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 learn about the effect of daprodustat given three times a week on haemoglobin in patients with anaemia due to chronic kidney disease.

Full Scientific Title: A phase 3 randomised, double-blind, active-controlled, parallel-group, multi-centre study in haemodialysis participants with anaemia of chronic kidney disease to evaluate the efficacy and safety of three-times weekly dosing of daprodustat compared to recombinant human erythropoietin, following a switch from recombinant human erythropoietin or its analogues.

Study Number: 204837

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 September 2018 and ended in June 2020.

What was the main objective of this study?

Chronic kidney disease (CKD) is a long-term disease of the kidneys. Some people with CKD cannot make enough red blood cells, which contain an oxygen-carrying protein called haemoglobin (Hgb). This condition is called renal anaemia.

Patients with renal anaemia may be treated with erythropoiesis-stimulating agents (ESAs), such as epoetin alfa. These agents trigger the body to make more red blood

cells, which leads to an increase in Hgb levels. Daprodustat is a medicine that is being tested to treat renal anaemia.

Researchers wanted to see how well daprodustat works in maintaining Hgb levels compared with epoetin alfa in patients with renal anaemia. Researchers also assessed the safety of these medicines.

Which medicines were studied?

On Day 1 of the 52-week treatment period, patients were included in one of the following two treatment groups by chance (randomisation).

- Daprodustat group: Patients received daprodustat tablets by mouth three times a week.
- Epoetin alfa group: Patients received epoetin alfa through a vein (intravenously) once or three times a week.

Twice as many patients received daprodustat compared with epoetin alfa.

Patients also received placebo (no active medicine) as tablets or intravenously. Neither patients nor study doctors knew who received 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 with renal anaemia were included in the study if they:

- Were 18 to 99 years old.
- Had Hgb levels between 8 grams per decilitre (g/dL) and 11.5 g/dL before Day 1.
- Had haemodialysis (a treatment that filters blood and removes waste) three times or more in a week for at least four months before Day 1.
- Had been taking an ESA for at least three months before Day 1.

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

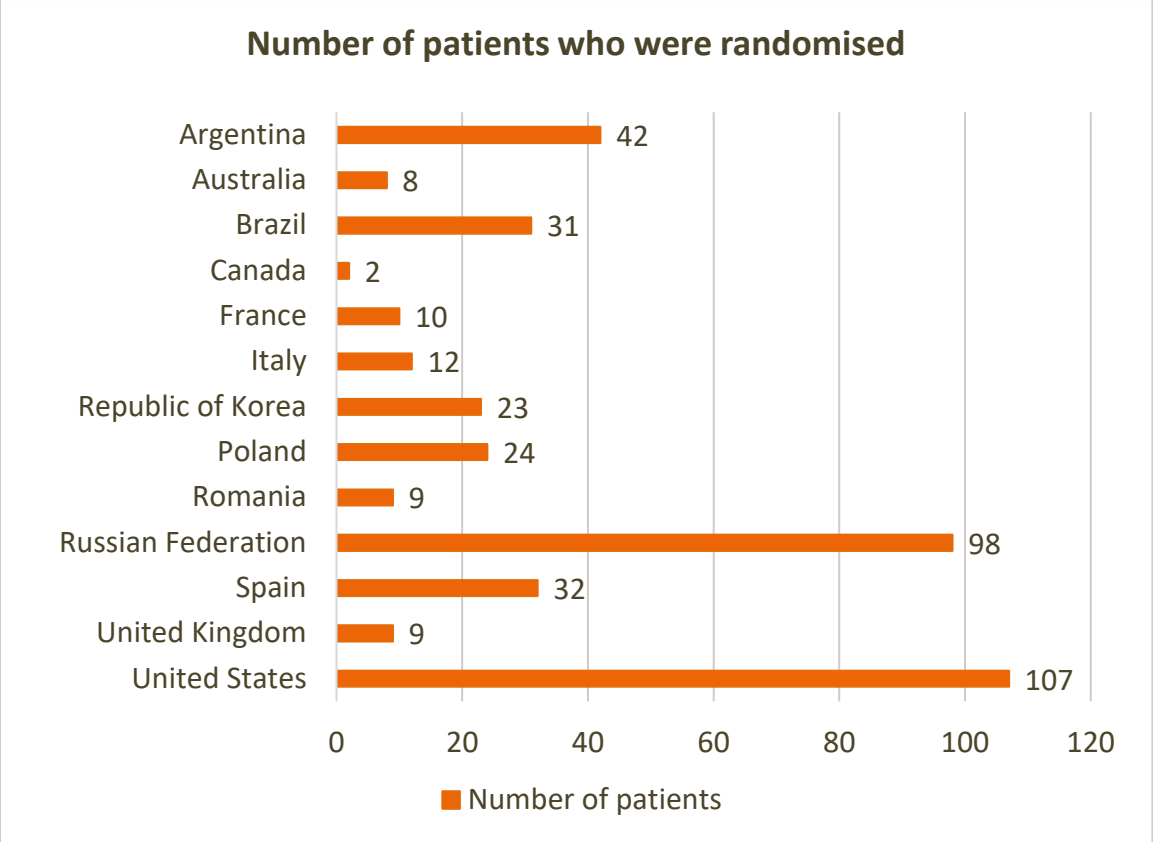
- A planned kidney transplant.
- Uncontrolled high blood pressure.
- A heart attack, stroke, or ministroke at least three months before Day 1.
- Another disease that could lead to anaemia.
- Stomach and intestinal bleeding at least three months before Day 1.
- Any other disease(s), abnormal test results, or other medication use that would put the patient at unacceptable risk or affect the results of the study.

