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: A study comparing the effects of a once a day inhaler containing three medicines and a twice a day inhaler containing two medicines in patients with chronic obstructive pulmonary disease (COPD).

Full Scientific Title: A phase III, 24 week, randomized, double blind, double dummy, parallel group study comparing the efficacy, safety and tolerability of the fixed-dose triple combination FF/UMEC/VI administered once daily in the morning via a dry powder inhaler with Budesonide/Formoterol 400mcg/12mcg administered twice-daily via a reservoir inhaler in subjects with chronic obstructive pulmonary disease.

Who sponsored this study?

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

General information about the clinical study

When was this study done?

The study started in January 2015 and ended in April 2016.

What was the reason for conducting this study?

COPD is a long-term disease of the lungs that makes it hard to breathe and gets worse over time.

GSK developed a potential new treatment for patients with COPD. This new treatment includes a combination of three medicines in one inhaler which is taken once a day.

This treatment is called triple therapy. A current treatment for COPD is a combination of two medicines in a single inhaler taken twice a day. This is called dual therapy.

The purpose of this study was to compare triple and dual therapy. After 24 weeks of treatment, researchers wanted to compare how well patients' lungs worked when taking the triple therapy compared with the dual therapy. They also wanted to see how the two treatments would affect health-related quality of life.

This was a Phase III study. Phase III studies collect information about how well new study medicines work and how safe they are. The results help regulators make decisions about whether to approve new medicines.

Which medicines were studied?

Patients were assigned to one of the two treatment groups by chance (randomisation). Neither patients nor study doctors knew who was receiving which treatment. This is called a double-blind study.

Triple Therapy Group Taken once a day	A combination of 3 medicines in one inahler: 1. **Fluticasone Furoate (FF)** 100 micrograms 2. **Umeclidinium Bromide (UM)** 62.5 micrograms 3. **Vilanterol (VI)** 25 micrograms
Dual Therapy Group Taken twice a day	A combination of 2 medicines in one inhaler: 1. **Budesonide (BUD)** 400 micrograms 2. **Formoterol (FOR)** 12 micrograms

The medicines in the Triple Therapy and Dual Therapy include the same general classes of medicines: **inhaled corticosteroids (ICS)** and **bronchodilators**.

- Fluticasone Furoate and Budesonide are an **inhaled corticosteroids (ICS)**. An inhaled corticosteroid is a medicine that reduces swelling and inflammation in the lungs.
- Umeclidinium bromide, vilanterol and formoterol are all **bronchodilators**. Bronchodilators are medicines that open the airways of the lung. The Triple therapy contains two different types of bronchodilators.

Study medicines were taken through a device called an inhaler. Inhalers are designed to deliver medicine to the lungs. All study participants used two different inhalers: one with an active study medicine and one with an inactive medicine (placebo). One inhaler was used two times a day and the other inhaler was used once a day in the morning. No one knew which inhaler contained the active medicine.

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, men and women could be included if they were:

- 40 years old or older
- Current smokers or had smoked a lot in the past
- Diagnosed with COPD and were taking daily medication for their COPD for at least 3 months before starting the study.

Patients were not allowed in the study if they had:

- Asthma, tuberculosis, lung cancer or other serious non-respiratory diseases
- Worsening of COPD or pneumonia within 14 days of study start.

