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 belimumab in patients with systemic lupus erythematosus.

Full Scientific Title: A randomised, double-blind, placebo-controlled 52-week study to assess adverse events of special interest in adults with active, autoantibody-positive systemic lupus erythematosus receiving belimumab.

Study Number: 115467

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 November 2012. Enrolment is closed, but the study was ongoing when this summary was finalised.

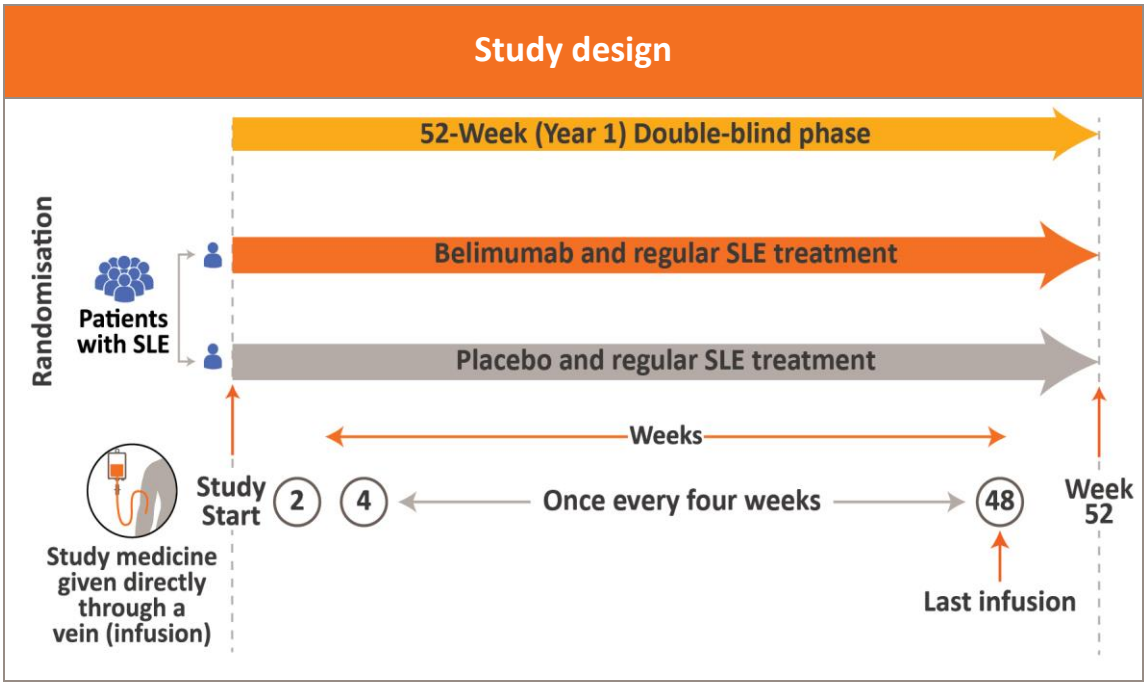
What was the main objective of this study?

Systemic lupus erythematosus (SLE) is a long-term autoimmune disease, in which a type of white blood cell (B cells) produce proteins called autoantibodies. Autoantibodies attack the body's own tissues and organs (for example, kidneys, heart, lungs, or brain). Common symptoms include skin rash and joint pain.

Belimumab is a medicine that decreases autoantibodies. The main focus of this study was to compare the safety of belimumab when added to regular SLE treatment with regular SLE treatment alone. The safety was assessed by comparing the number of patients who died or who had unwanted medical events (adverse events) which were serious or of special interest.

Which medicines were studied?

