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 see how well belimumab works and how safe it is in patients with lupus nephritis.

Full Scientific Title: A phase 3, randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of belimumab plus standard of care versus placebo plus standard of care in adult subjects with active lupus nephritis.

Study Number: 114054

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 July 2012 and ended in March 2020.

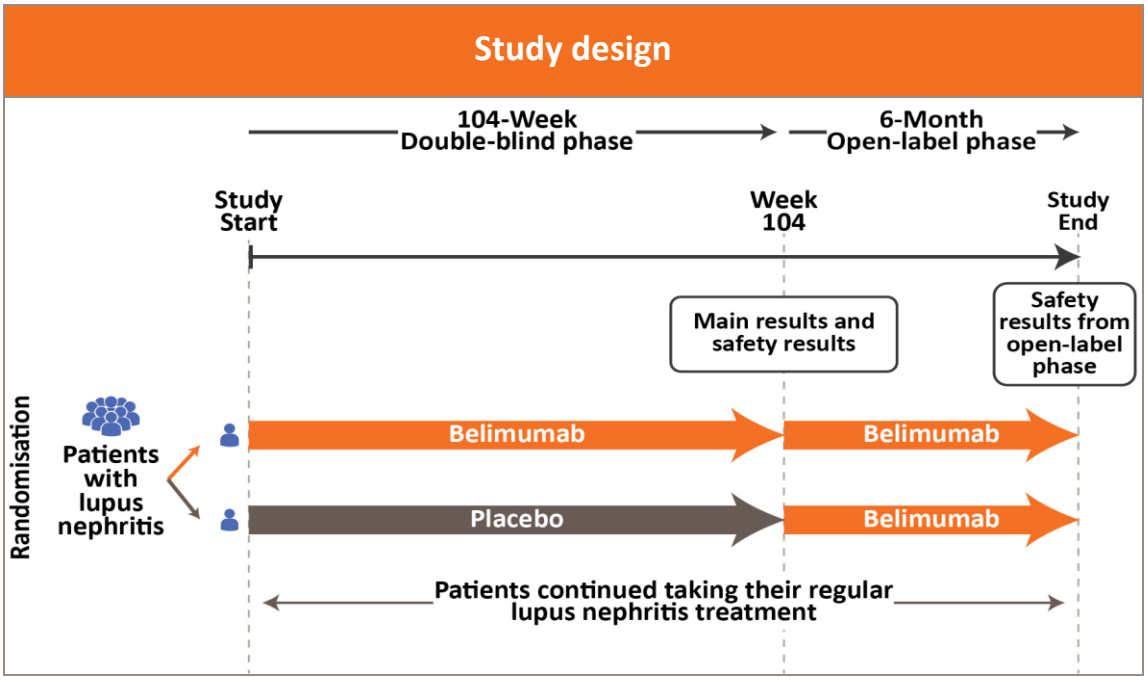
What was the main objective of this study?

Lupus nephritis is an inflammation of the kidneys caused by systemic lupus erythematosus (SLE). In patients with SLE, the body produces autoantibodies that attack its own tissues and organs. An autoantibody attack on the kidneys may cause reduced kidney function.

Belimumab is a medicine that decreases the number of autoantibodies. Researchers wanted to see how well belimumab works when added to regular lupus nephritis treatment. They also studied the safety of belimumab.

Which medicines were studied?

As shown in the figure below, patients were placed in one of the two treatment groups by chance (randomisation). Patients received belimumab or placebo (no active medicine) directly through a vein.



This study took place in two phases. During the first 104 weeks, neither the patients nor the study doctors knew who was receiving which treatment. This is called a double-blind phase. After Week 104, patients could continue in the open-label phase of the study and receive belimumab.

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 with lupus nephritis were included in the study if they:

- Were at least 18 years old.
- Had tested positive for lupus autoantibodies before starting the study.
- Had active kidney disease, which required regular lupus nephritis treatment within two months before starting the study.

