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 Identification

Short Title: Safety and benefit study of fluticasone propionate and salmeterol versus fluticasone propionate alone in children with asthma.

Full Scientific Title: A 6-month safety and benefit study of inhaled fluticasone propionate/salmeterol combination versus inhaled fluticasone propionate in the treatment of 6200 pediatric subjects 4-11 years old with persistent asthma.

Name and Contact Details of the Sponsor

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

General Information about the Study

Study Dates: The study started in November 2011 and ended in November 2015.

The Reason for Conducting This Study

This study was done to help answer an important safety question about long-acting beta-agonists, a type of medicine to treat asthma. The question is whether children taking inhaled corticosteroids together with salmeterol (in a single inhaler) have the same risk of having uncommon but serious problems when compared with patients taking inhaled corticosteroids alone. Serious problems include hospitalization, needing to have a tube put down their throat to help them breathe (intubation), or death due to asthma.

Background

Asthma is a long-term condition of the airways, the tubes that carry air to the lungs. When the airways are inflamed (irritated and swollen), they become narrow. This narrowing can cause coughing, wheezing, chest tightness, and shortness of breath. When these symtoms

of asthma are getting worse and it is hard to breathe, it is called an asthma attack, also known as an asthma exacerbation.

People can develop asthma at any age, but most children with asthma will experience their first symptoms before age 5 years.

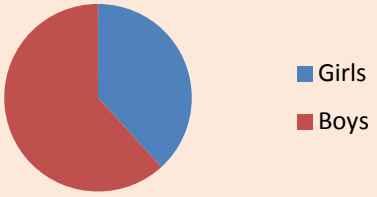
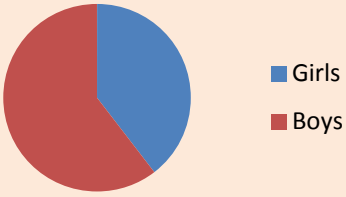
When an asthma attack does not improve with prompt treatment at home, it can become severe (severe asthma attack) and need emergency care in a hospital. A severe asthma attack can become a life-threatening emergency. A breathing tube may need to be inserted into the airways (this is called intubation). The tube is then connected to a ventilator, a machine which pushes air into the lungs and helps the person breathe. Very rarely a severe asthma attack can cause death.