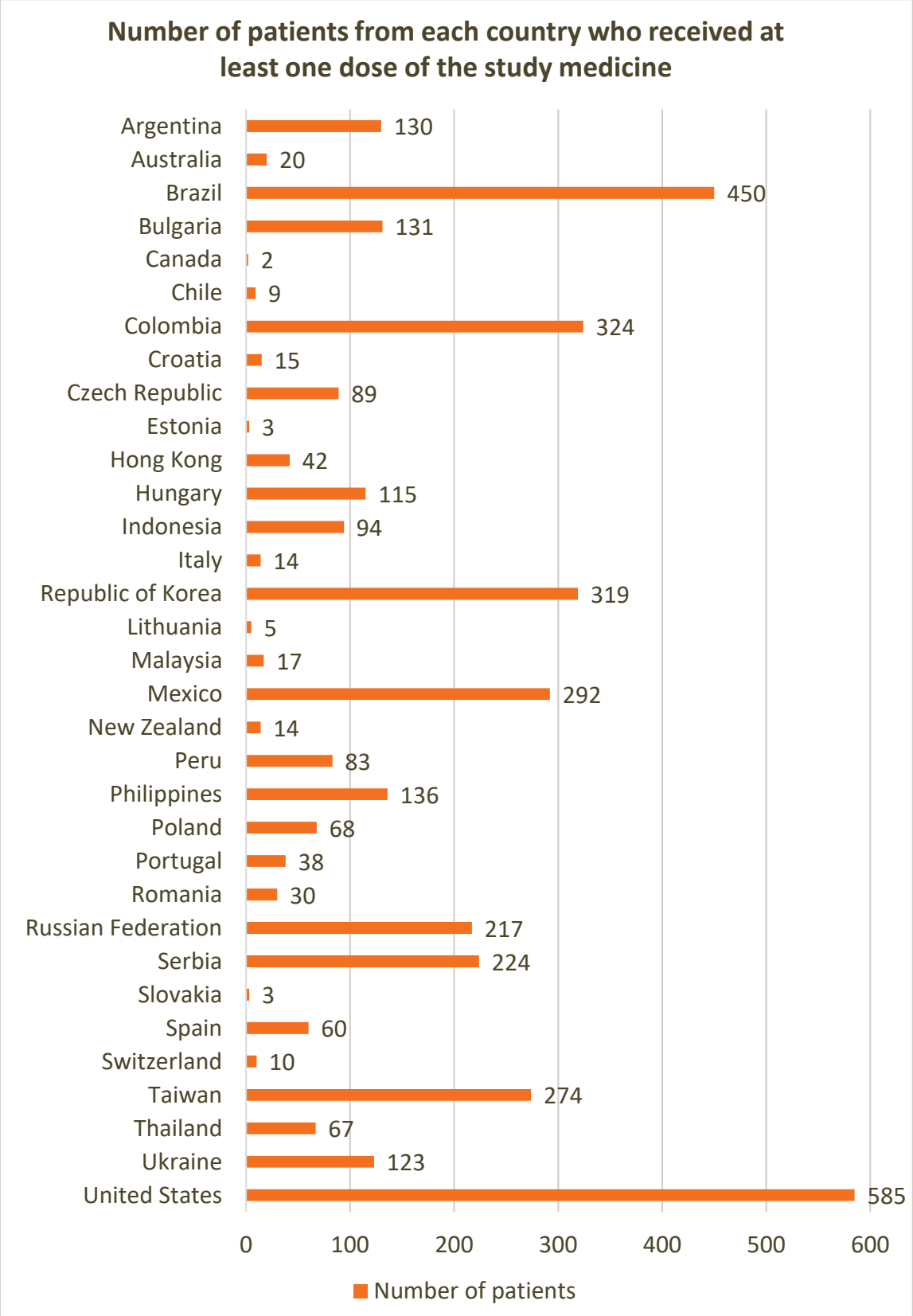
This study is taking place in two phases. During the first 52 weeks (Year 1), patients were placed in one of two treatment groups by chance (randomisation), as shown in the figure below. Patients received either belimumab or placebo (no active medicine) in addition to their regular SLE treatment. Neither the patients nor the study doctors knew who was receiving which treatment. This is called the double-blind phase.



After Week 52, all patients continued their regular SLE treatment and could choose to take belimumab, if approved by their regular doctor. The study doctors continued to monitor the safety of the patients for 4 years (follow up phase).

