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 triple therapy with dual therapy in patients with poorly controlled asthma.

Full Scientific Title: A Phase III, randomised, double-blind, active controlled, parallel group study, comparing the efficacy, safety and tolerability of the fixed dose combination of fluticasone furoate, umeclidinium, and vilanterol with the fixed dose dual combination of fluticasone furoate and vilanterol administered once-daily via a dry powder inhaler in subjects with inadequately controlled asthma.

Study Number: 205715

## 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 October 2016 and ended in February 2019.

What was the main objective of this study?

Asthma is a long-term condition of the airways. When the airways are inflamed, they become narrow. This narrowing can cause coughing, wheezing, chest tightness, and shortness of breath. For patients with asthma, inhaled medicines are an important part of treatment.

One of the approved treatments for asthma is a combination of two inhaled medicines (dual therapy). However, dual therapy may not be enough to control symptoms in patients with moderate to severe asthma. GSK has developed a combination of three inhaled medicines (triple therapy) by adding umeclidinium to the dual therapy. Researchers wanted to see how well the addition of umeclidinium to dual therapy improved patients' lung function compared with dual therapy alone in patients who had poorly controlled asthma.

## Which medicines were studied?

Patients were put into one of the six treatment groups by chance (randomisation). Four different doses of triple therapy and two different doses of dual therapy were used in this study (as shown in figure below).

| Treatment Groups | | | | | | |
|---|---|---|---|---|---|---|
| **Set** | **Set A – low-dose fluticasone furoate groups** | | | **Set B – high-dose fluticasone furoate groups** | | |
| **Therapy type** | **Dual** | **Triple** | | **Dual** | **Triple** | |
| **Treatment Groups** | **Group 1** | **Group 2** | **Group 3** | **Group 4** | **Group 5** | **Group 6** |
| **Fluticasone furoate** | 100 mcg | 100 mcg | 100 mcg | 200 mcg | 200 mcg | 200 mcg |
| **Vilanterol** | 25 mcg | 25 mcg | 25 mcg | 25 mcg | 25 mcg | 25 mcg |
| **Umeclidinium** | - | 31.25 mcg | 62.5 mcg | - | 31.25 mcg | 62.5 mcg |

mcg = microgram

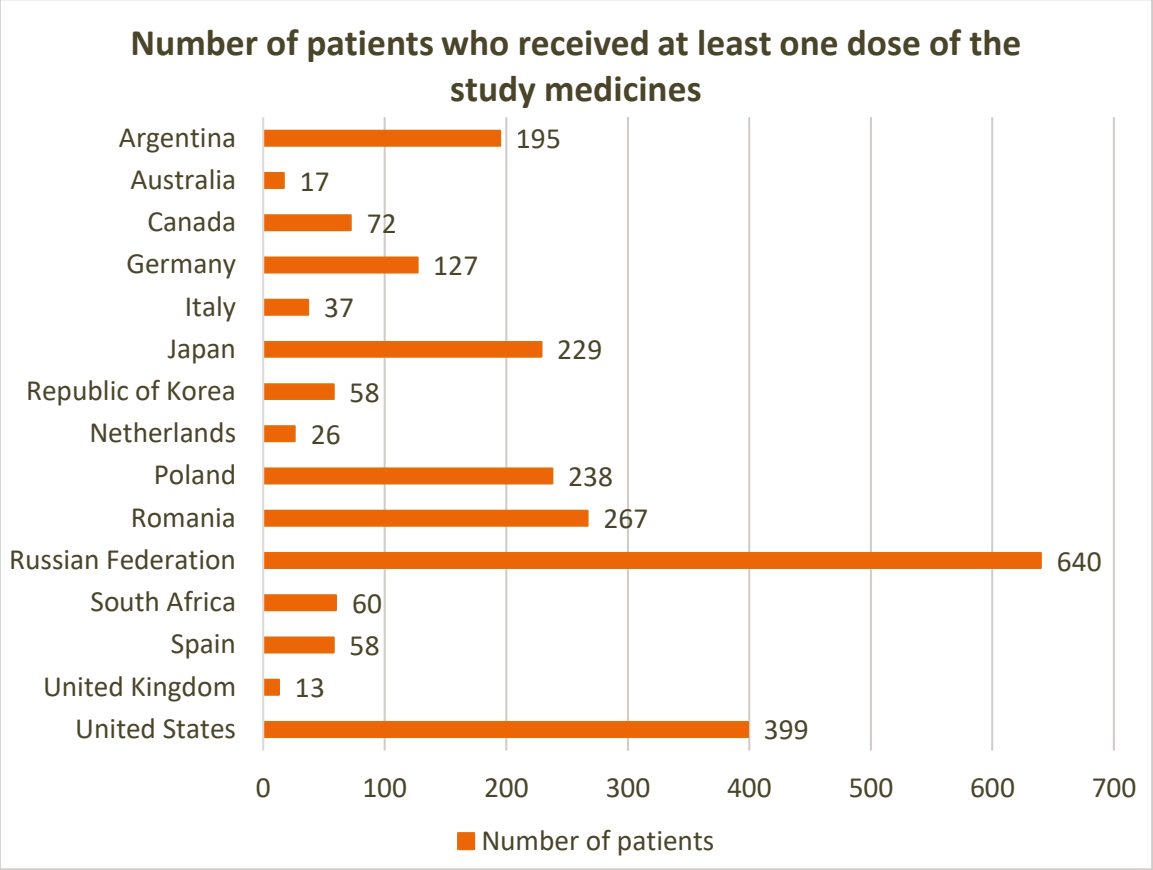
Fluticasone furoate is an inhaled corticosteroid (ICS), an inhaled medicine that reduces inflammation in the lungs.

