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 six different doses of nemiralisib with placebo when added to regular medicine(s) in patients with moderate to severe worsening of chronic obstructive pulmonary disease.

Full Scientific Title: A phase IIb, randomised (stratified), double-blind (sponsor open), parallel-group, placebo-controlled, dose-finding study of nemiralisib (GSK2269557) added to standard of care versus standard of care alone in participants diagnosed with an acute moderate or severe exacerbation of chronic obstructive pulmonary disease.

Study Number: 200879

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 November 2017 and ended in January 2019.

What was the main objective of this study?

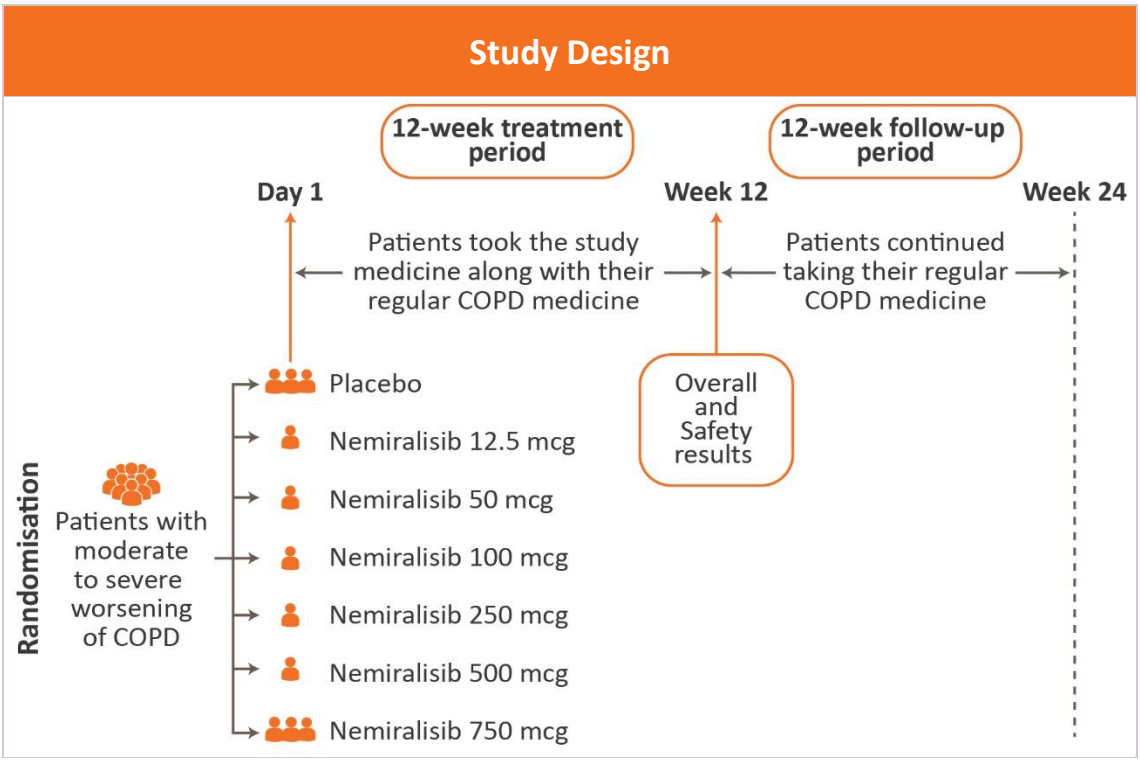
Chronic obstructive pulmonary disease (COPD) is a long-term disease of the lungs that makes it hard to breathe and gets worse over time. Patients with COPD have inflammation in the airways and/or lungs. This inflammation can cause shortness of breath, coughing, and chest tightness.

Reducing the severity of symptoms is important in the treatment of COPD. For patients with COPD, inhaled medicines are an important part of treatment. An inhaler is a handheld device that delivers medicine to the lungs.

Researchers wanted to see if nemiralisib, an inhaled medicine, reduced lung inflammation and improved lung function in patients with moderate to severe worsening of COPD. In this study, six different doses of nemiralisib were compared with placebo (no active medicine), when added to patients' regular COPD medicine(s) (standard of care). The study also assessed the safety of nemiralisib.

Which medicines were studied?

Patients were included in one of the seven treatment groups by chance (randomisation), as shown in figure below. Three times as many patients were included in the placebo group and nemiralisib 750 microgram (mcg) group compared with the other nemiralisib groups.