Participants

Patients Included

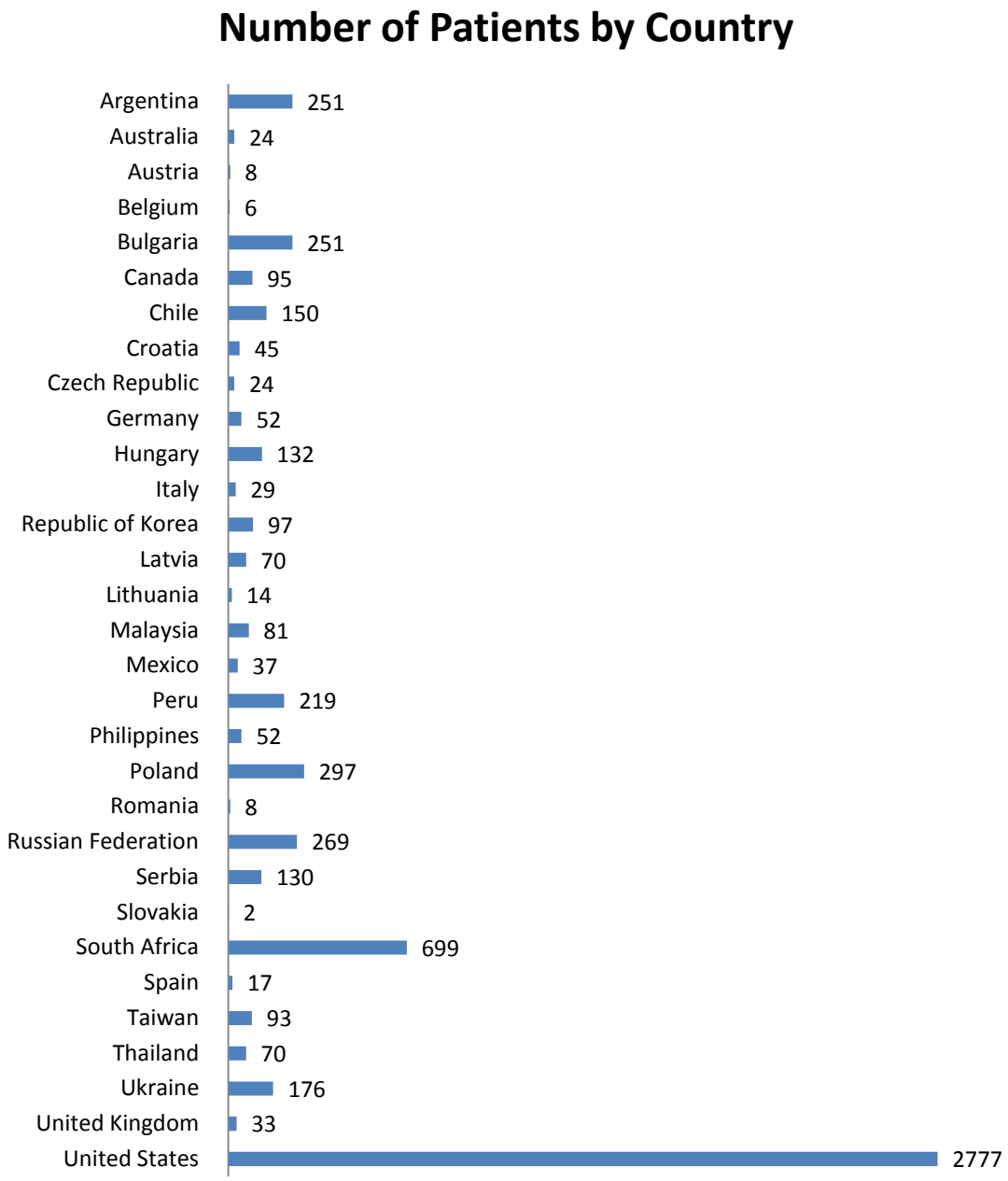
Patients with one or more asthma attacks in the year before the study started, were included in the study. Patients could not be included in the study if they had a history of life-threatening asthma or another lung disease, in addition to their asthma.

This study included 6208 patients. The youngest patient was 4 years old and the oldest was 12 years old.

Patient Population		
	Group A **Fluticasone Propionate and Salmeterol**	**Group B** **Fluticasone Propionate**
Patient Population and Gender of Patients	**3107 Patients** 	**3101 Patients** 
Average Age of Patients	**8 years old**	**8 years old**

Study Site Locations

Study sites were located in 31 countries. The graph below shows how many patients were from each country.



Investigational Medicinal Products Used

Medicines used

An inhaled corticosteroid is a medicine that reduces asthma inflammation and swelling of the lungs, which helps to control asthma. The inhaled corticosteroid used in this study was fluticasone propionate.

A long-acting beta-agonist is a medicine that relaxes (opens/dilates) the airways to make breathing easier. The long-acting beta-agonist used in this study was salmeterol.

The patients in the study had an equal chance, like flipping a coin, of being placed into either treatment Group A or treatment Group B. This equal chance is because of a process called randomization.

- Group A – patients who took two medicines (fluticasone propionate 100 or 250 micrograms and salmeterol 50 micrograms) in a single inhaler twice daily.
- Group B – patients who took one medicine (fluticasone propionate 100 or 250 micrograms) in an inhaler twice daily.

An inhaler is a medical device which delivers medicine straight to the lungs by breathing in the medicine. The inhalers looked the same for both groups to ensure that patients and study staff did not know which treatment each patient was taking (this is called a double-blinded study).

Patients in Groups A and B took their medicine twice every day for 6 months. Patients received the higher or lower dose depending on the severity of their asthma.

The medicines in this study work in different ways to treat the two main symptoms of asthma (inflammation and tightening of the airways).