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

Neither patients nor study doctors knew who was receiving which treatment. This is called a double-blind study.

## Where was this study done?

Study sites were in 15 countries.




## 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.

Men and women were included in the study if they:

- Were at least 18 years old.
- Had been diagnosed with asthma at least one year before starting the study.
- Were taking daily asthma treatment (medium to high dose of ICS, and LABA) for at least 12 weeks before starting the study.
- Had poorly controlled asthma as scored using an asthma survey.

Men and women were excluded from the study if they:

- Had worsening of asthma that required a change in the dose of ICS and LABA within six weeks before starting the study.
- Had chronic obstructive pulmonary disease or any other lung disease.
- Were current smokers or former smokers with a history of smoking at least 20 cigarettes daily for 10 years.
- Had any medical condition that the study doctor thought would affect the results of the study.

A total of 2436 patients received at least one dose of the study medicines. The table below shows the gender and age of these patients.

| Patients who received at least one dose of the study medicines | | | | | | |
|---|---|---|---|---|---|---|
| **Treatment Groups** | **Group 1**<br>**407 patients** | **Group 2**<br>**405 patients** | **Group 3**<br>**406 patients** | **Group 4**<br>**406 patients** | **Group 5**<br>**404 patients** | **Group 6**<br>**408 patients** |
| **Female** | 254 (62%) | 262 (65%) | 248 (61%) | 252 (62%) | 240 (59%) | 258 (63%) |
| **Male** | 153 (38%) | 143 (35%) | 158 (39%) | 154 (38%) | 164 (41%) | 150 (37%) |
| **Age Range (years)** | 19 to 85 | 18 to 88 | 18 to 80 | 20 to 84 | 18 to 82 | 18 to 78 |
| **Average Age (years)** | 53 | 52 | 53 | 54 | 54 | 54 |

For more detailed information about the patients included in this study, see the scientific results summaries (links to those summaries are provided at the end of this document).

## 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.

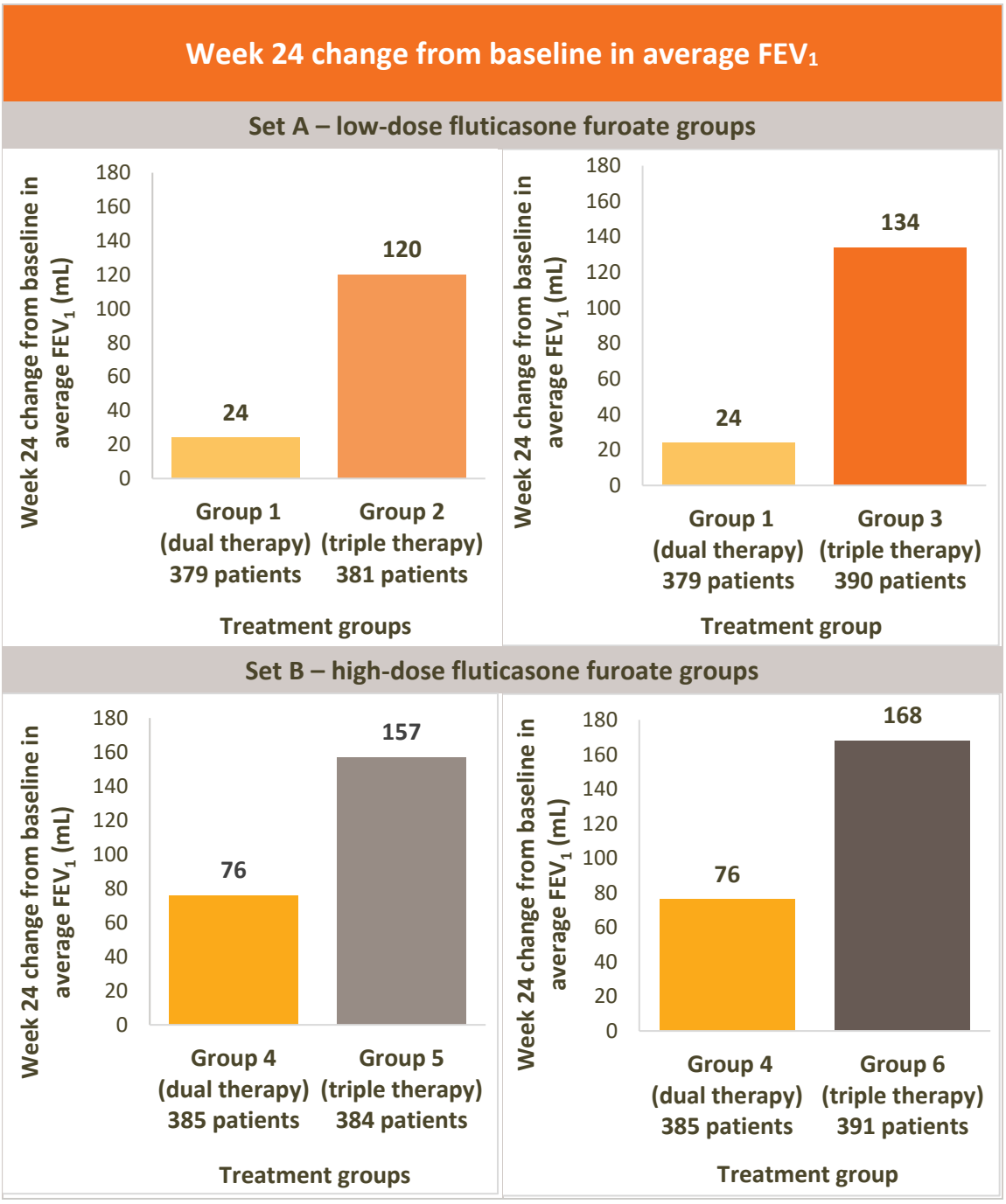
One measure of lung function is forced expiratory volume in one second ($FEV_1$). $FEV_1$ measures the amount of air a patient can breathe out in the first second when asked to blow as hard as possible into a tube connected to a machine (spirometer). Higher values of $FEV_1$ mean more air is flowing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

