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 five different doses of danirixin with placebo in patients with chronic obstructive pulmonary disease.

Full Scientific Title: Randomised, double-blind, placebo-controlled, multi-centre, dose ranging study to evaluate the efficacy and safety of danirixin tablets administered twice daily compared with placebo for 24 weeks in adult participants with chronic obstructive pulmonary disease.

Study Number: 205724

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 April 2017 and ended in October 2018.

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 inflamed airways and/or inflammation in the lungs. This inflammation can cause shortness of breath, coughing, and chest tightness. Reducing the severity of symptoms is important in the treatment of COPD.

Danirixin is a medicine that decreases inflammation. It was tested to see if it could reduce patients' COPD symptoms. In this study, researchers wanted to see how five different doses of danirixin worked in reducing COPD symptoms compared with placebo (no active medicine), when added to patients' regular COPD medicine(s). The study also assessed the safety of danirixin.

Which medicines were studied?

During the study, patients were included in one of the six treatment groups by chance (randomisation):

- Placebo
- Danirixin 5 milligram (mg)
- Danirixin 10 mg
- Danirixin 25 mg
- Danirixin 35 mg
- Danirixin 50 mg

Patients took either placebo or danirixin tablets twice daily for six months. Neither patients nor study doctors knew who was receiving which treatment. This is called a double-blind study.

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 between 40 to 80 years of age.
- Were current or former smokers.
- Had COPD with symptoms including long-term cough, increased phlegm, and shortness of breath on most days for at least the three months before starting the study.
- Had a history of moderate or severe worsening of COPD symptoms (exacerbations), which required treatment and/or hospitalisation in the year before starting the study.

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

- Lung problems other than COPD.
- Undergone lung surgery before starting the study.
- A specific genetic condition that led to COPD.
- Pneumonia within three months before starting the study.
- Liver or heart disease.
- Other disease(s) or use of certain medicine(s) that the study doctor thought could affect the results of the study.

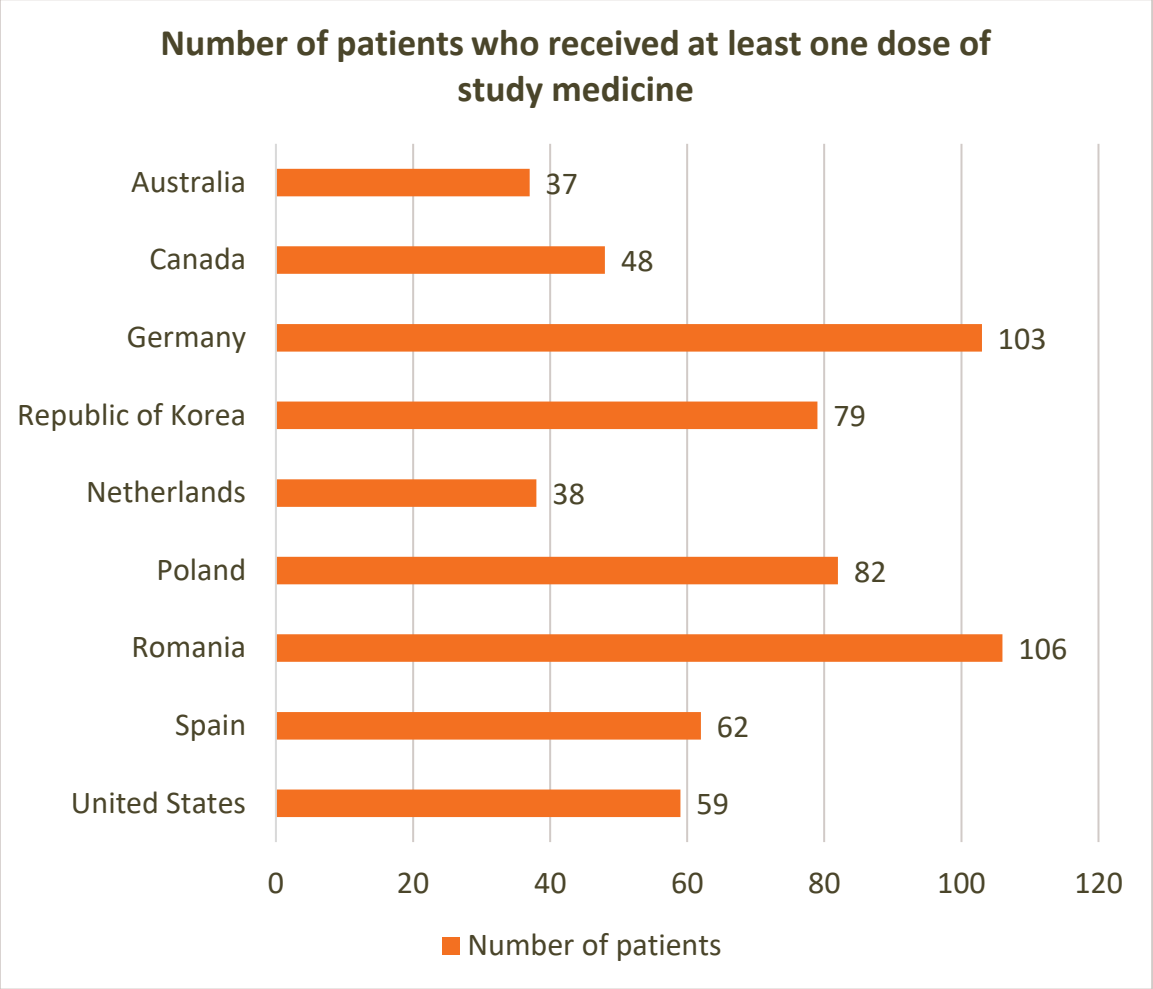
A total of 614 patients received at least one dose of the study medicine. The table below shows the gender and age of these patients.

