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 in participants with anaemia due to chronic kidney disease who were receiving dialysis.

Full Scientific Title: A phase 3, randomised, open-label (sponsor-blind), active-controlled, parallel-group, multi-centre, event driven study in dialysis subjects with anaemia associated with chronic kidney disease to evaluate the safety and efficacy of daprodustat compared to recombinant human erythropoietin, following a switch from erythropoietin-stimulating agents.

Study Number: 200807

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 2016 and ended in November 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. This condition is called anaemia due to CKD. Red blood cells contain an oxygen-carrying protein called haemoglobin (Hgb). When people have anaemia, they have reduced amount of Hgb in their blood.

Patients with anaemia may be treated with certain medicines called recombinant human erythropoietin (rhEPO), such as epoetin alfa and darbepoetin alfa. These medicines are also called erythropoiesis-stimulating agents (ESAs). These medicines trigger the body to make more red blood cells, which leads to an increase in Hgb levels. However, they may also increase the risk of developing cardiovascular disease (problems that affect the heart and/or the blood vessels) in the patients. There are other treatments in development that are being tested in clinical studies. Daprodustat is a medicine that is being tested to treat anaemia due to CKD.

Patients with anaemia due to CKD who were receiving dialysis (a treatment that removes waste from the body and filters blood when kidneys do not work well) took part in this study. Researchers wanted to see how well daprodustat worked in maintaining Hgb levels compared with rhEPO in these participants. Researchers also assessed the safety of these medicines, including if taking daprodustat increased the risk of a major cardiovascular problem (major adverse cardiovascular event [MACE]) compared with rhEPO.

Which medicines were studied?

On Day 1, participants were included in one of the following two treatment groups by chance (randomisation).

- Daprodustat group: Participants took daprodustat tablets by mouth once daily.
- rhEPO group: Participants received either epoetin alfa through a vein one or three times a week or darbepoetin alfa injections through a vein or under the skin once every one, two, or four weeks.

The participant and the study doctor knew which treatment the participant received. The study ended when at least 664 participants had a major cardiovascular problem.

Which participants took part in this study?

Studies have a list of requirements for participants 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 anaemia due to CKD 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 on Day 1.
- Had dialysis twice or more in a week for at least five 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:

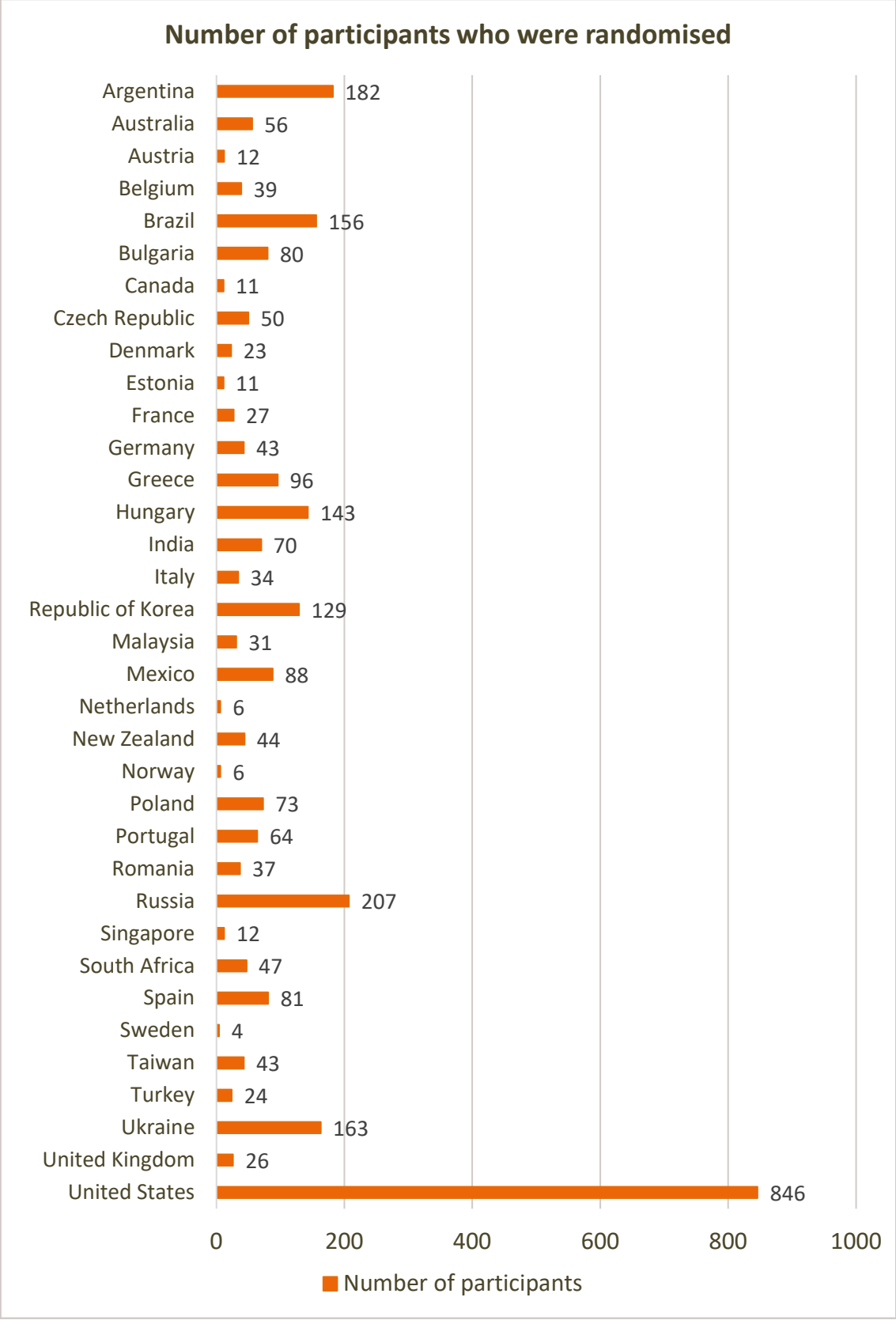
- A plan to have a kidney transplant within a year after Day 1.
- Uncontrolled high blood pressure.
- A heart attack, stroke, or ministroke within three months before Day 1.
- Stomach and intestinal bleeding within three months before Day 1.
- Another disease that could lead to anaemia.
- Any other disease(s),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

