help make sure any of the effects they see in the participants who take a treatment are actually caused by the treatment.

A computer program was used to randomly choose the treatment each participant received. 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.

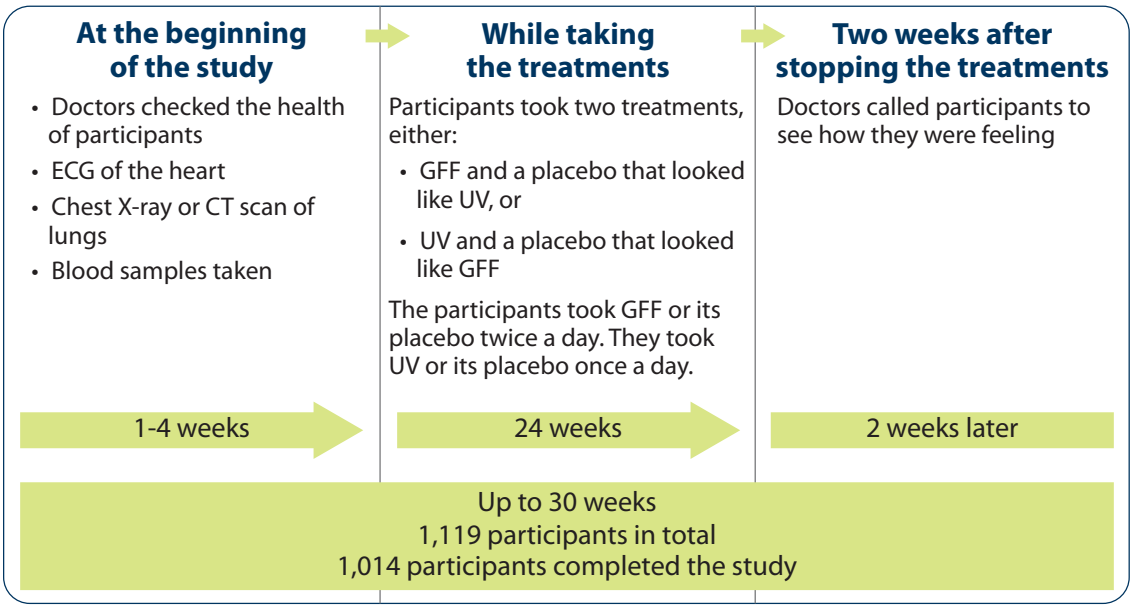
What happened during the study?

At the beginning of the study, participants visited the study site 2 times. At these visits, the doctors checked participants' overall health and lungs to make sure they could stay in the study. If participants were able to join the study, the doctors may have asked them to stop taking certain medicines. This helped make sure any effects the researchers saw in the participants were due to the treatments in the study.

While taking the treatments, the participants visited the study site 5 times. At each visit, the doctors or study staff measured how much air the participants could breathe out. The participants also completed questionnaires about how the treatments were affecting them.

Two weeks after stopping the treatments, the doctors called the participants to see how they were feeling.

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 the 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.

Some of the participants who started taking GFF or UV did not complete the study. These participants still contributed information up until the point at which they stopped the study.

Did GFF affect the amount of air participants could breathe out at least as much as UV did?

How much air the participants could breathe out in the morning before taking treatment