Patients who received at least one dose of the study medicine						
	Placebo 102 patients	**Danirixin 5 mg 102 patients**	**Danirixin 10 mg 103 patients**	**Danirixin 25 mg 103 patients**	**Danirixin 35 mg 102 patients**	**Danirixin 50 mg 102 patients**
Gender						
Female	29 (28%)	36 (35%)	32 (31%)	38 (37%)	35 (34%)	32 (31%)
Male	73 (72%)	66 (65%)	71 (69%)	65 (63%)	67 (66%)	70 (69%)
Age - in years						
Range	47 to 80	48 to 79	50 to 80	51 to 79	47 to 80	46 to 78
Average	66	66	66	66	65	66

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 nine countries.

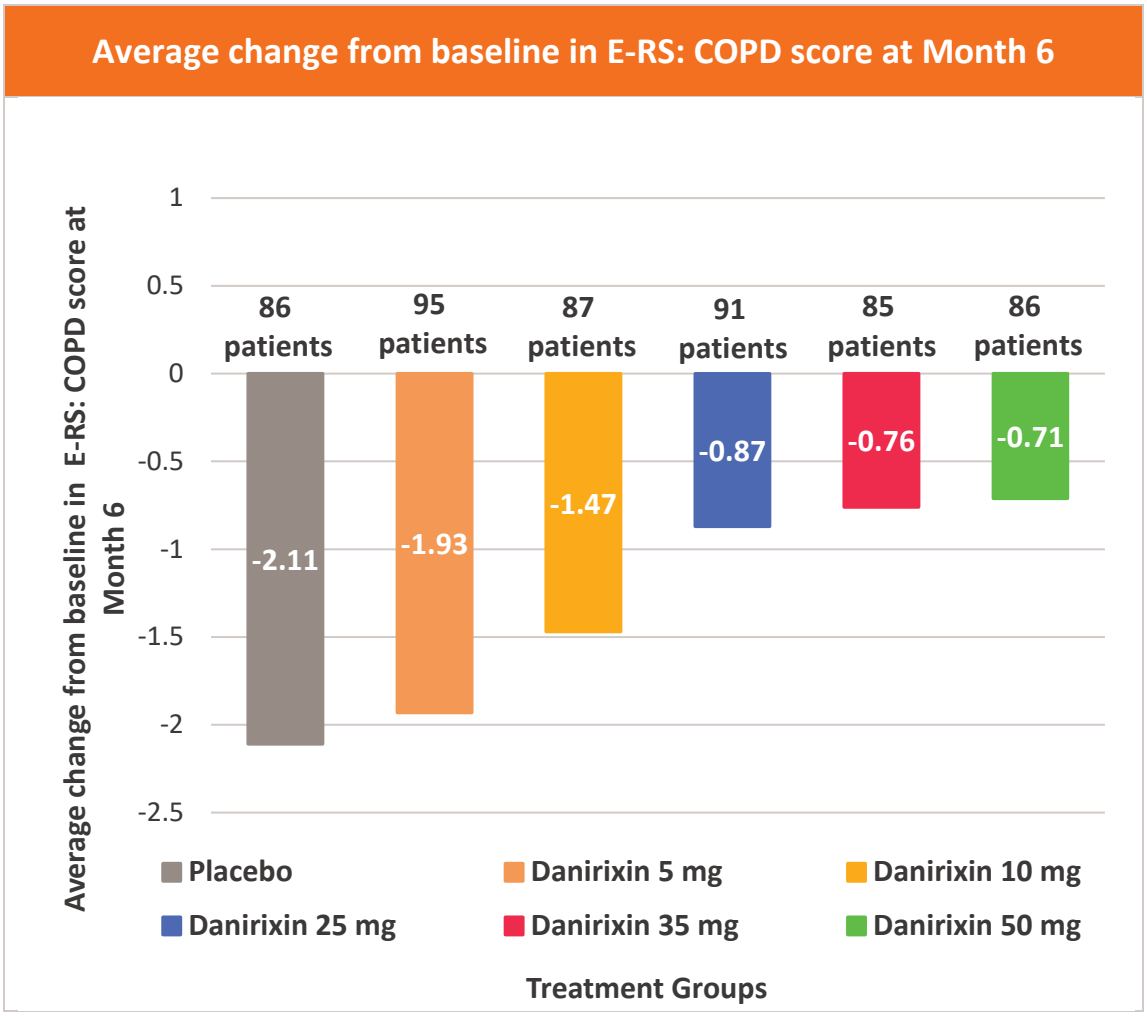


What were the overall results of the study?

In this study, patients scored their COPD symptoms (shortness of breath, cough and phlegm production, and chest tightness and chest congestion) once daily using the Evaluating Respiratory Symptoms in COPD (E-RS: COPD) tool. This tool helps measure the severity of COPD symptoms, where higher scores indicate more severe symptoms.

For each patient, the difference between E-RS: COPD score in the week before starting the study treatment (baseline) and Month 6 were calculated. This difference in patients' scores within each treatment group were combined and averaged to get the change from baseline scores. A decrease in the average E-RS: COPD score at Month 6 compared with the baseline score indicates a reduction in COPD symptoms during the study.

Results for 530 patients who recorded scores at baseline and Month 6 are shown in the figure below.



The placebo group showed the largest decrease in the average change from baseline in E-RS: COPD score. This means the placebo group showed a greater reduction of COPD symptoms at month 6 compared with all the danirixin 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 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.

