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

Study names

Short Title: The effect of fluticasone furoate and vilanterol compared with placebo on survival in patients with chronic obstructive pulmonary disease (COPD) who also have or are at risk of getting heart disease.

Full Scientific Title: A clinical outcomes study to compare the effect of fluticasone furoate/vilanterol inhalation powder 100/25mcg with placebo on survival in subjects with moderate chronic obstructive pulmonary disease (COPD) and a history of or at increased risk for cardiovascular disease.

Who sponsored this study?

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

General information about the clinical study

When was this study done?

The study started in January 2011 and ended in July 2015.

What was the reason for this study?

Chronic Obstructive Pulmonary Disease (COPD) is a long-term disease of the lungs that makes it hard to breathe and gets worse over time. It usually takes many years for COPD symptoms to appear, so COPD is more common in older people and past or current smokers. Heart disease is also more common in older people and smokers. People with both COPD and heart disease have a higher risk of dying at an earlier age than people in the general population.

What was the main objective of this study?

The goal was to see if different COPD medicines affected the overall survival of patients in the study. All patients had COPD and either heart disease or a high risk of getting heart disease.

Which medicines were studied?

For patients with COPD, inhaled medicines taken every day can be an important part of treatment. An inhaler is a device that is designed to deliver medicine to the lungs.

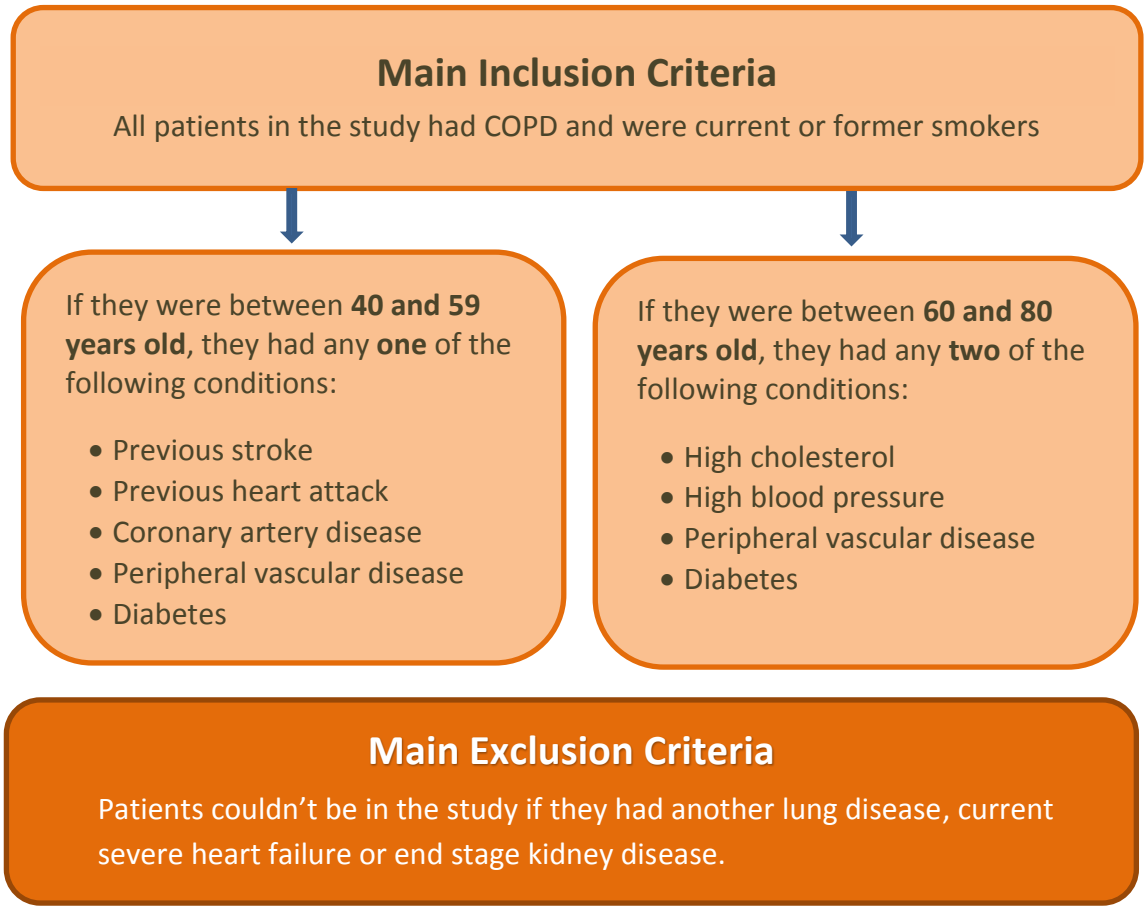
The patients who took part in this study were placed into one of four treatment groups based on chance (randomisation).

