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 the effect of daprodustat with darbepoetin alfa in participants with anaemia due to chronic kidney disease who were not on dialysis.

Full Scientific Title: A phase 3, randomised, open-label (sponsor-blind), active-controlled, parallel-group, multi-centre, event driven study in non-dialysis subjects with anaemia associated with chronic kidney disease to evaluate the safety and efficacy of daprodustat compared to darbepoetin alfa.

Study Number: 200808

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 April 2021.

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.

People with anaemia may be treated with erythropoiesis-stimulating agents (ESAs), such as darbepoetin alfa. These agents trigger the body to make more red blood cells, which leads to an increase in Hgb levels. However, these agents may also increase the risk of developing cardiovascular disease (problems that affect the heart and/or the blood vessels). 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.

People with anaemia due to CKD who were not on dialysis took part in this study. Dialysis is a treatment that removes waste from the body and filters blood when kidneys do not work well. Researchers wanted to see how well daprodustat worked in increasing and/or maintaining Hgb levels compared with darbepoetin alfa in these participants. Researchers also assessed the safety of these medicines, which included whether taking daprodustat increased the risk of a major cardiovascular problem (major adverse cardiovascular event [MACE]) compared with darbepoetin alfa.

Which medicines were studied?

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

- Daprodustat group: Participants received daprodustat tablets by mouth once daily.
- Darbepoetin alfa group: Participants received darbepoetin alfa as an injection under the skin or through a vein once every one, two, or four weeks.

The participant and the study doctor knew which treatment the participant received. The study was planned to end 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 moderate to severe CKD.
- Had the following Hgb levels on Day 1:
  - between 8 grams per decilitre (g/dL) and 10 g/dL and were not taking ESAs before Day 1.

    (or)
  - between 8 g/dL and 11 g/dL and were taking the same ESAs for at least three months before Day 1.

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

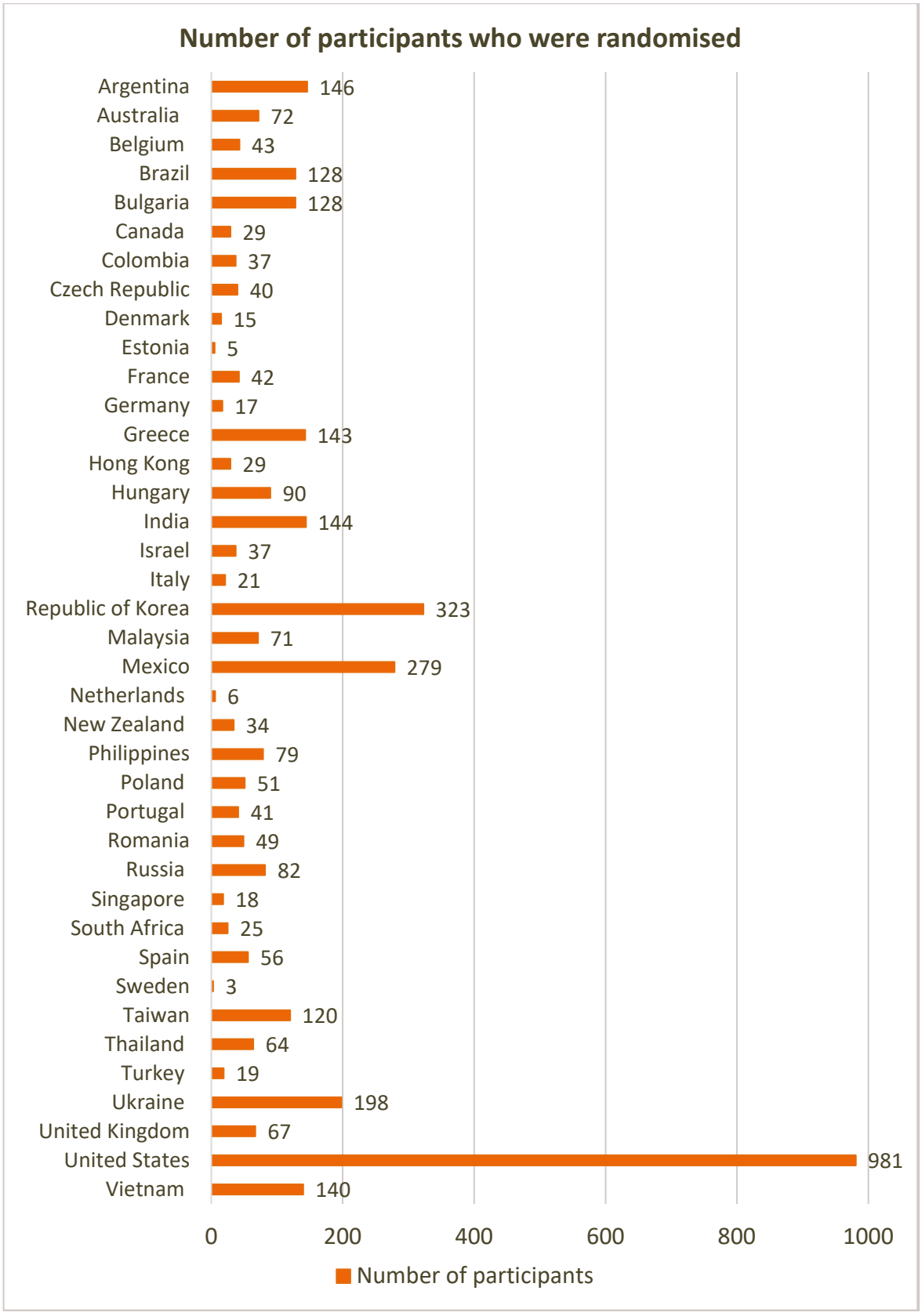
- Been on dialysis or would need to start dialysis within three months after Day 1.
- A plan to have a kidney transplant within a year after Day 1.
- Uncontrolled high blood pressure.
- A heart attack, stroke, or ministroke within three months before Day 1.
- Severe long-term heart failure.
- Stomach 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, 3872 participants were randomised. The study included 1699 men (44%) and 2173 women (56%). The average age was 65 years. The youngest participant was 18 years old and the oldest participant was 98 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 39 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 darbepoetin alfa in maintaining participants' Hgb levels from 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 during the testing period was calculated for each treatment group. Results are shown in the table below.

