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 assess the safety of GSK2330811 in patients with diffuse cutaneous systemic sclerosis.

Full Scientific Title: A multi-centre, randomised, double-blind (sponsor open), placebo-controlled, repeat-dose, proof of mechanism study to evaluate the safety and tolerability of GSK2330811 in participants with diffuse cutaneous systemic sclerosis.

Study Number: 201247

## 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 June 2017 and ended in July 2020.

What was the main objective of this study?

An autoimmune disease is a condition in which the body's immune system attacks its own tissues and organs. Diffuse cutaneous systemic sclerosis (dcSSc), a type of systemic sclerosis, is a rare and often serious autoimmune disease. Patients with dcSSc develop inflammation and fibrosis (thickening and hardening of the tissue) that usually starts on the skin of the hands, feet, and face. The fibrosis can affect blood vessels and later spread to internal organs.

GSK2330811 is a new medicine that may reduce inflammation and fibrosis.

The main objective of this study was to assess the safety of GSK2330811 in patients with dcSSc. Safety was measured by recording unwanted medical events (adverse events) and monitoring patients' blood and urine test results. Study doctors also monitored patients' heart health, blood pressure, and body temperature.

## Which medicines were studied?

This study had two parts. Each part had a 12-week treatment phase and a 16-week follow-up phase. On Day 1 of each part, patients were placed in one of the following treatment groups by chance (randomisation):

- Part 1: GSK2330811 100 milligrams (mg) or placebo (no active medicine)
- Part 2: GSK2330811 300 mg or placebo

In Part 1, four patients received GSK2330811 100 mg or placebo. When this smaller group of patients completed the treatment phase, study doctors reviewed their safety results. After the review, a larger group of 31 patients received GSK2330811 300 mg or placebo in Part 2.

During the treatment phase, study medicine was injected under the skin of the thigh, abdomen, or upper arm every two weeks up to Week 10. Neither the patients nor the 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.

Men and women were included in the study if they:

- Were at least 18 years old.
- Had dcSSc for up to five years before starting the study.
- Had active dcSSc, as assessed by the study doctor.

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

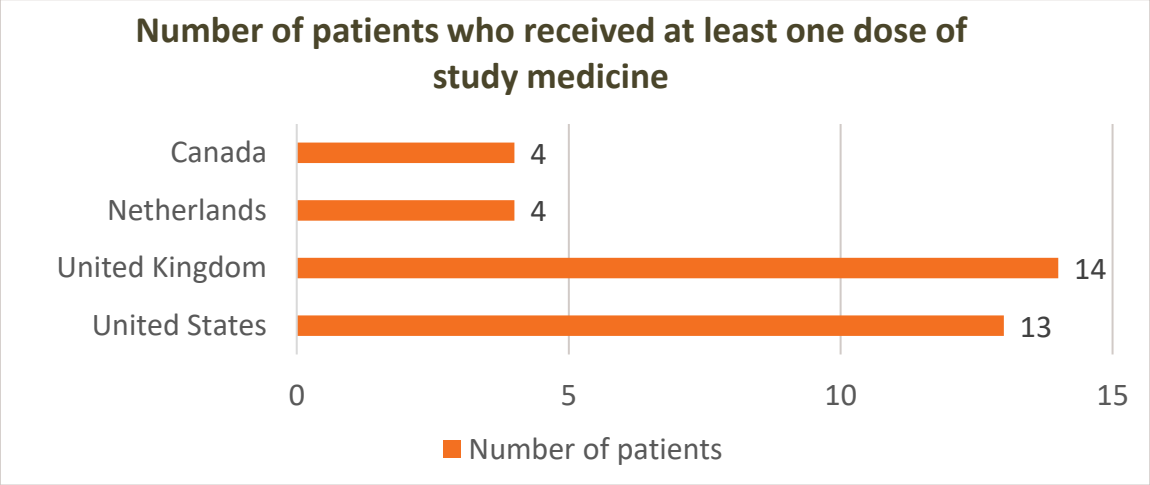
- Any other autoimmune disease in addition to dcSSc.
- Inflammation in the muscles caused by systemic sclerosis.
- Systemic sclerosis affecting the kidneys.
- High blood pressure in the blood vessels of the lungs.
- Abnormal blood test results before starting the study.
- Any major surgery, other disease(s), infection(s), and/or treatment(s) that the study doctor thought would affect the results of the study.