Where was this study done?

Study sites were in 33 countries.



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 SLE were included in the study if they:

- Were at least 18 years old.
- Tested positive for the presence of autoantibodies before starting the study.
- Were on stable regular SLE treatment before starting the study.

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

- Received treatment with belimumab before starting the study.
- Received any other treatment(s) that affected B cells.
- Been treated for severe kidney disease caused by SLE or inflammation of the kidneys within three months before starting the study treatment.
- Abnormalities of the nervous system caused by SLE (such as seizures, psychosis) requiring treatment before starting the study.
- Received treatment for an acute or chronic infection within two months of starting the study.
- Other disease(s) or taken medicine(s) that the study doctor thought would affect the results of the study.

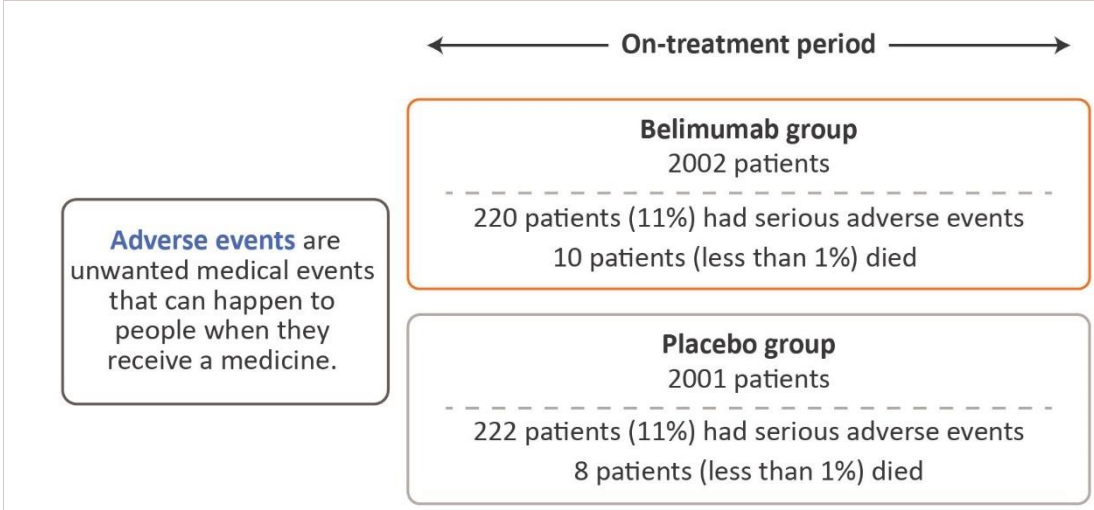
Overall, 4003 patients received at least one dose of the study medicine. The study included 302 (8%) men and 3701 (92%) women. The average age was 41 years. The youngest patient was 17 years old and the oldest patient was 86 years old.

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).

What were the overall results of the study?

The figure below shows the number and percentage of patients who had serious adverse events including those who died during the on-treatment period (Day 1 to four weeks after they received the last infusion of the study medicine).

Number of patients (percent) who had serious adverse events including those who died during the on-treatment period



The numbers of patients who had serious infections were similar between the two treatment groups. The numbers of patients who died in each treatment group were similar. Despite this, there were more infection-related deaths in the belimumab group (9 out of 10 patients) compared with the placebo group (3 out of 8 patients).

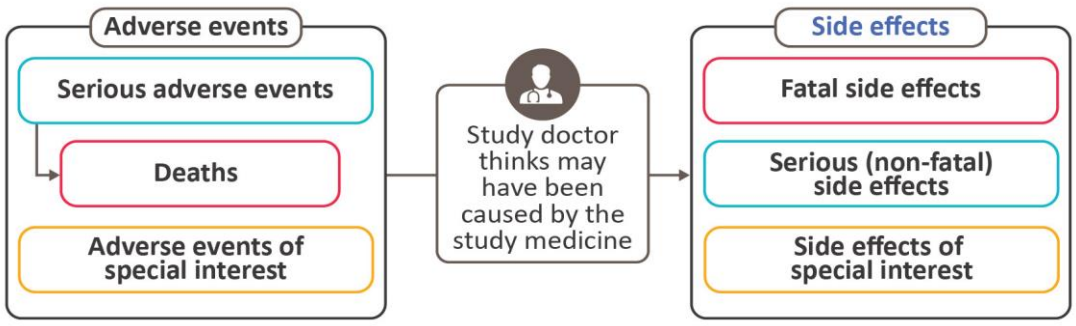
The table below shows the number of patients (percent) with adverse events of special interest reported during the on-treatment period.