	Placebo	Fluticasone Furoate	Vilanterol	Fluticasone Furoate and Vilanterol
Medicine	No active medicine	Decreases swelling and irritation in the lungs	Relaxes and opens the air passages of the lungs	Combination medicine which both decreases swelling and opens the air passages of the lungs
Dose	None	100 micrograms	25 micrograms	100 and 25 micrograms
How was the medicine taken	Each medicine was delivered though identical inhaler devices			

Patients took their medicines once a day in the morning. No one knew which treatment each patient was taking. This is called a double-blind study.

What 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 in the figure below. For more detailed information, see the links to the summaries provided at the end of this document.

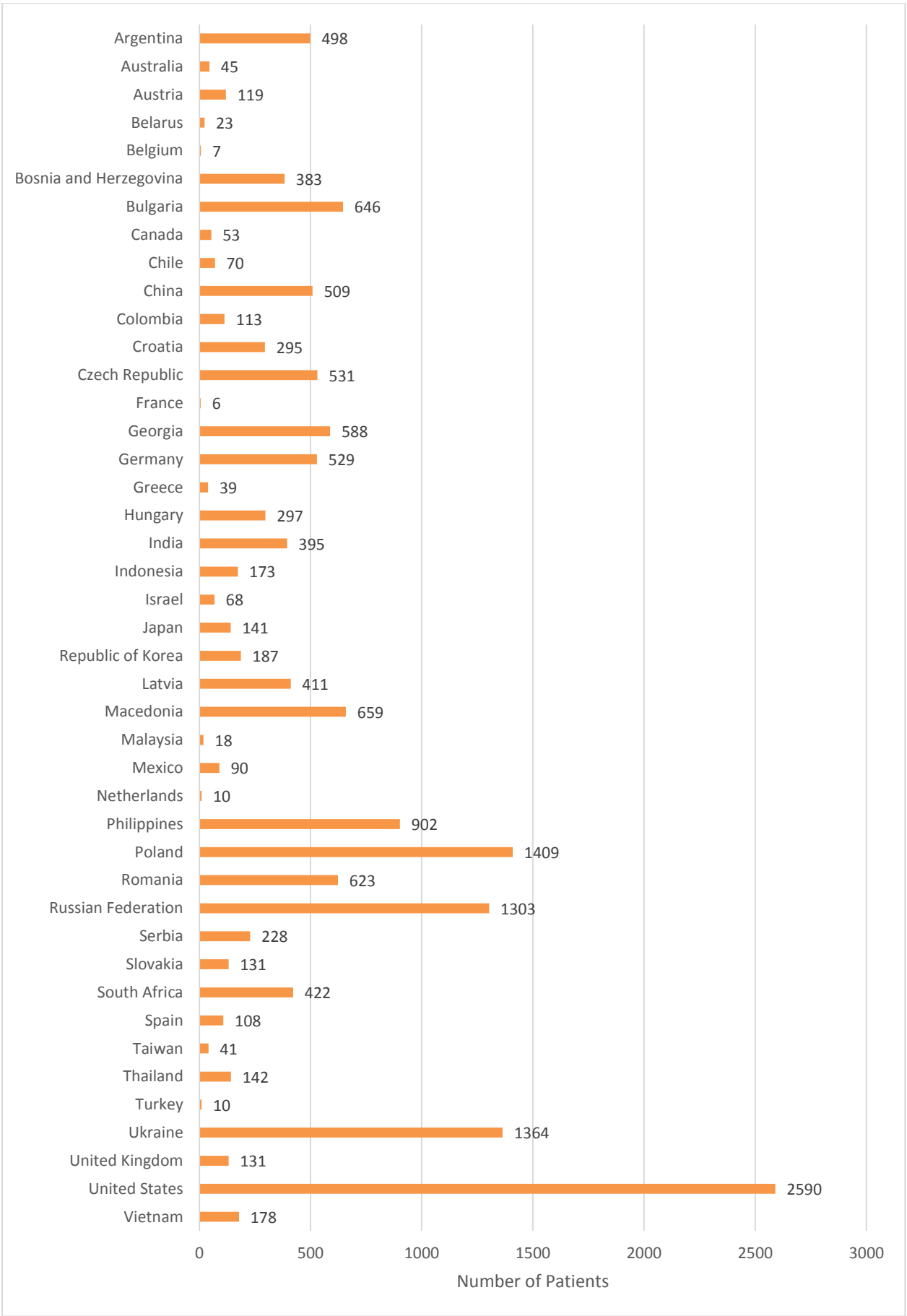


A total of 16,485 men and women between 40 and 80 years of age participated in this study. This is called the intent-to-treat population. The average age of the patients was 65 years. This study included three times more men than women.