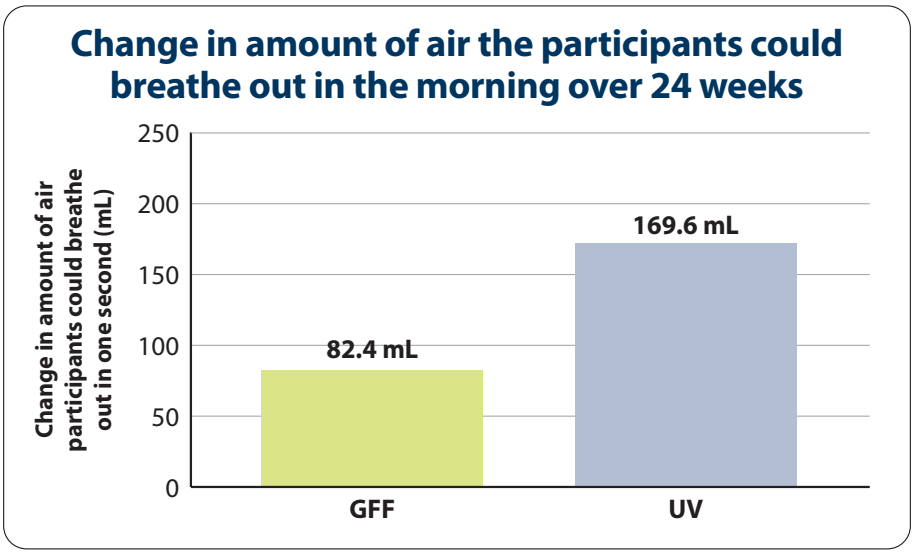
The amount of air participants could breathe out in the morning before taking treatment was not as large for participants taking GFF compared with those taking UV.

At the beginning of the study, researchers measured the amount of air participants breathed out in 1 second in the morning before taking their first dose of the treatment. They repeated this measurement in the morning of each study visit before the participant took the morning treatment dose. Researchers then compared these measurements to the measurements before the first dose of treatment. The amount of air breathed out was measured in milliliters, also called mL.

Over the 24 weeks of the study:

- The participants taking GFF breathed out an average of 82.4 mL more air in the morning than they did at the start of the study.
- The participants taking UV breathed out an average of 169.6 mL more air in the morning than they did at the start of the study.

The graph below shows these results.



How much air the participants could breathe out 2 hours after taking treatment

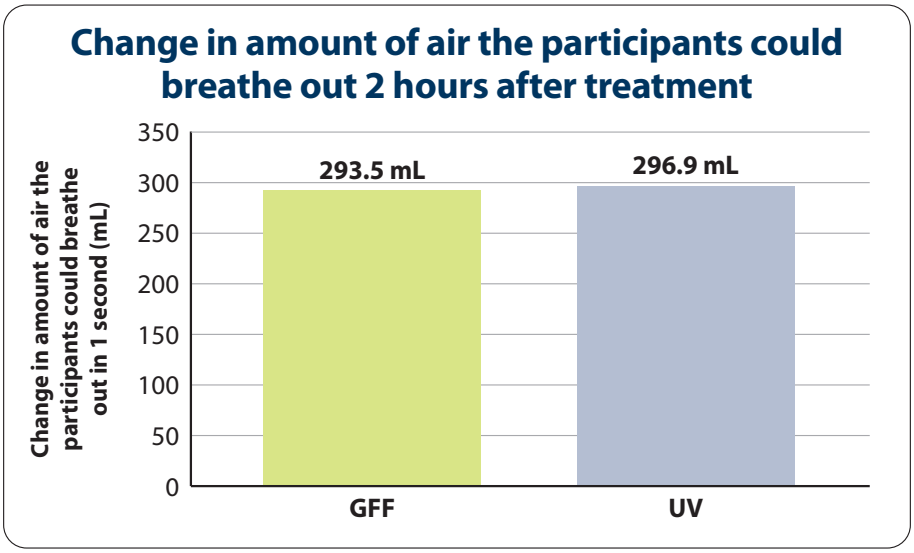
After 24 weeks of treatment, the researchers found that there were not meaningful differences between the GFF and UV treatments in how much air the participants could breathe out in 1 second 2 hours after taking the drug.

At the beginning of the study, researchers measured the amount of air participants breathed out in 1 second in the morning before taking their first dose of treatment. At each visit, they measured the maximum amount of air participants breathed out in 1 second in the morning up to 2 hours after taking treatment. Researchers then compared these measurements to the measurements they took before the first dose of treatment. The amount of air breathed out was measured in mL.

Over the 24 weeks of the study:

- The participants taking GFF breathed out an average of 293.5 mL more air after taking treatment.
- The participants taking UV breathed out an average of 296.9 mL more air after taking treatment.