Average change from baseline in Hgb levels		
	Daprodustat 1937 participants	**Darbepoetin alfa 1935 participants**
Average increase from baseline in Hgb levels	0.74 g/dL	0.66 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 1937 participants	**Darbepoetin alfa 1935 participants**
Number of participants (percent)	378 (20%)	371 (19%)

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 3870 participants (1937 participants in the daprodustat group and 1933 participants in the darbepoetin alfa 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 six participants (less than 1%) in the daprodustat group and one participant (less than 1%) in the darbepoetin alfa group.

The table below shows the number of participants with fatal serious side effects.

Number of participants (percent) with fatal serious side effects		
	Daprodustat 1937 participants	**Darbepoetin alfa 1933 participants**
Death	1 (less than 1%)	1 (less than 1%)
Hardening of artery walls	1 (less than 1%)	0
Cancer that had spread from an unknown source	1 (less than 1%)	0
Intestinal damage due to poor blood supply	1 (less than 1%)	0
Life-threatening failure of the heart to pump enough blood to the body	1 (less than 1%)	0
Life-threatening response to an infection	1 (less than 1%)	0

Non-fatal serious side effects were reported by 30 participants (2%) in the daprodustat group and nine participants (less than 1%) in the darbepoetin alfa group. No specific 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 93 participants (5%) in the daprodustat group and 60 participants (3%) in the darbepoetin alfa group. No specific 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 darbepoetin alfa in increasing and/or maintaining Hgb levels in participants with anaemia due to CKD who were not on dialysis. The study showed that taking daprodustat did not increase the risk of a major cardiovascular problem compared with darbepoetin alfa. The side effects reported were as expected in participants with anaemia due to CKD who were not receiving dialysis.

Are there plans for further studies?

Other studies of daprodustat in participants with anaemia due to CKD have been completed. Some studies 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)	2016-000542-65[1]
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	NCT02876835[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 people with anaemia due to CKD who were not on dialysis.

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

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-000542-65
[2] https://clinicaltrials.gov/ct2/show/NCT02876835