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 on forearm blood flow in participants with anaemia due to chronic kidney disease.

Full Scientific Title: A randomised, repeat dose, open label, parallel group, multi-centre study to evaluate the effect of daprodustat compared to darbepoetin alfa on forearm blood flow in participants with anaemia of chronic kidney disease that are not dialysis dependent.

Study Number: 205767

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 and where was this study done?

The study started in January 2019 and ended in May 2019. The study was stopped earlier than planned. All study sites were in the United Kingdom.

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 anaemia due to CKD. 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 darbepoetin alfa. These medicines trigger the body to make more red blood cells, leading to an increase in Hgb levels. However, they may also increase the risk of developing problems that affect the heart and/or the blood vessels in these patients. Daprodustat is a medicine that is being tested to treat anaemia due to CKD.

Endothelial dysfunction is a condition in which blood vessels become narrow and do not open fully. Patients with endothelial dysfunction have a higher risk of having a stroke or heart attack. One way to assess the endothelial function is to check if the patient has normal forearm blood flow (FBF).

The FBF is assessed by measuring the increase in forearm blood vessel size when tight blood pressure cuffs are placed at the wrist and above the elbow. Forearm blood vessel size increases if the blood flow into the arm is normal.

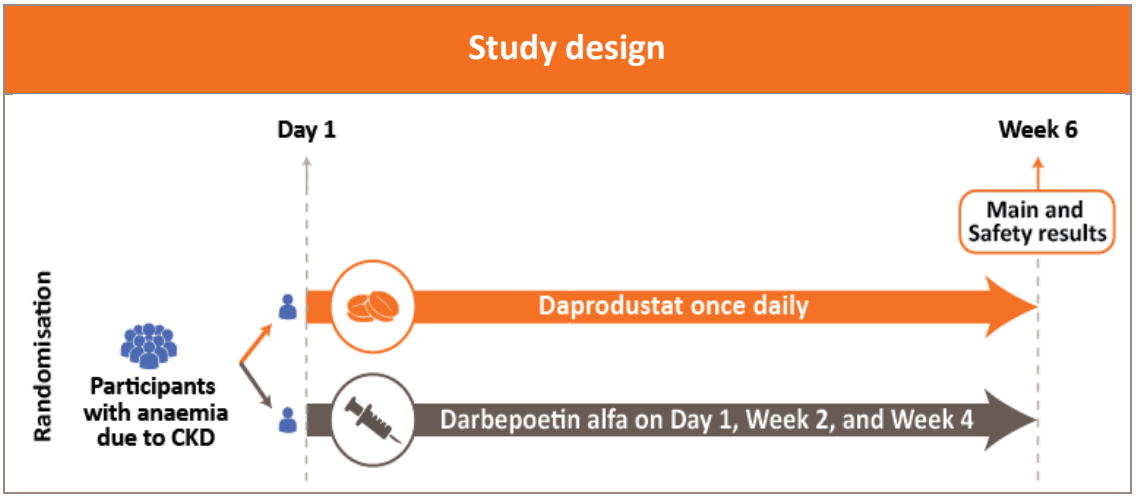
Patients with anaemia due to CKD who were not receiving dialysis took part in this study. Dialysis is a treatment that removes waste from the body and filters blood when kidneys do not work well. Researchers wanted to see the effect of daprodustat on FBF compared with darbepoetin alfa in these participants. Researchers also assessed the safety of these medicines.

Which medicines were studied?

On Day 1 of the treatment period, participants were assigned by chance (randomisation) to receive one of the following two study medicines.

- Daprodustat as a tablet.
- Darbepoetin alfa as an injection under the skin.

The participant and the study doctor knew which treatment the participant received.



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 at least 18 years old.
- Had moderate to severe CKD.
- Had Hgb levels of up to 11 grams per decilitre (g/dL) on Day 1.
- Had a clearly seen blood vessel at the inner side of the elbow.

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

- Been on dialysis or would need to start dialysis or have a kidney transplant within three months after Day 1.
- Used an rhEPO within four months before Day 1.
- An abnormal connection between two blood vessels.

It was initially planned to have at least 50 participants in the study. When the study was stopped, only five participants had received at least one dose of the study medicine.

The study included three men (60%) and two women (40%). The average age was 57 years. The youngest participant was 36 years old and the oldest participant was 67 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).

What were the main results of the study?

Study doctors measured each participant's FBF on Day 1 and at Week 6. The difference in the participant's FBF values on Day 1 and at Week 6 was calculated. This is called the change from baseline for each participant. The average change from baseline in FBF was calculated for each treatment group.

The results were obtained only from four participants, who completed the study. These were not enough to compare the effect of daprodustat with darbepoetin alfa on FBF in participants with anaemia due to CKD. Hence, no conclusions could be drawn from these results.

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.

No side effects were reported in this study.

How has this study helped participants and researchers?

Researchers could not compare the effect of daprodustat with darbepoetin alfa on FBF. This could be because the study was stopped earlier than planned and the number of participants in the study was too small. No side effects were reported during this study.

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)	2017-002268-42[1]
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	NCT03446612[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.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=2017-002268-42
[2] https://clinicaltrials.gov/ct2/show/NCT03446612

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 who were not receiving dialysis.

The content for this document was finalised by GSK on 24 February 2022. The information in this summary does not include additional information available after this date.