Study doctors measured $FEV_1$ values, before patients took the study medicines, on Day 1 (baseline), and at Week 24. The difference between $FEV_1$ values at baseline 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 of the dual therapy group were compared with each of the two triple therapy groups within in each set:

- Set A (low-dose fluticasone furoate groups):
    - Group 1 (dual therapy) compared with Group 2 (triple therapy)
    - Group 1 (dual therapy) compared with Group 3 (triple therapy).
- Set B (high-dose fluticasone furoate groups):
    - Group 4 (dual therapy) compared with Group 5 (triple therapy)
    - Group 4 (dual therapy) compared with Group 6 (triple therapy).

The Week 24 change from baseline in $FEV_1$ could be calculated for 2310 patients who had both Day 1 and Week 24 values. The results are shown in the figure below.




mL = millilitre

After 24 weeks, the improvement in the average $FEV_1$ of patients in the triple therapy groups was greater compared with the dual therapy groups.

More information about the study results is available in the scientific results summaries (links to those summaries are provided 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 these events can be found in the scientific results summaries (links to those summaries are provided at the end of this document).

If the study doctor thinks that the event was caused by the study medicines, 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 medicines. The side effects in this summary may be different to those in the Informed Consent or other documents related to the study medicines.

Two serious side effects were reported. One patient (less than 1%) in Group 2 had a serious side effect of a blood clot that went to the lung and resulted in the death of the patient (fatal serious side effect). A review of this possible side effect was done using results from other studies. The review showed that blood clots caused by the study medicines is unlikely. One patient (less than 1%) in Group 6 reported a serious side effect of abnormal rapid, irregular heartbeat. No serious side effects were reported in the other treatment groups.

The table below shows the number of patients (percent) with non-serious side effects that were reported by one percent or more of patients in any treatment group.

| Number of patients (percent) with non-serious side effects that were reported by one percent or more of patients in any treatment group | | | | | | |
|---|---|---|---|---|---|---|
| **Treatment Groups** | **Group 1**<br><br>**407 patients** | **Group 2**<br><br>**405 patients** | **Group 3**<br><br>**406 patients** | **Group 4**<br><br>**406 patients** | **Group 5**<br><br>**404 patients** | **Group 6**<br><br>**408 patients** |
| **Hoarse voice** | 3 (less than 1%) | 0 | 4 (less than 1%) | 5 (1%) | 2 (less than 1%) | 3 (less than 1%) |

## How has this study helped patients and researchers?

This was a Phase III study. Phase III studies collect information about how well new medicines work and how safe they are. The results help government regulators make decisions about new medicines for their country. Researchers concluded that addition

of umeclidinium to dual therapy, when treating patients with poorly controlled asthma, showed a greater improvement in lung function compared with dual therapy alone. The side effects reported in this study were limited.

## Are there plans for further studies?

Other studies of fluticasone furoate, umeclidinium, and vilanterol in patients with asthma have been conducted and more are being planned.

## 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.

| Organisation | Website | Study Number |
|---|---|---|
| **European Medicines Agency** | www.clinicaltrialsregister.eu | 2016-001304-37[1] |
| **United States National Institutes of Health (NIH)** | www.clinicaltrials.gov | NCT02924688[2] |

Your doctor can help you understand more about this study and the results. Speak to your doctor about the treatment options available in your country. 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 asthma.

The content for this document was finalised by GSK on the 27th of January 2020. The information in this summary does not include additional information available after this date.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-001304-37

[2] https://clinicaltrials.gov/ct2/show/study/NCT02924688