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

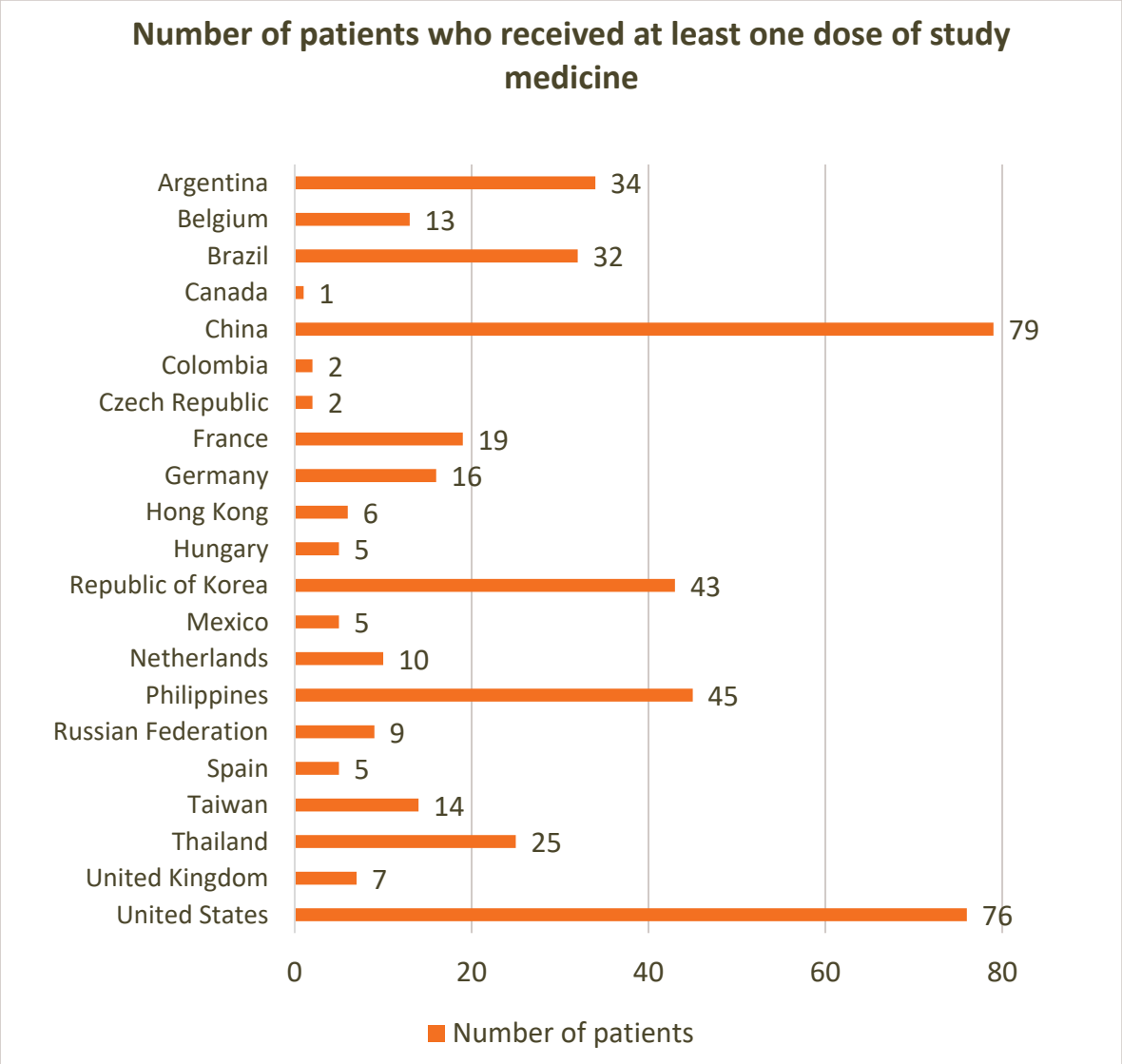
- Not responded well to regular lupus nephritis treatment.
- Severe abnormalities of the nervous system caused by SLE (such as seizures, psychosis) that required treatment within two months before starting the study.
- Used a machine that filters the blood and removes waste (dialysis) within one year before starting the study.
- Reduced rate at which kidneys filter out waste from the blood at study start.
- A history of cancerous tumor within five years before starting the study.
- Any other disease(s) or major organ transplant or had taken any medicine(s) before starting the study, that the study doctor thought would affect the results of the study.

Overall, 448 patients received at least one dose of study medicine. The study included 54 (12%) men and 394 (88%) women. The average age was 33 years. The youngest patient was 18 years old and the oldest patient was 77 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 21 countries.



What were the main results of the study?

Study doctors monitored patients' kidney function to assess how belimumab works in patients with lupus nephritis.

Patients were considered to have responded if:

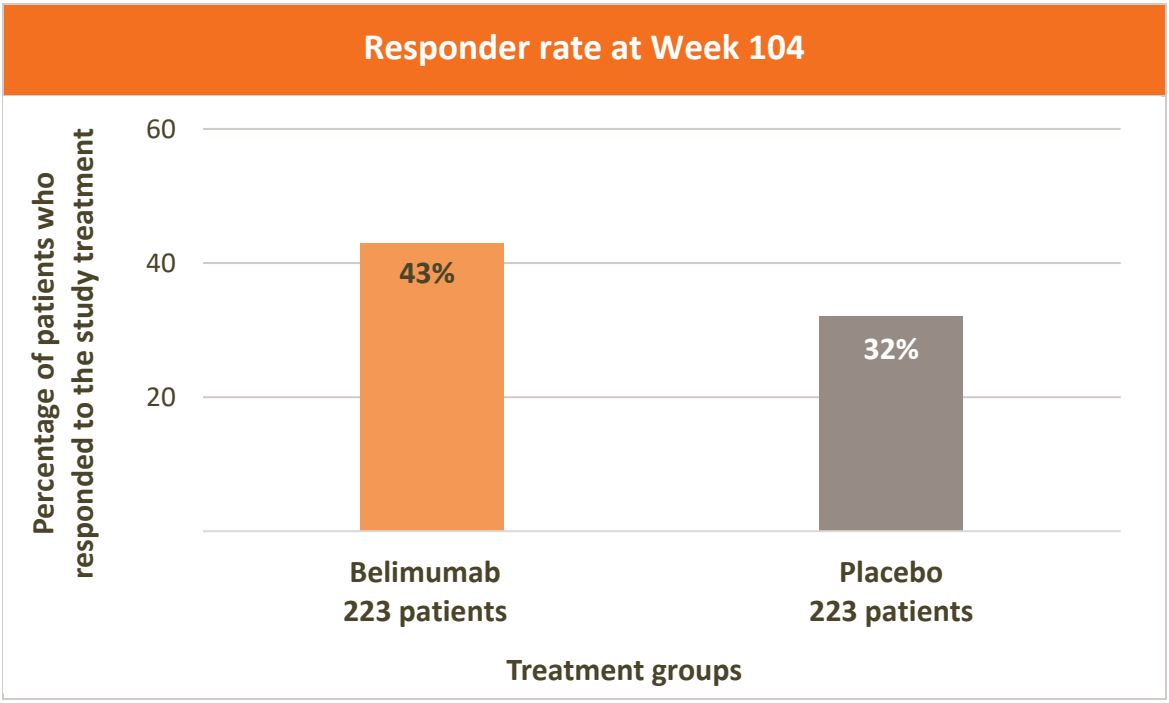
- They continued taking the study treatment up to Week 104.

AND

- Their kidney function improved to the required levels.

The percentage of patients who responded (responder rate) at Week 104 was calculated.

The results for 446 patients are shown in the figure below.



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

In this summary, side effects refer to those events that the study doctor thinks may have been caused by belimumab or placebo. The side effects in this summary may be different to those in the Informed Consent or other documents related to the study medicine.

Side effects reported during double-blind phase

Serious side effects were reported by 24 patients (11%) in the belimumab group and 26 patients (12%) in the placebo group. The table below shows the number of patients (percent) with serious side effects that were reported by one percent or more of patients.

Number of patients (percent) with serious side effects reported by one percent or more of patients during the double-blind phase		
	Belimumab 224 patients	**Placebo 224 patients**
Pneumonia	3 (1%)	4 (2%)
Herpes zoster viral infection (such as shingles)	3 (1%)	2 (less than 1%)

Of the patients who reported serious side effects during the double blind phase, three patients in each of the treatment groups reported side effects that led to death (fatal side effects).

- Belimumab: Two patients had pneumonia and one patient had severe shortness of breath and high blood pressure.
- Placebo: One patient had blood poisoning (sepsis), one patient had a disorder that affects the brain, and one patient had a seizure.

Non-serious side effects were reported by 116 patients (52%) in the belimumab group and 108 patients (48%) in the placebo group. The table below shows the number of patients (percent) with non-serious side effects that were reported by five percent or more of patients.

Number of patients (percent) with non-serious side effects reported by five percent or more of patients during the double-blind phase		
	Belimumab 224 patients	**Placebo 224 patients**
Upper respiratory tract infection	26 (12%)	25 (11%)
Urinary tract infection	14 (6%)	12 (5%)
Bronchitis	11 (5%)	11 (5%)

Side effects reported during open-label phase

After Week 104, 132 patients from the belimumab group and 123 patients from the placebo group continued in the open-label phase. All 255 patients received belimumab in this phase.

During this phase, no fatal side effects were reported. No serious side effects were reported by one percent or more of patients. No non-serious side effects were reported by five percent or more of patients.

How has this study helped patients and researchers?

This study showed that belimumab, when added to regular lupus nephritis treatment, worked better compared with regular lupus nephritis treatment alone. Similar side effects were reported for both treatment groups.

Are there plans for further studies?

Other studies of belimumab in patients with lupus nephritis have been conducted. No further studies are planned at this time.

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)	2011-004570-28[1]
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	NCT01639339[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 lupus nephritis.

The content for this document was finalised by GSK on the 18th of November 2020. The information in this summary does not include additional information available after this date.

[1] https://www.clinicaltrialsregister.eu/ctr-search/trial/2011-004570-28/results

[2] https://clinicaltrials.gov/ct2/show/NCT01639339?term=114054&draw=2&rank=1