	Placebo 4111 patients	Fluticasone Furoate 4135 patients	Vilanterol 4118 patients	Fluticasone Furoate and Vilanterol 4121 patients
Gender -Number of patients (percent)				
Women	1040 (25%)	1082 (26%)	1065 (26%)	1009 (24%)
Men	3071 (75%)	3053 (74%)	3053 (74%)	3112 (76%)
Age – in years				
Range	40 to 80	40 to 80	40 to 80	40 to 80
Average	65	65	65	65

Where was this study done?

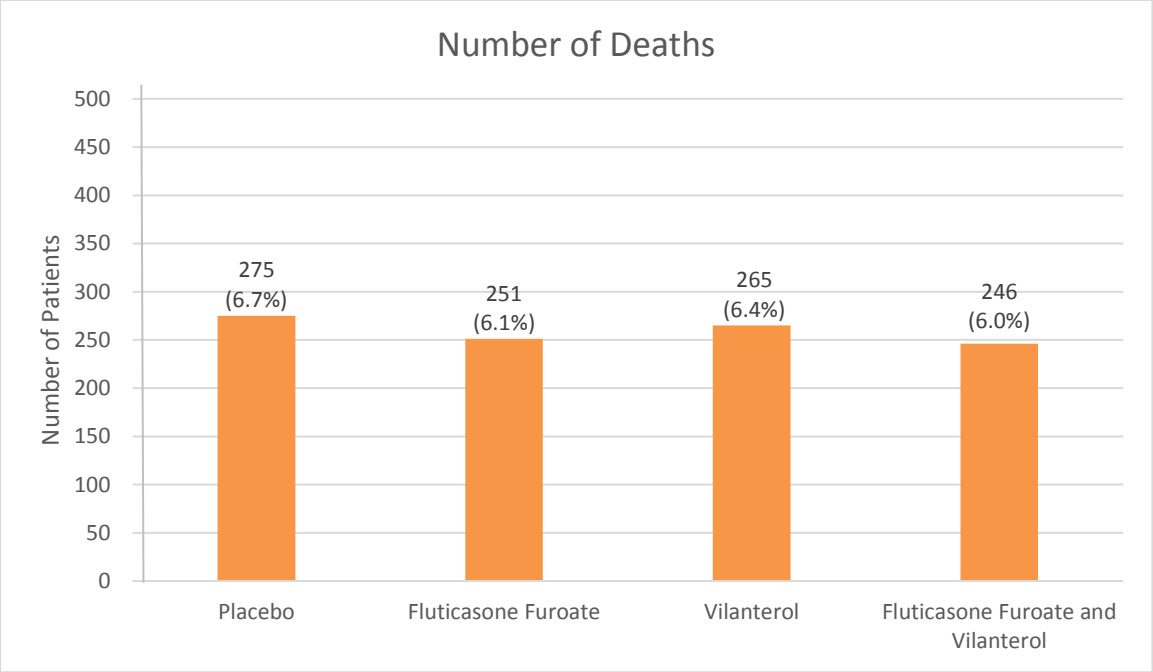
The study was carried out in 43 countries. The number of patients from each country is listed below. This figure includes patients in the intent to treat population.


Argentina 498
Australia 45
Austria 119
Belarus 23
Belgium 7
Bosnia and Herzegovina 383
Bulgaria 646
Canada 53
Chile 70
China 509
Colombia 113
Croatia 295
Czech Republic 531
France 6
Georgia 588
Germany 529
Greece 39
Hungary 297
India 395
Indonesia 173
Israel 68
Japan 141
Republic of Korea 187
Latvia 411
Macedonia 659
Malaysia 18
Mexico 90
Netherlands 10
Philippines 902
Poland 1409
Romania 623
Russian Federation 1303
Serbia 228
Slovakia 131
South Africa 422
Spain 108
Taiwan 41
Thailand 142
Turkey 10
Ukraine 1364
United Kingdom 131
United States 2590
Vietnam 178
0
500
1000
1500
2000
2500
3000
Number of Patients

What were the overall results of the study?