Overall, 407 patients were randomised. The study included 230 men (57%) and 177 women (43%). The average age was 58 years. The youngest patient was 21 years old and the oldest patient was 90 years old.

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 13 countries.



What were the main results of the study?

The main objective was to compare daprodustat with epoetin alfa in maintaining patients' Hgb levels during Week 28 to Week 52 (testing period) of the study.

Study doctors collected blood samples from the patients. They measured each patient's Hgb levels on Day 1 (baseline) and during the testing period. The difference in the patient's baseline Hgb value and the average Hgb value during the testing period was calculated. This is called the change from baseline for each patient.

The average change from baseline in Hgb levels was calculated for each treatment group. These values were similar for both the treatment 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 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.

A total of 406 patients (270 patients in the daprodustat group and 136 patients in the epoetin alfa group) received at least one dose of study medicine. Side effects were reported for these patients during the 52-week treatment period.

Serious side effects

Serious side effects were reported by three patients (1%) in the daprodustat group and four patients (3%) in the epoetin alfa group. No serious side effect was reported by more than one patient in either treatment group.

Non-serious side effects

Non-serious side effects were reported by 37 patients (14%) in the daprodustat group and 18 patients (13%) in the epoetin alfa group. The table below shows the non-serious side effects that were reported by 1% or more of patients in either treatment group.

Number of patients (percent) with non-serious side effects reported by 1% or more of patients		
	Daprodustat 270 patients	**Epoetin alfa 136 patients**
High blood pressure	5 (2%)	3 (2%)
Diarrhoea	4 (1%)	2 (1%)
Nausea	3 (1%)	1 (less than 1%)

How has this study helped patients and researchers?

Researchers concluded that daprodustat was similar to epoetin alfa in maintaining Hgb levels in patients with renal anaemia. The side effects reported were similar between the treatment groups.

Are there plans for further studies?

Other studies of daprodustat in patients with renal anaemia have been conducted and some are ongoing or 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.

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 and Website	Study Number
European Medicines Agency (www.clinicaltrialsregister.eu)	2017-004372-56[1]
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	NCT03400033[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 renal anaemia.

The content for this document was finalised by GSK on 27 June 2021. The information in this summary does not include additional information available after this date.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=2017-004372-56
[2] https://clinicaltrials.gov/ct2/show/NCT03400033?term=NCT03400033&rank=1