Clinical trial results:
A Phase 3, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, 104-Week Study to Evaluate the Efficacy and Safety of Belimumab Administered in Combination with Rituximab to Adult Subjects with Systemic Lupus Erythematosus (SLE)

Summary

EudraCT number	2016-003050-32
Trial protocol	DE NL ES
Global end of trial date	07 July 2021

Results information

Result version number	v1 (current)
This version publication date	18 April 2022
First version publication date	18 April 2022

Trial information

Trial identification

Sponsor protocol code	205646

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 September 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of belimumab and a single cycle of rituximab administered in a combination regimen to adult participants with SLE.

Protection of trial subjects:

Specific eligibility, monitoring and individual participant/study treatment stopping rules were implemented in the study protocol to mitigate potential risks. An independent data monitoring committee performed periodic review of unblinded safety data. The protocol was amended to ensure safety monitoring during the corona virus disease-19 (COVID-19) pandemic, including recommendations for a safety contact with subjects in the event they could not attend clinic visits and a local analysis of laboratory assessments if central lab results could not be obtained. Also, provisions were made to allow short term treatment with hydroxychloroquine for experimental treatment of COVID-19 and direct supply of Belimumab to participants if participant was unable to visit the site.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	United States: 105
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Netherlands: 18
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Argentina: 15
Country: Number of subjects enrolled	Brazil: 20
Country: Number of subjects enrolled	Korea, Republic of: 26
Country: Number of subjects enrolled	Mexico: 9
Country: Number of subjects enrolled	Russian Federation: 46
Worldwide total number of subjects	292
EEA total number of subjects	59

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	284
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multicenter study conducted at 71 centers in 11 countries. This was a randomized, placebo-controlled, parallel study where participants received treatment in any one of the treatment arms.

Pre-assignment

Screening details:

A total of 396 participants were screened, of which 104 were screen failures. A total of 292 participants were enrolled in the study (Intent-to-Treat Population: It comprised of all randomized participants who received at least one dose of study treatment [Belimumab or Rituximab or Placebo]).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Belimumab + Placebo

Arm description:

Participants received Belimumab 200 milligrams (mg) administered subcutaneously (SC) on Day 1 and then weekly (i.e., every 7 days) through Week 52. Participants also received rituximab-placebo administered by intravenous (IV) infusions at Weeks 4 and 6 in double blind manner. Participants received standard therapy excluding Immunosuppressants and including anti-malarials, non-steroidal anti-inflammatory drugs (NSAIDs), and/or corticosteroids tapered down to prednisone equivalent of less than or equal to (<=) 5 mg/day until Week 104. Participants did not receive treatment after 52 weeks and were in observation until Week 104.

Arm type	Placebo
Investigational medicinal product name	Belimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Belimumab 200 milligrams (mg) was administered subcutaneously (SC) on Day 1 and then weekly (i.e., every 7 days) through Week 52 (Belimumab + Placebo and Belimumab + Rituximab) and through Week 104 for Belimumab + Standard therapy.

Investigational medicinal product name	Rituximab-placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Rituximab-placebo was administered by intravenous (IV) infusions at Weeks 4 and 6.

Investigational medicinal product name	Standard therapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Standard therapy was administered.

Arm title	Belimumab + Rituximab

Arm description:

Participants received Belimumab 200 mg administered SC on Day 1 and then weekly (i.e., every 7 days) through Week 52. Participants also received rituximab 1000 mg administered by IV infusions at Weeks 4 and 6 in double blind manner. Participants received standard therapy excluding Immunosuppressants and including anti-malarials, NSAIDs, and/or corticosteroids tapered down to prednisone equivalent of <= 5 mg/day until Week 104. Participants did not receive treatment after 52 weeks and were in observation until Week 104.

Arm type	Experimental
Investigational medicinal product name	Belimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Belimumab 200 milligrams (mg) was administered subcutaneously (SC) on Day 1 and then weekly (i.e., every 7 days) through Week 52 (Belimumab + Placebo and Belimumab + Rituximab) and through Week 104 for Belimumab + Standard therapy.

Investigational medicinal product name	Standard therapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Standard therapy was administered.

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Rituximab 1000 mg was administered by IV infusions at Weeks 4 and 6.

Arm title	Belimumab + Standard therapy

Arm description:

Participants received open-label Belimumab 200 mg administered SC on Day 1 and then weekly (i.e., every 7 days) until Week 104. Participants also received standard therapy including immunosuppressant, anti-malarials, NSAIDs, and/or corticosteroids tapered down to prednisone equivalent of <= 5 mg/day until Week 104.

Arm type	This was a part of exploratory analysis of study.
Investigational medicinal product name	Standard therapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Standard therapy was administered.