Researchers looked at the number of patients in each group who had died by the end of the study and the time from the start of the study until they died. Patients were counted if they died for any reason and not just because of COPD or heart disease. The study continued until about 1000 patients had died. This is called an event-driven study.

The number of deaths for any reason is listed in the figure below.



The number of deaths was highest in the placebo group. Numerically fewer patients who received active medicines died compared with patients who received placebo. These differences in the number and percentage of deaths were not statistically significant. This means that any differences were likely to have been due to chance rather than the study medicines. The risk of death over time (hazard ratio) between each of the treatment groups was also not significantly different. Cardiovascular disorders were the most common primary cause of death.

What were the side effects?

Study doctors collect information about the safety of study medicines. They document the side effects that are reported by patients during the study. If they believe that the side effect was caused by the medicine, they note that as well. This plain language summary reports adverse events that may be related to the study medicine. These are called adverse reactions.

- An ***adverse reaction*** is a medical problem that develops during the study that the doctor thinks could have been caused by the patient's study medicine.

- A ***serious adverse reaction*** is an adverse reaction that is life threatening, requires hospitalisation, or results in death or permanent damage.

No serious adverse reactions were reported by 1% or more of the patients in any treatment group. The serious adverse reactions reported by 5 or more patients in at least one treatment group and the adverse reactions (serious and non-serious) reported by 1% or more of patients in at least one treatment group are shown in the tables below. The number of patients in the tables below includes all patients who received at least one dose of the medicine. All of these patients were included as part of the safety population. There are more patients in the safety population than in the intent to treat population.

Serious Adverse Reactions				
	Placebo 4131 patients	**Fluticasone Furoate** 4157 patients	**Vilanterol** 4140 patients	**Fluticasone Furoate and Vilanterol** 4140 patients
Pneumonia	3 of 4131 (less than 1%)	12 of 4157 (less than 1%)	3 of 4140 (less than 1%)	11 of 4140 (less than 1%)
Worsening COPD	10 of 4131 (less than 1%)	7 of 4157 (less than 1%)	5 of 4140 (less than 1%)	5 of 4140 (less than 1%)
Abnormal Rapid, Irregular Heartbeat (Atrial Fibrillation)	3 of 4131 (less than 1%)	None of 4157 (0%)	5 of 4140 (less than 1%)	3 of 4140 (less than 1%)

Adverse Reactions (serious and non-serious)				
	Placebo 4131 patients	**Fluticasone Furoate** 4157 patients	**Vilanterol** 4140 patients	**Fluticasone Furoate and Vilanterol** 4140 patients
Worsening COPD	72 of 4131 (2%)	51 of 4157 (1%)	47 of 4140 (1%)	31 of 4140 (less than 1%)
Yeast infection in the mouth (Oral candidiasis)	19 of 4131 (less than 1%)	46 of 4157 (1%)	16 of 4140 (less than 1%)	51 of 4140 (1%)

For further information, including the adverse events that study doctors did not think were related to the study medicine, please see the scientific summaries using the links provided at the end of this document.

How has this study helped patients and researchers?

This study helped study doctors learn more about possible treatments for COPD in patients with COPD and heart disease or a higher chance of getting heart disease. Between each of the four treatment groups, study doctors did not find a significant difference in survival at the end of the study.

Are there plans for further studies?

Other studies of fluticasone furoate and vilanterol in patients with COPD are currently ongoing. The results of these studies will also be available on GSK's Study Register after the studies end and the results are analysed. The link is below.

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 adverse events.

Organization	Website	Study Number
European Medicines Agency	www.clinicaltrialsregister.eu	2010-021638-72
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT01313676
GlaxoSmithKline (GSK)	www.gsk-clinicalstudyregister.com	113782

*

For readers of this document in printed form, the websites that go with the internet links above are

https://www.clinicaltrialsregister.eu/ctr-search/search?query=2010-021638-72
https://clinicaltrials.gov/ct2/show/NCT01313676?term=113782&rank=1
https://www.gsk-clinicalstudyregister.com/search/?search_terms=113782

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. The results of this study will help answer scientific questions about treating patients with COPD.

This document was developed and approved by GSK on 18th December 2017. The information in this summary does not include additional information available after this date.