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 to see how well daprodustat works and how safe it is in Japanese patients with renal anaemia due to chronic kidney disease who were either not on dialysis or were on peritoneal dialysis.

Full Scientific Title: A 52-week, Phase III, open-label, multi-center study to evaluate efficacy and safety of GSK1278863 (daprodustat) in Japanese non-dialysis and peritoneal dialysis subjects with anaemia associated with chronic kidney disease.

Study Number: 201753

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

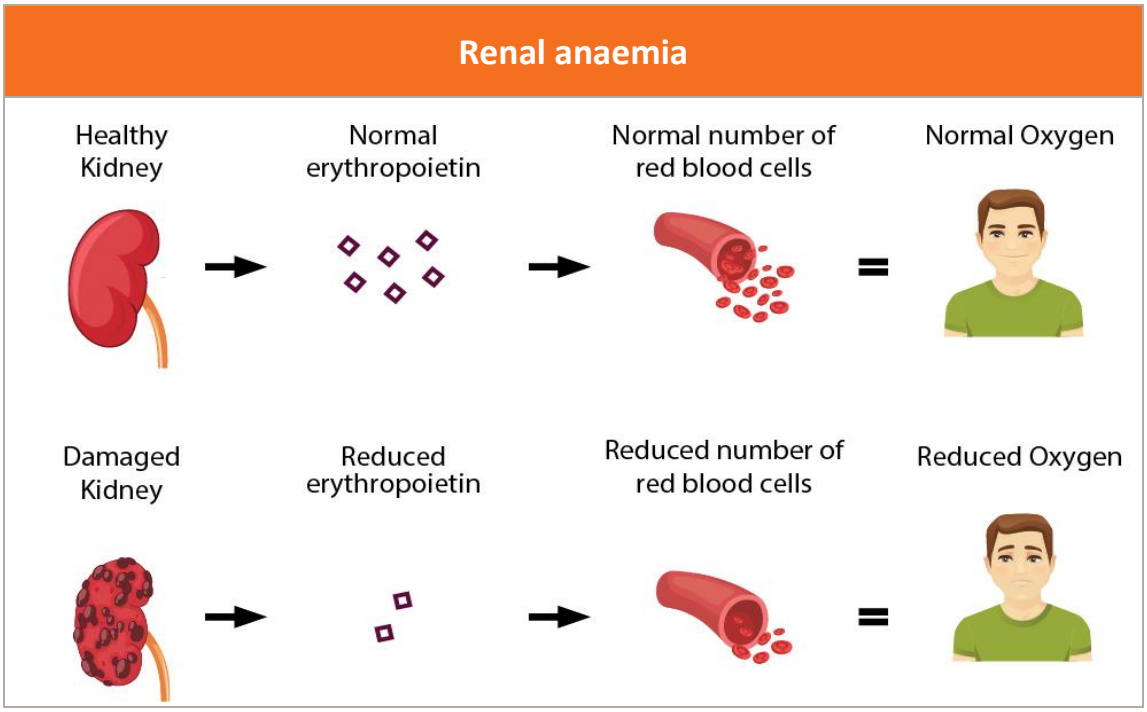
When and where was this study done?

The study started in June 2016 and ended in October 2018. All study sites were in Japan.

What was the main objective of this study?

Patients with chronic kidney disease may develop anaemia. Anaemia is a condition that arises because the blood does not have enough healthy red blood cells or haemoglobin (Hgb). Haemoglobin 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 chronic kidney disease have diseased or damaged kidneys that cannot 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 (or oxygen) 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 or epoetin beta pegol. These agents trigger the bone marrow to make more red blood cells.

Daprodustat is a medicine that prompts the body to make more EPO, and EPO prompts the bone marrow to make 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 epoetin beta pegol in maintaining Hgb levels in Japanese patients with renal anaemia, who were not on dialysis at the beginning of the study (non-dialysis patients). Dialysis is a procedure that removes waste products and excess fluid from the blood when the kidneys stop working properly. This document provides a short summary of the results for non-dialysis patients.