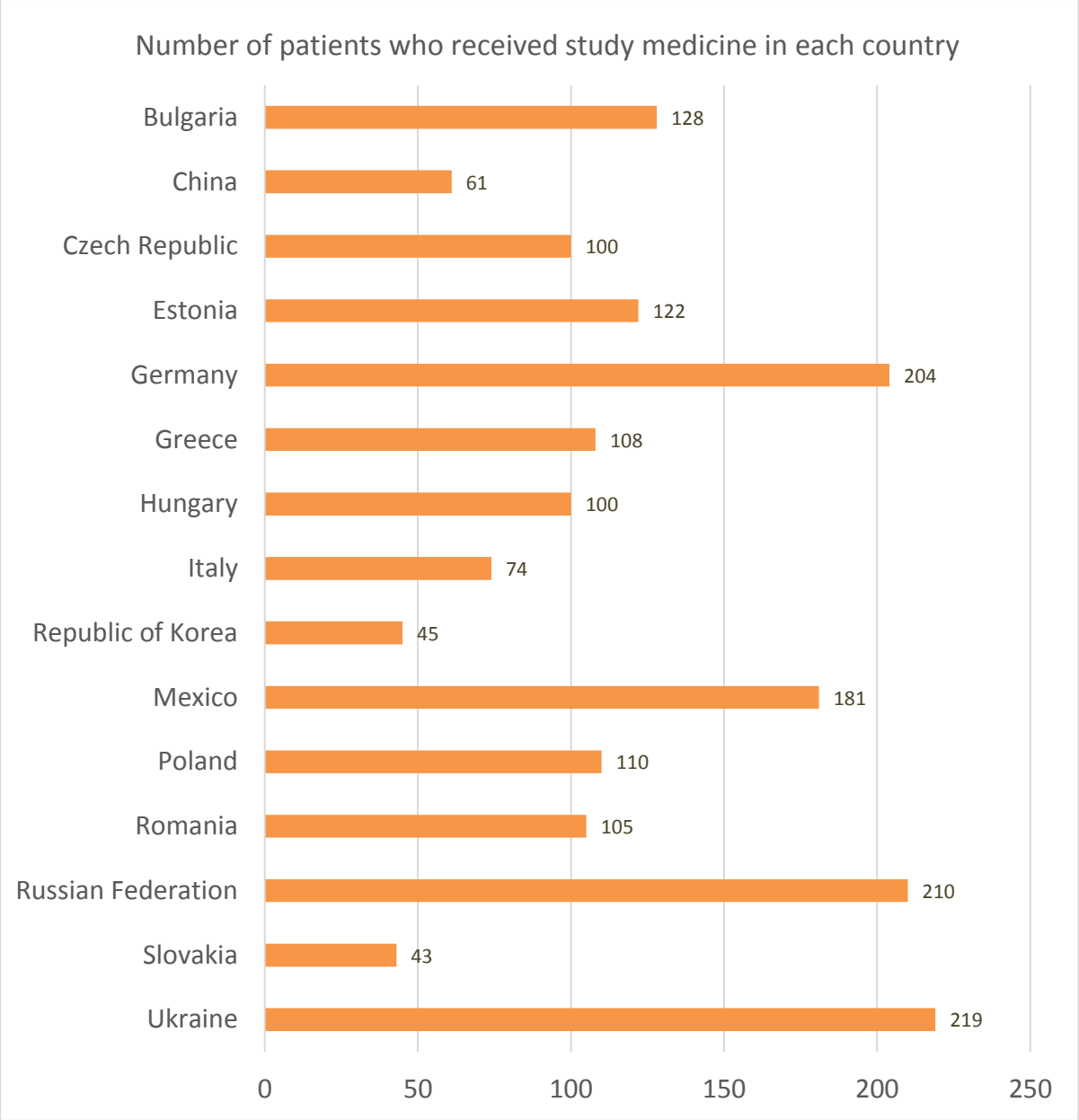
For more detailed information about the patients included in this study, see the scientific summary on the GSK Study Register (see link provided at the end of this document).

A total of 1810 patients met the study requirements and received study medicine. The table below provides the gender and ages of these patients.

	Triple Therapy Group 911 patients	Dual Therapy Group 899 patients
Gender - Number of patients (percent)		
Female	233 (26%)	236 (26%)
Male	678 (74%)	663 (74%)
Age - in years		
Range	39 to 99	41 to 92
Average	64	64

Where was this study done?

The study sites were located in 15 countries.



What were the overall results of the study?

Lung Function

Lung function tests measure how well lungs are moving air in and out of the body. Doctors can use 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).

To compare the lung function of the Triple Therapy Group with the Dual Therapy Group, study doctors measured each patient's lung function at the beginning of the study (baseline FEV_1) and after 24 weeks of treatment (FEV_1 after treatment). The difference between the two values for FEV_1 is called the change from baseline.

The results from patients in each study group were combined and averaged. The difference between the two groups was compared.

After 24 weeks of treatment, the average lung function of the Triple Therapy Group improved and the average lung function of the Dual Therapy group got worse. The difference in FEV_1 between the two groups was 171 mL. This difference was statistically significant. Statistically significant means that the difference was not likely due to chance alone.