Overall, 2964 participants were randomised. The study included 1698 men (57%) and 1266 women (43%). The average age was 57 years. The youngest participant was 18 years old and the oldest participant was 95 years old.

For more detailed information about the participants 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 35 countries.



What were the main results of the study?

Participants' were assessed for change in Hgb levels and whether there was a risk of developing a major cardiovascular problem.

Hgb levels

Researchers wanted to compare daprodustat with rhEPO in maintaining participants' Hgb levels during Week 28 to Week 52 (testing period) of the study.

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

The average change from baseline in Hgb levels was calculated for each treatment group. Results are shown in the table below.

Average change from baseline in Hgb levels during the testing period		
	Daprodustat 1487 participants	**rhEPO 1477 participants**
Average change from baseline in Hgb levels	0.28 g/dL	0.10 g/dL

Major cardiovascular problem

Study doctors recorded the number of participants who had a major cardiovascular problem. For this study, a major cardiovascular problem included a heart attack, stroke, or death. Researchers wanted to compare the risk of a major cardiovascular problem between treatment groups, during the study.

Results are shown in the table below.

Participants who had a major cardiovascular problem		
	Daprodustat 1487 participants	**rhEPO 1477 participants**
Number of participants (percent)	374 (25%)	394 (27%)

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 2956 participants (1482 participants in the daprodustat group and 1474 participants in the rhEPO group) received at least one dose of study medicine. Side effects were reported for these participants while they were receiving study medicine.

Serious side effects

In this study, serious side effects were reported as fatal serious side effects and non-fatal serious side effects.

Fatal serious side effects were reported by four participants (less than 1%) in the daprodustat group and one participant (less than 1%) in the rhEPO group.

The table below shows the fatal serious side effects.

Number of participants (percent) with fatal serious side effects		
	Daprodustat 1482 participants	**rhEPO 1474 participants**
Bacterial infection in the heart	1 (less than 1%)	0
Breathing stopped and heart stopped beating	1 (less than 1%)	0
Heart stopped beating	1 (less than 1%)	0
High blood pressure	1 (less than 1%)	0
Heart attack	0	1 (less than 1%)

Non-fatal serious side effects were reported by 25 participants (2%) in the daprodustat group and 26 participants (2%) in the rhEPO group. No non-fatal serious side effects were reported by 1% or more of participants in either treatment group.

Non-serious side effects

Non-serious side effects were reported by 85 participants (6%) in the daprodustat group and 61 participants (4%) in the rhEPO group. No non-serious side effects were reported by 1% or more of participants in either treatment group.

How has this study helped participants and researchers?

Researchers concluded that daprodustat was similar to rhEPO in maintaining Hgb levels in participants with anaemia due to CKD. The study showed that taking daprodustat did not increase the risk of a major cardiovascular problem compared with rhEPO. The side effects reported were as expected in patients with anaemia due to CKD who were receiving dialysis.

Are there plans for further studies?

Other studies of daprodustat in participants with anaemia due to CKD have been completed 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)	2016-000541-31[1]
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	NCT02879305[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 participants who contributed to this study. The results of this study will help answer scientific questions about treating patients with anaemia due to CKD.

The content for this document was finalised by GSK on 28 January 2022. The information in this summary does not include additional information available after this date.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-000541-31
[2] https://clinicaltrials.gov/ct2/show/NCT02879305