Researchers also wanted to see if daprodustat could maintain Hgb levels in Japanese patients with renal anaemia, who were on peritoneal dialysis at the beginning of the

study. For information on peritoneal dialysis patients, see the scientific results summary (a link to the summary is provided at the end of this document).

Which medicines were studied?

During the study, non-dialysis patients were assigned to one of the two treatment groups by chance (randomisation). The patients knew which treatment they received. This is called open-label study.

Medicines used in the study	
Daprodustat	Patients received daprodustat tablet(s) once daily* for 52 weeks.
Epoetin beta pegol	Patients received epoetin beta pegol via an injection below the skin once every two or four weeks** for 52 weeks.

*Daprodustat was given at a dose of 2 or 4 milligram (mg) 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 achieve and/or maintain the patient's Hgb levels within a target Hgb range[#].

**Epoetin beta pegol dose ranged from 25 micrograms (mcg) to 250 mcg once every two or four weeks. The dose could be raised or lowered every four weeks to achieve and/or maintain the patient's Hgb levels within a target range[#].

[#]Target Hgb range = 11 to 13 grams per decilitre (g/dL).

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.

Non-dialysis patients with chronic kidney disease were included in the study if they were:

- At least 20 years old.
- Not on dialysis for at least 12 weeks before starting the study.
- ESA users:
  - using the same ESA for at least eight weeks before starting the study.
  - with Hgb levels from 9 g/dL to 13 g/dL before starting the study.
- Not ESA users:
  - not used any ESA for at least eight weeks before starting the study.
  - with Hgb levels from 8 g/dL to 11 g/dL before starting the study.

Non-dialysis patients (men and women) with chronic kidney disease were excluded from the study if they had:

- A planned kidney transplant or dialysis during the study period.
- Another disease that could lead to anaemia.
- Been diagnosed with heart disease, unstable liver disease, or cancer.

A total of 299 non-dialysis patients received at least one dose of the study medicine. The table below shows the gender and age of these patients.

Non-dialysis patients who received at least one dose of the study medicine		
	Daprodustat 149 patients	**Epoetin beta pegol 150 patients**
Gender – Number of patients (percent)		
Female	53 (36%)	58 (39%)
Male	96 (64%)	92 (61%)
Age - in years		
Range	28 to 86	34 to 86
Average	68	70

For more detailed information about the patients included in this study, see the scientific results summary (a link to the summary is provided at the end of this document).

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 then every four weeks during the study.

The main objective of the study was to see whether daprodustat was similar to epoetin beta pegol in maintaining patients' Hgb levels during Week 40 to Week 52. The patients' Hgb levels at Week 40, 44, 48, and 52 were combined and averaged.

The average Hgb levels for the 217 non-dialysis patients who met criteria were considered for the results. Results are shown in the table below.

Average haemoglobin level in non-dialysis patients (Week 40 to Week 52)		
	Daprodustat 108 patients	**Epoetin beta pegol 109 patients**
Average Hgb level	11.97 g/dL	11.86 g/dL
Difference in average Hgb level between daprodustat group and epoetin beta pegol group	0.10 g/dL	

During 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 (a link to the summary is 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 all these events can be found in the scientific results summary (a link to the summary is 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.

The table below shows the number of non-dialysis patients (percent) reporting serious side effects during this study.

Number of non-dialysis patients (percent) for all serious side effects		
	Daprodustat 149 patients	**Epoetin beta pegol 150 patients**
Buildup of fluid in the lungs	0	1 (less than 1%)
Stroke	1 (less than 1%)	0

One patient (less than 1%) in the daprodustat group and three patients (2%) in the epoetin beta pegol group reported a non-serious side effect of high blood pressure. No other 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. The results showed that daprodustat was similar to epoetin beta pegol in maintaining the Hgb levels in non-dialysis patients. The side effects reported in these patients were similar between the treatment groups. These results will help regulators make decisions about whether to approve daprodustat for treatment of renal anaemia in Japanese non-dialysis patients.

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 adverse events.

Organisation	Website	Study Number
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT02791763[1]

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 the 8th of October 2019. The information in this summary does not include additional information available after this date.

[1] https://clinicaltrials.gov/ct2/show/NCT02791763