Number of patients (percent) with adverse events of special interest reported during the on-treatment period		
	Belimumab 2002 patients	**Placebo 2001 patients**
Serious infections	75 (4%)	82 (4%)
Other infections	36 (2%)	50 (2%)
Thoughts of committing suicide as assessed using a suicidality scoring scale	28 (1%)	23 (1%)
Allergic reactions to the study medicine	8 (less than 1%)	2 (less than 1%)
Serious depression	7 (less than 1%)	1 (less than 1%)
Cancer other than of the skin	5 (less than 1%)	5 (less than 1%)
Skin cancer	4 (less than 1%)	3 (less than 1%)

What were the side effects?

If the study doctor thinks that an adverse event was caused by the study medicine, they record this as a possible side effect (adverse reaction).

Difference between adverse events and side effects in this summary



In this summary, **side effects** refer to those events that the study doctor thinks may have been caused by the study medicine up to week 52. The side effects in this summary may be different to those in the Informed Consent or other documents related to the study medicine.

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.

Fatal side effects occurred in eight patients (less than 1%) in the belimumab group and two patients (less than 1%) in the placebo group. In the belimumab group, two patients had two side effects each that played a part in their death. In line with the overall study results, there were more infection-related fatal side effects in the belimumab group than the placebo group.

The table below shows the fatal side effects.

Number of patients (percent) with fatal side effects		
	Belimumab 2002 patients	**Placebo 2001 patients**
Dangerously low blood pressure caused by a life-threatening response to an infection	3 (less than 1%)	1 (less than 1%)
Pneumonia	3 (less than 1%)	0
Life-threatening response to an infection	2 (less than 1%)	0
Tuberculosis in the lung	1 (less than 1%)	0
Viral infection (Cytomegalovirus)	1 (less than 1%)	0
Cardiac arrest	0	1 (less than 1%)

Serious (non-fatal) side effects occurred in 80 patients (4%) in the belimumab group and 59 patients (3%) in the placebo group. All serious side effects were reported by less than 1% of patients in either treatment group.

Non-serious side effects of special interest occurred in 15 patients (less than 1%) in the belimumab group and 26 patients (1%) in the placebo group. All non-serious side

effects of special interest were reported by less than 1% of patients in either treatment group.

How has this study helped patients and researchers?

This study compared the safety of belimumab when added to regular SLE treatment with regular SLE treatment alone in patients with SLE. The numbers of patients who died or had serious adverse events in this study were similar between the two treatment groups. The number of patients who died from infection-related adverse events was higher in the belimumab group. Adverse events of special interest reported in this study were similar between the two treatment groups, except for the numbers of patients who had serious depression or allergic reaction to the study medicine which were higher in the belimumab group.

Are there plans for further studies?

Other studies on belimumab in patients with SLE 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 numbers associated with this study are shown below with internet links to scientific summaries and other information.

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. When the follow-up phase of this study is complete, final results will be available in the scientific summaries.

Organisation	Website	Study Number
European Medicines Agency	www.clinicaltrialsregister.eu	2011-005667-25[1]
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT01705977[2]

[1] https://www.clinicaltrialsregister.eu/ctr-search/trial/2011-005667-25/results
[2] https://clinicaltrials.gov/ct2/show/study/NCT01705977

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 SLE.

The content for this document was finalised by GSK on the 17th of March 2020. The information in this summary does not include additional information available after this date.