This document provides a short summary of this study for a general audience. You can find more information in the scientific summaries of the study. Links to those summaries are provided at the end of this document.

Study names

Short Title: A study to compare a combination of umeclidinium and vilanterol with umeclidinium alone and salmeterol alone in patients with chronic obstructive pulmonary disease.

Full Scientific Title: A 24-week treatment, multi-centre, randomised, double-blind, double-dummy, parallel group study to compare Umeclidinium/Vilanterol, Umeclidinium, and Salmeterol in subjects with chronic obstructive pulmonary disease (COPD).

Study Number: 201749

Who sponsored this study?

GlaxoSmithKline (GSK)
GSK Clinical Support Help Desk
Website: clinicalsupporthd.gsk.com/contact.html
Email: GSKClinicalSupportHD@gsk.com

General information about the clinical study

When was this study done?

The study started in June 2017 and ended in June 2018.

What was the main objective of this study?

Chronic obstructive pulmonary disease is a long-term disease of the lungs that makes it hard to breathe and gets worse over time. For patients with COPD, inhaled medicines are an important part of treatment.

The main objective of this study was to compare lung function in patients with COPD using a combination of umeclidinium and vilanterol in a single inhaler with

umeclidinium alone. Researchers also compared these treatments with salmeterol. They assessed the safety of these medicines in the patients.

Which medicines were studied?

Patients took the study medicine(s) through inhalers for 24 weeks. An inhaler is a handheld device that is designed to deliver medicine to the lungs.

Patients in this study were put into one of the following three treatment groups by chance. This is called randomisation.

Medicines used in the study	
Umeclidinium and vilanterol	• A combination of umeclidinium 62.5 microgram (mcg) and vilanterol 25 mcg **once daily** via ELLIPTA inhaler
Umeclidinium	• Umeclidinium 62.5 mcg **once daily** via ELLIPTA inhaler
Salmeterol	• Salmeterol 50 mcg **twice daily** via DISKUS inhaler

Bronchodilators are medicines that relax and open the airways in the lungs. Umeclidinium is an inhaled long-acting muscarinic antagonist (LAMA). Vilanterol and salmeterol are inhaled long-acting beta agonists (LABA). LAMA and LABA are different types of bronchodilators.

In addition to the above medicine(s), the patients in each treatment group also received placebo via inhaler (containing no active medicine).

All the patients received a total of three doses in a day: two doses (morning and evening) via the DISKUS inhaler and one dose (morning) via the ELLIPTA inhaler. Neither patients nor study doctors knew who was receiving which treatment. This is called a double-blind study.

Which patients were included in this study?

Studies have a list of requirements for patients who can enrol (inclusion criteria) and those who can't (exclusion criteria). For this study, the main inclusion and exclusion criteria are listed below.

Main Inclusion Criteria

Men and women were included in the study if they:

- Were at least 40 years old.
- Had COPD with symptoms.
- Were current or former smokers.

Main Exclusion Criteria

Men and women were excluded from the study if they had:

- Asthma or any other lung problem.
- A specific genetic condition that led to COPD.
- Received inhaled corticosteroid (ICS) alone or in combination with LABA in the six weeks before starting the study. An ICS is a medicine that reduces swelling and irritation in the lungs.
- Been hospitalised for COPD or pneumonia in the 12 weeks before starting the study.
- Unresolved pneumonia, or moderate or severe COPD exacerbation.
- Liver or heart disease.

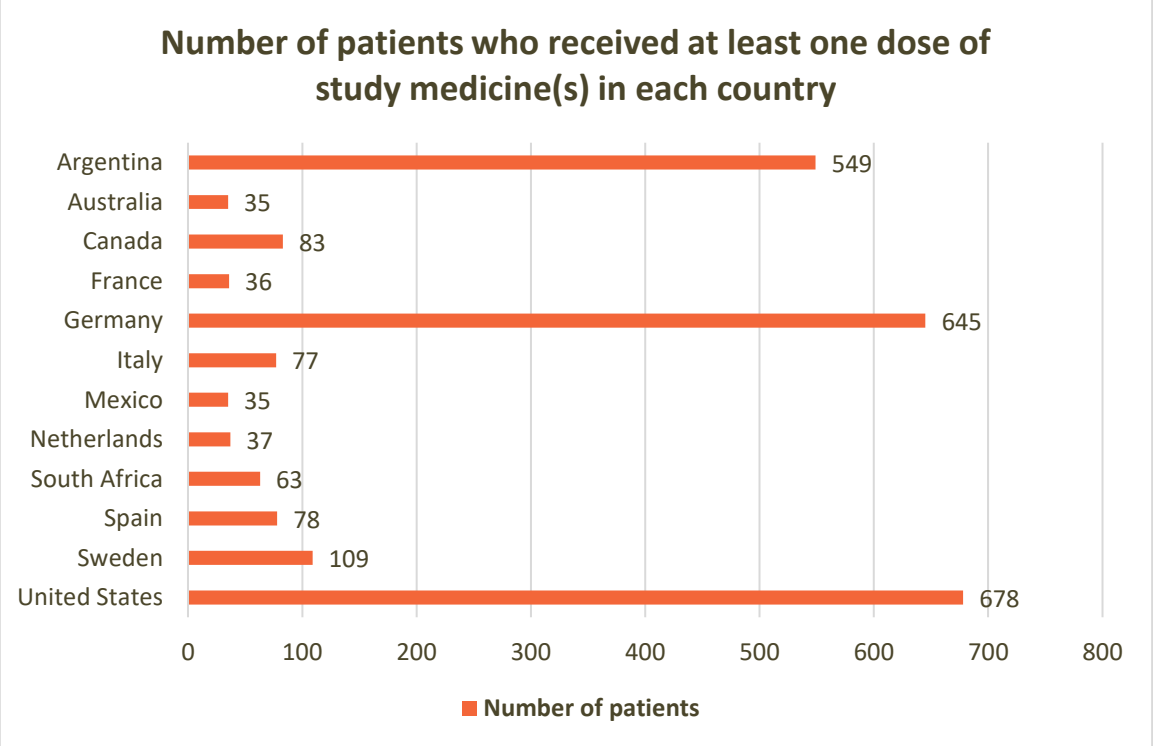
For more detailed information about the patients included in this study, see the scientific summary on the ClinicalTrials.gov website (see link provided at the end of this document).