Lung Function Results at Week 24		
	Triple Therapy Group	**Dual Therapy Group**
Number of patients with a baseline value and at least one value after baseline (so change could be measured)	895 patients	874 patients
Average FEV_1 change from baseline to after 24 week treatment	142 mL higher	29 mL lower
Difference between Triple Therapy Group and Dual Therapy Group	171 mL	

Health-Related Quality of Life

This study used a questionnaire called the St. George's Respiratory Questionnaire for COPD (referred to as SGRQ-C) to measure the effects of COPD and its treatment on

quality of life. This questionnaire is a useful tool to evaluate a COPD patient's overall well-being, symptoms and daily activity. Scores range from 0 to 100 units, with a lower score indicating better health-related quality of life.

In this study, the SGRQ-C score was converted to a SGRQ total score. Study doctors measured each patient's questionnaire scores at the beginning of the study and after 24 weeks of treatment with the study medicines. The difference between the two values for SGRQ total score is called the change from baseline.

The results from patients in each study group where combined and averaged. The average change from baseline between the two groups was then compared.

Patients in both treatment groups recorded improvements from baseline in average SGRQ total scores. The difference in SGRQ total scores between the two groups was 2.2 units. This difference was statistically significant.

SGRQ Total Score Results at Week 24		
	Triple Therapy Group	**Dual Therapy Group**
Number of patients with a baseline value and at least one value after baseline (so change could be measured)	887 patients	866 patients
Average SGRQ total score change from baseline to after 24 week treatment (lower scores indicate better health-related quality of life)	6.6 unit decrease	4.3 unit decrease
Difference in average SGRQ total score after treatment between Triple Therapy and Dual Therapy Groups	2.2 units	

What were the side effects?

Study doctors collect information about the safety of study medicines. Any medical events including symptoms reported by patients in the clinical study are called adverse events. These adverse events can be found in the scientific summary (see link provided at the end of this document).

The study doctors record if they think any of these events may be caused by the medicine. If the study doctor believes that the event was caused by the medicine, they record this adverse event as a possible side effect. In a clinical study these are called **adverse reactions**. A **serious adverse reaction** is an adverse reaction that is life threatening, requires hospitalisation, or results in death or permanent damage.

This plain language summary describes those side effects (adverse reactions including serious adverse reactions) recorded by study doctors.

Two patients in the Triple Therapy Group and one patient in the Dual Therapy Group reported serious adverse reactions.

Serious Adverse Reactions up to Week 24		
	Triple Therapy Group 911 patients	**Dual Therapy Group 899 patients**
Abnormal Heartbeat (Atrial flutter)	0 of 911	1 of 899 (less than 1%)
Heart Failure (Cardiac Failure)	1 of 911 (less than 1%)	0 of 899
Lung Infection	1 of 911 (less than 1%)	0 of 899
Pneumonia	1 of 911 (less than 1%)	0 of 899

The adverse reactions (serious and non-serious) reported by 5 or more patients in at least one treatment group are shown in the table below.

Adverse Reactions in 5 or More Patients up to Week 24		
	Triple Therapy Group 911 patients	**Dual Therapy Group 899 patients**
Muscle spasms (non-serious)	5 of 911 (less than 1%)	1 of 899 (less than 1%)
Pneumonia (serious and non-serious)	5 of 911 (less than 1%)	0 of 899

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

How has this study helped patients and researchers?

The results of this study were submitted to regulators for approval so that doctors can use triple therapy to treat COPD patients.

Are there plans for further studies?

Other studies of a fixed-dose triple therapy in adults with COPD have been conducted and more are underway. The results of these studies will also be available on the GSK Study Register (see link provided at the end of this document).

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	2013-003073-10
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT02345161
GlaxoSmithKline (GSK)	www.gsk-clinicalstudyregister.com	116853

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

https://www.clinicaltrialsregister.eu/ctr-search/trial/2013-003073-10/results

https://clinicaltrials.gov/ct2/show/NCT02345161?term=116853&rank=1

https://www.gsk-clinicalstudyregister.com/search/?study_ids=116853

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 developed and approved by GSK on 20th February 2018. The information in this summary does not include additional information available after this date.