The graph below shows these results



Compared with participants taking UV, how breathless were participants taking GFF during common daily activities?

After 24 weeks of treatment, the researchers found that there were not meaningful differences in how breathless participants were between those taking GFF and those taking UV.

Throughout the study, on average, participants taking either GFF or UV treatment reported having improved COPD symptoms and were able to breathe more easily during daily activities.

The doctors used a questionnaire to ask the participants about how breathless they were during common daily activities. Over the 24 weeks of the study, the scores from the questionnaire had increased by an average of 1.2 units for the GFF participants and 1.6 units for the UV participants. An increase in the scores of this questionnaire meant their symptoms had improved.

Did GFF affect the early morning symptoms of COPD at least as much as UV did?

After 24 weeks of treatment, the researchers found that there were not meaningful differences in the early morning symptoms of COPD between the participants taking GFF and the participants taking UV in this questionnaire.

Over the study, on average, all participants taking either GFF or UV treatment reported having less severe early morning symptoms of COPD.

The participants filled out a questionnaire about their early morning COPD symptoms. They repeated this questionnaire during the morning of each study visit. The researchers compared the questionnaire scores to the questionnaire scores at the start of the study. Over the 24 weeks of the study, the scores from the questionnaire had decreased by an average of 0.14 units for the GFF participants and 0.18 units for the UV participants. A decrease in the scores from this questionnaire meant their symptoms had improved.

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 have been caused by the study treatments. A lot of research is needed to know whether a treatment 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 during the study.

How many participants had adverse reactions?

- There were 0.9% of participants who had adverse reactions during the study. This was 10 out of 1,104 participants whose safety data was available during the study.
  - There were 1.3% of participants taking GFF who had adverse reactions during the study. This was 7 out of 552 participants.
  - There were 0.5% of participants taking UV who had adverse reactions related to the treatment during the study. This was 3 out of 552 participants.
- There were 0.5% of participants who stopped taking GFF because of adverse reactions. This was 3 out of 552 participants.
- There were 0.2% of participants who stopped taking UV because of adverse reactions. This was 1 out of 552 participants.

What adverse reactions did the participants have?

The table below shows the adverse reactions that happened in 1 or more participants in either treatment group. Some participants taking UV had more than 1 adverse reaction during the study.

Most common adverse reactions

	GFF (out of 552 participants)	UV (out of 552 participants)
Vertigo, which is a kind of dizziness	0.4% (2)	0.0% (0)
Losing their voice	0.4% (2)	0.0% (0)
Anxiety	0.2% (1)	0.0% (0)
Wheezing	0.2% (1)	0.0% (0)
Painful or difficult urination	0.2% (1)	0.0% (0)
Headache	0.0% (0)	0.2% (1)
Dizziness	0.0% (0)	0.2% (1)
Loss of feeling on one side of the body and loss of pain and temperature sense on the other	0.0% (0)	0.2% (1)
Difficulty breathing	0.0% (0)	0.2% (1)
Swollen stomach	0.0% (0)	0.2% (1)
Abnormal physical weakness or lack of energy	0.0% (0)	0.2% (1)
Chest discomfort	0.0% (0)	0.2% (1)

How has this study helped patients and researchers?

This study helped researchers learn how GFF worked in participants with moderate to very severe 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 one study. Other studies may provide new information or different results.

Further studies comparing GFF and UV are not currently planned.

Where can I learn more about this study?

More information about this study is available on the website 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 "**NCT03162055**" into the search box and click "**Search**".
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5970C00002"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Randomized, Double-Blind, Double-Dummy, Multicentre, Parallel Group Study to Assess the Efficacy and Safety of Glycopyrronium/Formoterol Fumarate fixed-dose combination relative to Umeclidinium/Vilanterol fixed-dose combination over 24 Weeks in Patients with Moderate to Very Severe Chronic Obstructive Pulmonary Disease (AERISTO).

National Clinical Trials number: NCT03162055

AstraZeneca Protocol Number: D5970C00002

AstraZeneca AB sponsored this study and has its headquarters in Mölndal, 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 participants.