Overall, 35 patients received at least one dose of study medicine. The study included 9 men (26%) and 26 women (74%). The average age was 57 years. The youngest patient was 21 years old and the oldest patient was 72 years old.

For more detailed information about the patients 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 four countries.

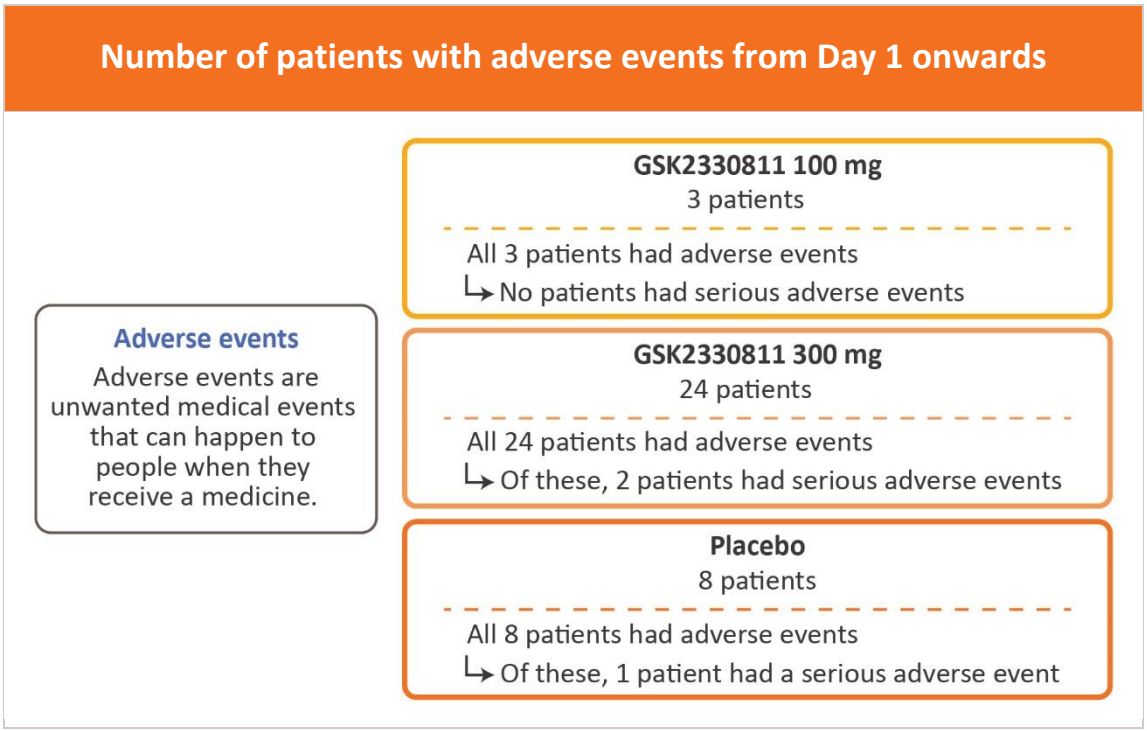



## What were the main results of the study?

Safety was measured by recording adverse events and monitoring patients' test results.

Adverse events

The figure below shows the number of patients who had adverse events, including serious adverse events, from Day 1 onwards.



Test results

Results for the urine test, heart health, blood pressure, and body temperature were within acceptable limits.

Most blood test results were within acceptable limits. Blood test results for abnormal (lower or higher than normal) levels of haemoglobin (oxygen-carrying proteins), platelets (blood clotting cells), and white blood cells are shown for 34 patients in the table below. Results were not available for one patient in the GSK2330811 300 mg group.

