This document provides a short summary of this study for a general audience. You can find more information in the scientific summary of the study. A link to the summary is provided at the end of this document.

Study names

Short Title: A study comparing daprodustat with darbepoetin alfa in Japanese patients with renal anaemia due to chronic kidney disease who were being treated with haemodialysis and erythropoiesis-stimulating agents.

Full Scientific Title: A 52-week, Phase III, double-blind, active-controlled, parallel-group, multi-centre study to evaluate efficacy and safety of daprodustat compared to darbepoetin alfa in Japanese haemodialysis-dependent subjects with anaemia associated with chronic kidney disease who are currently erythropoiesis-stimulating agent users.

Study Number: 201754

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

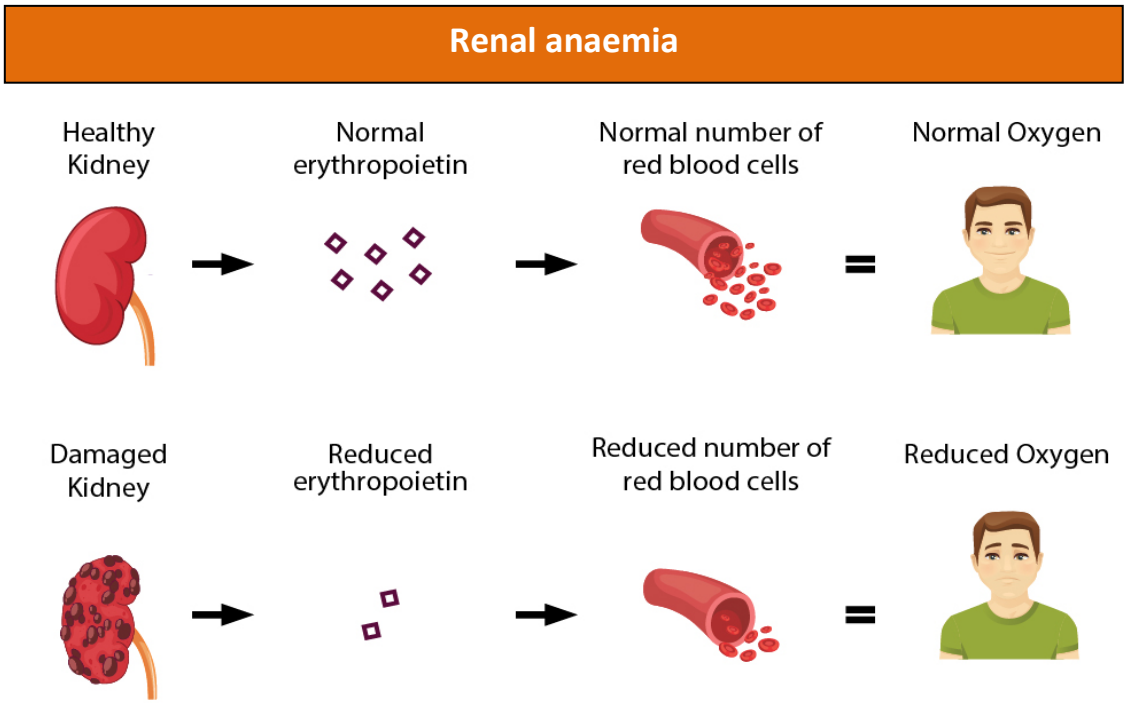
When and where was this study done?

The study started in November 2016 and ended in July 2018. All study sites were in Japan.

What was the main reason for this study?

Patients with chronic kidney disease (CKD) may develop anaemia. Anaemia is a condition that arises because the blood does not have enough healthy red blood cells or haemoglobin. Haemoglobin (Hgb) is a protein in the red blood cells that carries oxygen to all parts of the body.

Healthy kidneys make a hormone called erythropoietin (EPO). Erythropoietin prompts the bone marrow to make red blood cells, which then carry oxygen in the blood. Patients with CKD have diseased or damaged kidneys that do not make enough EPO. As a result, the bone marrow makes fewer red blood cells, causing renal anaemia. Patients with low levels of red blood cells may struggle with daily activities like walking or climbing stairs. See figure below.