Name of Medicine	Class of Medicine	How Medicine Works
Fluticasone propionate	Inhaled Corticosteroid (ICS)	Reduces swelling and inflammation in the lungs
Salmeterol	Long-acting beta agonist (LABA)	Relaxes and open the airways

Patients in both groups were also given a separate rescue inhaler containing a bronchodilator medicine to quickly relax the muscles around air passages to open them up. Patients could use this rescue inhaler as needed during the study.

Results of the Study

Results

For this study, the main safety outcome was defined as the number of hospitalizations, intubations (breathing tube inserted in the patient's throat) or deaths that were asthma related.

Main Safety Outcome		
	Group A **Fluticasone Propionate Plus Salmeterol** **3107 patients**	**Group B** **Fluticasone Propionate** **3101 patients**
Hospitalization Due to Asthma	27 of 3107 (Less than 1%)	21 of 3101 (Less than 1%)
Breathing Tube	0 of 3107 (0%)	0 of 3101 (0%)
Death	0 of 3107 (0%)	0 of 3101 (0%)

During the 6 month study, 265 of 3107 patients (9%) in Group A had an asthma attack (exacerbation). In Group B, 309 of 3101 patients (10%) had an asthma attack.

Description of Adverse Reactions and Their Frequency

Serious Adverse Reactions

A serious adverse reaction is defined as a problem that the study doctor believes is related to the medicine that also leads to one or more of the following outcomes: a hospital stay, a life-threatening problem, permanent damage, death, or other important medical reason.

For this study, the table below lists the drug-related serious adverse reactions that occurred after the patients were assigned to their study group. There were no deaths.

Serious Adverse Reactions		
	Group A **Fluticasone Propionate Plus Salmeterol** **3107 patients**	**Group B** **Fluticasone Propionate** **3101 patients**
Asthma	4 of 3107 (less than 1%)	1 of 3101 (less than 1%)
Allergic Reaction (Hypersensitivity)	0 of 3107 (0%)	1 of 3101 (less than 1%)

Non-Serious Adverse Reactions

In this study, doctors also collected information about non-serious adverse events (any medical problems which were not life threatening and did not lead to a hospital stay) but only if these adverse events caused the patient to stop taking study medicine. For further information about these non-serious adverse events and information about the patients

who dropped out of the study, see the scientific summary on GSK's Clinical Study Register using the following link - 115358.

Comments on the Outcome of the Study

What did this study tell researchers?

This study provides evidence that in patients 4 to 12 years old, the combination of fluticasone propionate and salmeterol (in a single inhaler) results in no increased risk of hospitalization, intubation, or death related to asthma compared with fluticasone propionate alone. No patients required a breathing tube or died during the study.

This study was a Phase IV study. Phase IV studies are studying medicines that are already approved in some countries.

This summary shows the results from one study. Other studies may have different results.

We would like to thank the patients who participated and their parents. The results of this study will help answer important scientific questions about asthma in children.

Further Studies

Other studies of fluticasone propionate and salmeterol in combination (in a single inhaler) in children with asthma, have been conducted and more are underway. The results of these studies will also be available on GSK's Clinical Study Register after the studies end and the results are analysed (see link below).

Where Additional Information Can Be Found

Clinical studies have unique study numbers, which are included in publications and other information about the study. Here are the unique study numbers associated with this study. The links below provide you with scientific summaries and other information on the Internet.*

Organization	Website	Study Number
European Medicines Agency	www.clinicaltrialsregister.eu	2011-001643-79
US National Institutes of Heath (NIH)	www.clinicaltrials.gov	NCT01462344
GlaxoSmithKline (GSK)	www.gsk.clinicalstudyregister.com	115358

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 to change by your doctor.

This document was developed and approved by GSK on January 4, 2017. The information in this summary doesn't include information available after this date.

*For readers of this document in text form, the websites associated with the hyperlinks above are
http://www.gsk-clinicalstudyregister.com/study/115358?study_ids=115358#rs
https://clinicaltrials.gov/ct2/show/NCT01462344?term=115358&rank=1
https://www.clinicaltrialsregister.eu/ctr-search/trial/2011-001643-79/results