**Number of patients who developed abnormal blood test results during the study**

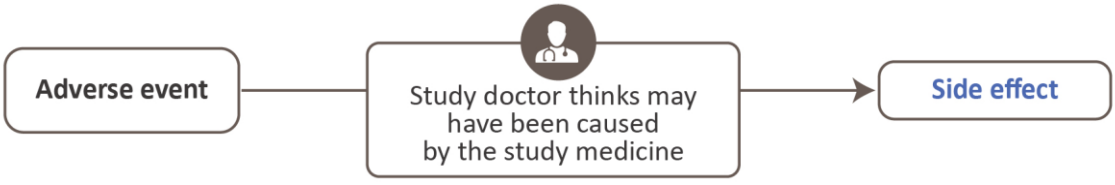
| | GSK2330811 100 mg | GSK2330811 300 mg | Placebo |
|---|---|---|---|
| **Lower than normal levels of haemoglobin** | 1 of 3 patients | 20 of 23 patients | 2 of 8 patients |
| **Lower than normal levels of platelets** | 0 of 3 patients | 9 of 23 patients | 0 of 8 patients |
| **Lower than normal levels of white blood cells** | 0 of 3 patients | 5 of 23 patients | 1 of 8 patients |

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?

In this summary, side effects refer to those adverse events that the study doctor thinks may have been caused by the study medicine, as shown in the figure below.

**Difference between an adverse event and a side effect**




In blinded studies, the doctor does not know which study medicine the patient is taking. In some cases, side effects will be assigned to placebo.

The side effects in this summary may be different to those in the Informed Consent or other documents related to the study medicine.

From Day 1 onwards, 1 of 24 patients in the GSK2330811 300 mg group had a serious side effect of kidney cancer. This side effect was reported more than a year after the patient completed the study. A review of this possible side effect showed that the link between kidney cancer and the study medicine remains unclear.

No serious side effects were reported by patients in the GSK2330811 100 mg group or the placebo group.

Non-serious side effects were reported by 1 of 3 patients in the GSK2330811 100 mg group, 21 of 24 patients in the GSK2330811 300 mg group, and 4 of 8 patients in the placebo group.

The table below shows the number of patients with non-serious side effects that were reported by three or more patients in any treatment group.

| **Number of patients with non-serious side effects reported by three or more patients from Day 1 onwards** | | | |
|---|---|---|---|
| | **GSK2330811 100 mg** | **GSK2330811 300 mg** | **Placebo** |
| **Lower than normal levels of haemoglobin reported as "haemoglobin decreased"** | 0 of 3 patients | 6 of 24 patients | 0 of 8 patients |
| **Lower than normal levels of haemoglobin reported as "anaemia"** | 0 of 3 patients | 4 of 24 patients | 0 of 8 patients |
| **Lower than normal levels of platelets reported as "platelet count decreased"** | 0 of 3 patients | 3 of 24 patients | 0 of 8 patients |
| **Lower than normal levels of platelets reported as "thrombocytopenia"** | 0 of 3 patients | 3 of 24 patients | 0 of 8 patients |

## How has this study helped patients and researchers?

Researchers concluded that treatment with GSK2330811 300 mg given every two weeks was not favourable in patients with dcSSc. More patients in the GSK2330811 300 mg group had lower than normal levels of haemoglobin, platelets, and white blood cells compared with the other two groups.

## Are there plans for further studies?

No studies of GSK2330811 in patients with dcSSc are currently planned or ongoing.

## 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)** | 2016-003417-95[1] |
| **United States National Institutes of Health (NIH) (www.clinicaltrials.gov)** | NCT03041025[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 patients who contributed to this study. The results of this study will help answer scientific questions about treating patients with dcSSc.

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=2016-003417-95
[2] https://clinicaltrials.gov/ct2/show/study/NCT03041025?term=NCT03041025&rank=1

The content for this document was finalised by GSK on 13 May 2021. The information in this summary does not include additional information available after this date.