One patient in the danirixin 50 mg group had a serious side effect of pneumonia.
No patients in any other treatment group had serious side effects.

The table below shows the non-serious side effects reported by more than one patient in any treatment group.

Non-serious side effects reported by more than one patient in any treatment group						
	Placebo 102 patients	**Danirixin 5 mg 102 patients**	**Danirixin 10 mg 103 patients**	**Danirixin 25 mg 103 patients**	**Danirixin 35 mg 102 patients**	**Danirixin 50 mg 102 patients**
Diarrhoea	3 (3%)	2 (2%)	1 (less than 1%)	2 (2%)	1 (less than 1%)	2 (2%)
Nose and throat infection (common cold)	0	1 (less than 1%)	0	0	2 (2%)	0

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 danirixin did not offer any benefit in reducing COPD symptoms. The side effects reported in this study were similar between the treatment groups.

Are there plans for further studies?

Other studies of danirixin as a treatment for COPD have been conducted and are completed. There are no plans for any further studies of danirixin in COPD.

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 side effects.

Organisation	Website	Study Number
European Medicines Agency	www.clinicaltrialsregister.eu	2016-003675-21[1]
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT03034967[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 22nd of August 2019. The information in this summary does not include additional information available after this date.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-003675-21

[2] https://clinicaltrials.gov/ct2/show/NCT03034967?term=205724&rank=1