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

For results reported during the 12-week follow-up period, see the scientific results summaries (links to those summaries are provided at the end of this document).

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 with COPD were included in the study if they were:

- Between 40 to 80 years of age.
- Current or former smokers.
- Experiencing sudden worsening of COPD symptoms requiring additional COPD medicines.

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

- Asthma.
- Pneumonia.
- Any other lung problems such as tuberculosis.
- Removal of part of the lung.
- Liver or unstable heart disease.
- Other disease(s) or medicine(s) that the study doctor thought could affect the results of the study.

A total of 938 patients received at least one dose of the study medicine. The table below shows the gender and age of these patients.

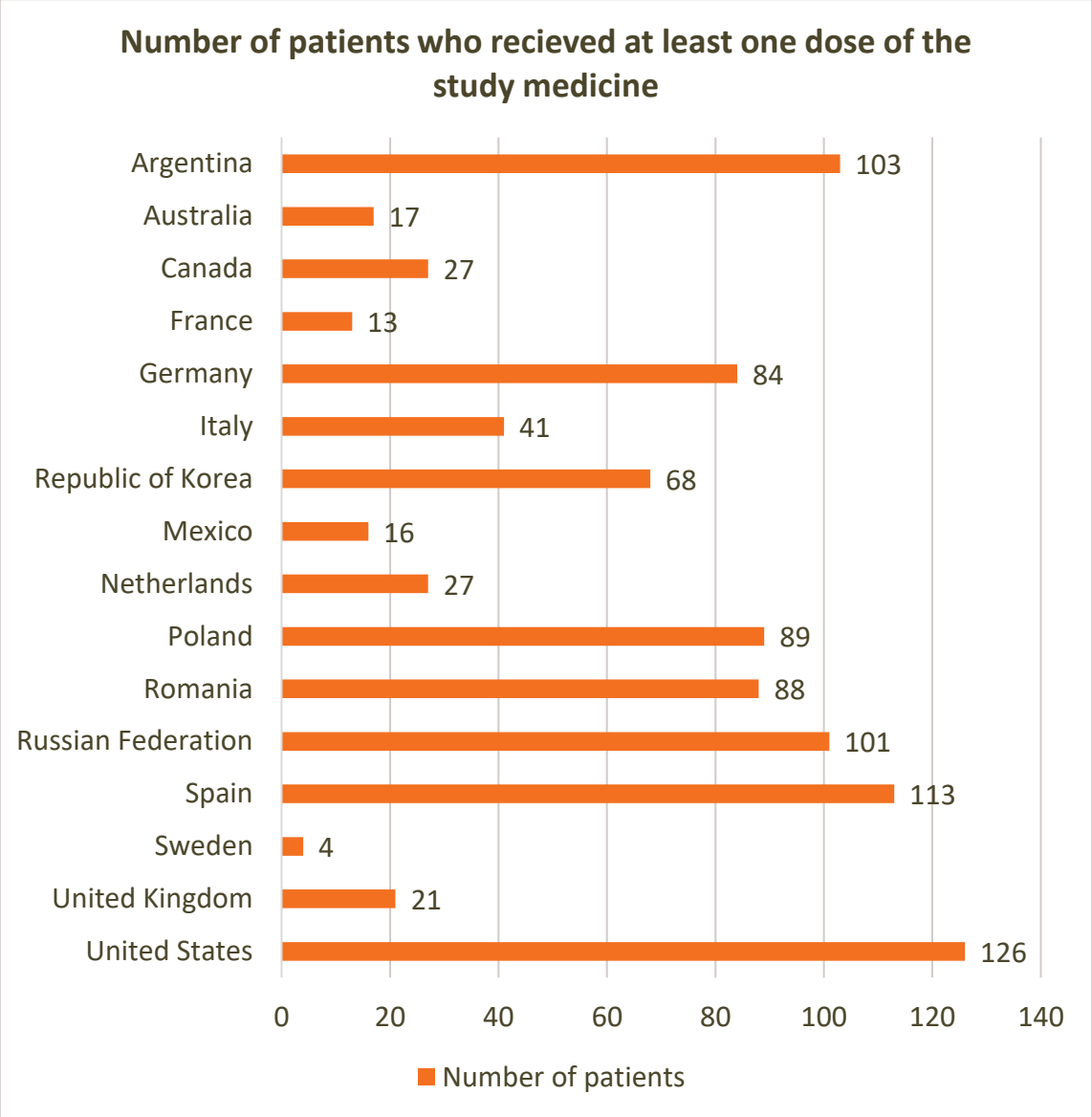
Patients who received at least one dose of the study medicine							
	Placebo	Nemiralisib					
		12.5 mcg	50 mcg	100 mcg	250 mcg	500 mcg	750 mcg
	276 patients	22 patients*	91 patients	92 patients	90 patients	89 patients	278 patients
Gender – Number of patients (percent)							
Female	86 (31%)	6 (27%)	35 (38%)	29 (32%)	31 (34%)	22 (25%)	100 (36%)
Male	190 (69%)	16 (73%)	56 (62%)	63 (68%)	59 (66%)	67 (75%)	178 (64%)
Age - in years							
Range	40 to 80	56 to 79	44 to 79	46 to 78	49 to 78	45 to 80	41 to 80
Average	65	68	63	65	66	65	65