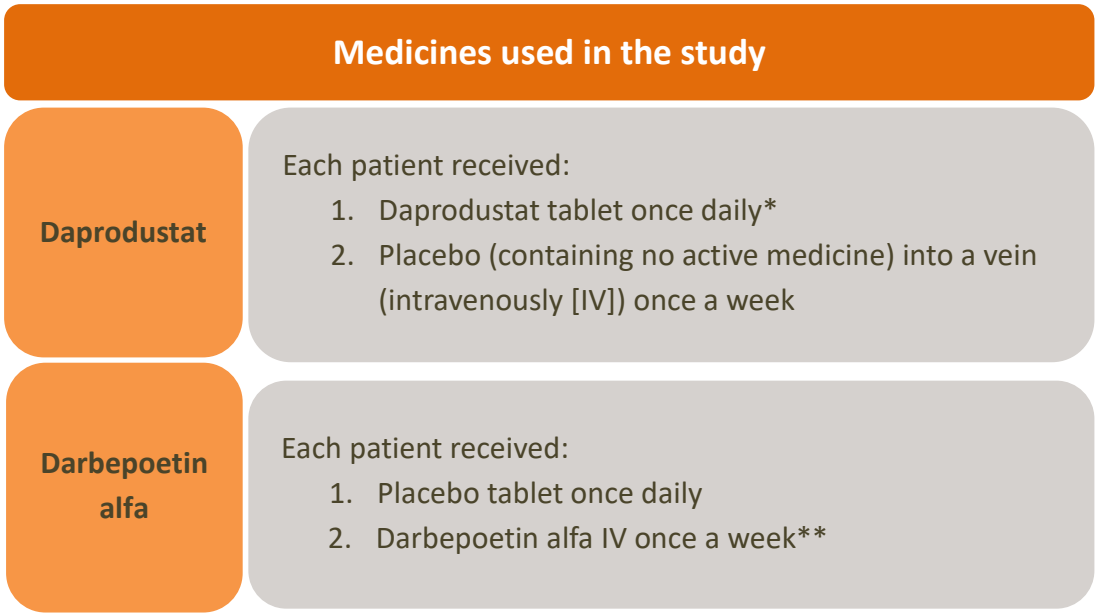
Patients with renal anaemia may be treated with medicines called erythropoiesis-stimulating agents (ESAs) such as darbepoetin alfa. Erythropoiesis-stimulating agents triggers the bone marrow to make more red blood cells.

Daprodustat is a medicine that prompts the body to make more EPO, which increases the number of red blood cells. More red blood cells lead to an increase in Hgb and oxygen levels in the blood.

In this study, researchers wanted to see if daprodustat is similar to darbepoetin alfa in maintaining Hgb levels in Japanese patients with renal anaemia, who were being treated with haemodialysis and ESAs.

Which medicines were studied?

During the study, patients were included in one of the following two treatment groups by chance (randomisation). The patients switched the ESA, which they were previously taking, with the study medicine(s) as shown in the figure below.



*Daprodustat was given as 4 milligram (mg) tablet for the first four weeks, the dose could be raised or lowered every four weeks thereafter (dose ranged from 1 mg to 24 mg) to maintain the patient's Hgb levels within a target Hgb range[#].

**Darbepoetin alfa starting dose varied depending on which ESA a patient was previously taking. At Week 2, the dose ranged from 10 micrograms (mcg) to 60 mcg. It could be raised or lowered every two weeks to maintain the patient's Hgb levels within a target Hgb range[#].

[#]Target Hgb range = 10.0 to 12.0 grams per decilitre (g/dL).

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.

Main Inclusion Criteria

Men and women were included in the study if they:

- Were at least 20 years old.
- Had a Hgb level between 9.5 g/dL and 12.5 g/dL before starting the study treatment.
- Used a machine that filters the blood and removes waste (haemodialysis) for at least 12 weeks before starting the study.
- Had been taking the same ESA for at least 10 weeks before starting the study.

Main Exclusion Criteria

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

- A planned kidney transplant during the study period.
- Another disease that could lead to anaemia.
- Stomach and intestinal bleeding within 10 weeks before starting the study.
- Been diagnosed with heart disease, unstable liver disease, or cancer.

For more detailed information about the patients included in this study, see the scientific summary on the ClinicalTrials.gov website (see link provided at the end of this document).

A total of 271 patients received at least one dose of study medicine. The table below shows the gender and age of these patients.

Patients who received at least one dose of study medicine		
	Daprodustat 136 patients	**Darbepoetin alfa 135 patients**
Gender		
Female	45 (33%)	46 (34%)
Male	91 (67%)	89 (66%)
Age - in years		
Range	34 to 87	34 to 89
Average	64	64

What were the overall results of the study?

Study doctors collected blood samples from all patients. They measured each patient's Hgb level on Day 1 and every four weeks during the study.

The main focus of the study was to see whether daprodustat is similar to darbepoetin alfa in maintaining Hgb levels between Week 40 to Week 52. All patients' Hgb levels at Weeks 40, 44, 48, and 52 were combined and averaged.

The Hgb levels were not measured for four patients after administration of study medicine. Results are shown for 267 patients in the table below.

Average haemoglobin level between Week 40 to Week 52		
	Daprodustat 133 patients	**Darbepoetin alfa 134 patients**
Average Hgb level	10.89 g/dL	10.83 g/dL
Difference in average Hgb level between daprodustat group and darbepoetin alfa group	0.06 g/dL	

Between Week 40 to Week 52, average Hgb levels in the two treatment groups were similar.

More information about the study results is available in the scientific results summary (see the link 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 summary (see the link 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 serious side effects were reported by the patients in this study.

No non-serious side effects were reported by more than one patient in either treatment group.

How has this study helped patients and researchers?

This was a Phase III study. Phase III studies collect information about how well new medicines work and how safe they are. This study showed that daprodustat was similar to darbepoetin alfa in maintaining the patients' Hgb levels. These results will help regulators make decisions about whether to approve daprodustat for treatment of renal anaemia in Japanese patients being treated with haemodialysis and ESAs.

Are there plans for further studies?

Other studies of daprodustat as a treatment for renal anaemia have been conducted and more are underway.

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 number associated with this study is shown below with an internet link to the scientific summary and other information.

The scientific summary includes 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
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT02969655 [1]

Your doctor can help you understand more about this study and the results. 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 the 11th of June 2019. The information in this summary does not include additional information available after this date.

[1] https://clinicaltrials.gov/ct2/show/NCT02969655