A total of 2425 patients were randomised and received at least one dose of study medicine(s) in this study. The table below shows the gender and age of these patients.

Patients who were randomised and received at least one dose of study medicine(s)			
	Umeclidinium and vilanterol 812 patients	Umeclidinium 804 patients	Salmeterol 809 patients
Gender			
Female	319 (39%)	327 (41%)	342 (42%)
Male	493 (61%)	477 (59%)	467 (58%)
Age - in years			
Range	41 to 89	41 to 89	40 to 92
Average	65	65	64

Where was this study done?

Study sites were in 12 countries.



What were the overall results of the study?

Lung function tests measure how well a patient's lungs move air in and out of the body. Doctors can use the results of these tests to see if lung function is stable, getting better, or getting worse.

One measure of lung function is Forced Expiratory Volume in one second (FEV_1). FEV_1 measures the amount of air that a patient can breathe out in the first second when asked to blow as hard as possible into a tube connected to a machine (spirometer). Higher values of FEV_1 mean more air is flowing out of the lungs and that lung function is better. FEV_1 is measured in millilitres (mL).

Study doctors measured the FEV_1 values of the patients during the study. The difference between the FEV_1 at the beginning of the study (baseline FEV_1) and after 24 weeks of treatment is called the Week 24 change from baseline in FEV_1.

The Week 24 change from baseline in FEV_1 values from individual patients in each treatment group were combined and averaged. These averaged values were compared between the three treatment groups. Out of the 2425 patients, the Week 24 change from baseline in FEV_1 could be calculated for 1966 patients who had both baseline and week 24 values measured. The results are shown in the table below.

Week 24 change from baseline in average FEV_1			
	Umeclidinium and vilanterol	**Umeclidinium**	**Salmeterol**
Number of patients with FEV_1 values at baseline and at Week 24	691 patients	621 patients	654 patients
Week 24 change from baseline in average FEV_1	122 mL higher	56 mL higher	19 mL lower

After 24 weeks of treatment, the improvement in the average FEV_1 of patients in the umeclidinium and vilanterol combination group was higher compared with each of the other two treatment groups. The differences in average FEV_1 between umeclidinium and vilanterol combination group and the other two treatment groups were statistically significant. This means that the difference was not likely due to chance alone.

More information about the study results are available in the scientific results summaries (see the links at the end of this document).

What were the side effects?

Unwanted medical events (adverse events) can happen to people when they receive a medicine. Study doctors record these events. A summary of all these events can be found in the scientific results summaries (see the links at the end of this document).

If the study doctor thinks that the event was caused by the study medicine, they record this as a possible side effect (adverse reaction).

In this summary, “side effects*” refer to those events that the study doctor thinks may have been caused by the study medicine(s).

* The side effects in this summary may be different to those in the Informed Consent or other documents related to the study medicine(s).

No serious side effects were reported by patients in the study.

No non-serious side effects were reported by more than one percent of patients in any of the three treatment groups.

How has this study helped patients and researchers?

This study showed that the umeclidinium and vilanterol combination group was more effective than umeclidinium or salmeterol alone in treating COPD.

Are there plans for further studies?

Other studies with the combination of umeclidinium and vilanterol in patients with COPD have been conducted. No further studies are planned at this time.

Where can I find more information about this study?

Clinical studies have unique study numbers that are included in publications and other information about the study. The unique study numbers associated with this study are shown below with internet links to scientific summaries and other information.

The scientific summaries include more details about the requirements for study enrolment, the study visit schedule, results from other endpoints and more detailed information about side effects.

Organisation	Website	Study Number
European Medicines Agency	www.clinicaltrialsregister.eu	2016-002513-22[1]
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT03034915[2]

Your doctor can help you understand more about this study and the results. You should not make changes to your care based on the results of this or any single study. Keep taking your current treatment unless instructed by your doctor.

We would like to thank the patients who contributed to this study. The results of this study will help answer scientific questions about treating patients with COPD.

The content for this document was finalised by GSK on 13th of May 2019. The information in this summary does not include additional information available after this date.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-002513-22

[2] https://clinicaltrials.gov/ct2/show/study/NCT03034915