*The study protocol was changed part way through the study to add the Nemiralisib 12.5 mcg treatment group.

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).

Where was this study done?

Study sites were in 16 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.

Study doctors measured the FEV_1 values on Day 1 (baseline) and then again at Week 12. The difference between the FEV_1 values at baseline and after 12 weeks of treatment is called the Week 12 change from baseline in FEV_1.

The Week 12 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 seven treatment groups. The Week 12 change from baseline in FEV_1 could be calculated for 721 patients who had both baseline and Week 12 values measured. The results are shown in the table below.

Week 12 change from baseline in average FEV_1							
	Placebo	Nemiralisib					
		12.5 mcg	50 mcg	100 mcg	250 mcg	500 mcg	750 mcg
Number of patients with FEV_1 values at baseline and at Week 12	215	16	72	75	69	58	216
Week 12 change from baseline in average FEV_1 (in millilitres [mL])	52 mL	31 mL	26 mL	14 mL	58 mL	49 mL	49 mL

After 12 weeks of treatment, the change from baseline in the average FEV_1 (lung function) in patients was similar across all treatment groups, including placebo.

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

In blinded studies, the doctor does not know which study medicine the patient is taking. In some cases, side effects will be assigned to placebo.

No serious side effect was reported by more than one percent of patients in any treatment group up to Week 12. Three patients (one each from the placebo group, nemiralisib 50 mcg group, and nemiralisib 750 mcg group) reported a serious side effect of worsening symptoms of COPD. The patient from the nemiralisib 750 mcg group also reported low blood pressure. No patients in the other nemiralisib (12.5, 100, 250, and 500 mcg) groups reported serious side effects.

The table below shows the number of patients (percent) with non-serious side effects that were reported by two or more percent of patients up to Week 12.

Number of patients (percent) with non-serious side effects that were reported by two or more percent of patients up to Week 12							
	Placebo	Nemiralisib					
		12.5 mcg	50 mcg	100 mcg	250 mcg	500 mcg	750 mcg
	276 patients	22 patients	91 patients	92 patients	90 patients	89 patients	278 patients
Cough	8 (3%)	0	10 (11%)	9 (10%)	21 (23%)	28 (31%)	89 (32%)
Headache	3 (1%)	0	1 (1%)	2 (2%)	1 (1%)	0	1 (less than 1%)
Throat irritation	1 (less than 1%)	0	0	0	0	0	5 (2%)

How has this study helped patients and researchers?

This was a Phase II study. A Phase II study aims to collect information about the safety of the medicine and may also provide early information about how well the medicine works against the disease. This study showed that addition of nemiralisib to regular COPD medicine for patients with moderate-severe worsening of COPD did not show improvements in lung function. The number of side effects reported by patients in the

nemiralisib groups were higher than in placebo group. Cough was the most common non-serious side effect in all the treatment groups.

Are there plans for further studies?

Other studies on nemiralisib 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 adverse events.

Organisation	Website	Study Number
European Medicines Agency	www.clinicaltrialsregister.eu	2017-001074-42[1]
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT03345407[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 COPD.

The content for this document was finalised by GSK on the 18th of November 2019. The information in this summary does not include additional information available after this date.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=200879

[2] https://clinicaltrials.gov/ct2/show/NCT03345407?term=NCT03345407&rank=1