Investigational medicinal product name	Belimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Belimumab 200 milligrams (mg) was administered subcutaneously (SC) on Day 1 and then weekly (i.e., every 7 days) through Week 52 (Belimumab + Placebo and Belimumab + Rituximab) and through Week

104 for Belimumab + Standard therapy.

Number of subjects in period 1	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy
Started	72	144	76
Completed	55	114	57
Not completed	17	30	19
Adverse event, serious fatal	1	2	-
Physician decision	3	4	2
Consent withdrawn by subject	9	14	10
Adverse event, non-fatal	-	4	1
Lost to follow-up	2	3	2
Protocol deviation	2	3	4

Baseline characteristics

Reporting groups	
Reporting group title	Belimumab + Placebo
Reporting group description:	
Participants received Belimumab 200 milligrams (mg) administered subcutaneously (SC) on Day 1 and then weekly (i.e., every 7 days) through Week 52. Participants also received rituximab-placebo administered by intravenous (IV) infusions at Weeks 4 and 6 in double blind manner. Participants received standard therapy excluding Immunosuppressants and including anti-malarials, non-steroidal anti-inflammatory drugs (NSAIDs), and/or corticosteroids tapered down to prednisone equivalent of less than or equal to (<=) 5 mg/day until Week 104. Participants did not receive treatment after 52 weeks and were in observation until Week 104.	
Reporting group title	Belimumab + Rituximab
Reporting group description:	
Participants received Belimumab 200 mg administered SC on Day 1 and then weekly (i.e., every 7 days) through Week 52. Participants also received rituximab 1000 mg administered by IV infusions at Weeks 4 and 6 in double blind manner. Participants received standard therapy excluding Immunosuppressants and including anti-malarials, NSAIDs, and/or corticosteroids tapered down to prednisone equivalent of <= 5 mg/day until Week 104. Participants did not receive treatment after 52 weeks and were in observation until Week 104.	
Reporting group title	Belimumab + Standard therapy
Reporting group description:	
Participants received open-label Belimumab 200 mg administered SC on Day 1 and then weekly (i.e., every 7 days) until Week 104. Participants also received standard therapy including immunosuppressant, anti-malarials, NSAIDs, and/or corticosteroids tapered down to prednisone equivalent of <= 5 mg/day until Week 104.	

Reporting group values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy
Number of subjects	72	144	76
Age categorical			
Baseline characteristics were presented for Intent-to-Treat Population.			
Units: Participants			
All participants	72	144	76
Age Continuous			
Baseline characteristics were presented for Intent-to-Treat Population.			
Units: years			
arithmetic mean	40.6	40.1	41.0
standard deviation	± 12.58	± 11.45	± 12.75
Sex: Female, Male			
Baseline characteristics were presented for Intent-to-Treat Population.			
Units: Participants			
Female	66	129	73
Male	6	15	3
Race/Ethnicity, Customized			
Baseline characteristics were presented for Intent-to-Treat Population.			
Units: Subjects			
White -Arabic/North African Heritage	0	1	1
White-White/Caucasian/European Heritage	39	100	47
Asian - Central/South Asian Heritage	0	1	1
Asian - East Asian Heritage	7	14	10

Asian - South East Asian Heritage	3	2	1
African American/African Heritage	21	22	13
American Indian or Alaskan Native	1	3	3
Native Hawaiian or Other Pacific Islander	1	1	0

Reporting group values	Total		
Number of subjects	292		
Age categorical			
Baseline characteristics were presented for Intent-to-Treat Population.			
Units: Participants			
All participants	292		
Age Continuous			
Baseline characteristics were presented for Intent-to-Treat Population.			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Baseline characteristics were presented for Intent-to-Treat Population.			
Units: Participants			
Female	268		
Male	24		
Race/Ethnicity, Customized			
Baseline characteristics were presented for Intent-to-Treat Population.			
Units: Subjects			
White -Arabic/North African Heritage	2		
White-White/Caucasian/European Heritage	186		
Asian - Central/South Asian Heritage	2		
Asian - East Asian Heritage	31		
Asian - South East Asian Heritage	6		
African American/African Heritage	56		
American Indian or Alaskan Native	7		
Native Hawaiian or Other Pacific Islander	2		

End points

End points reporting groups

Reporting group title	Belimumab + Placebo

Reporting group description:

Participants received Belimumab 200 milligrams (mg) administered subcutaneously (SC) on Day 1 and then weekly (i.e., every 7 days) through Week 52. Participants also received rituximab-placebo administered by intravenous (IV) infusions at Weeks 4 and 6 in double blind manner. Participants received standard therapy excluding Immunosuppressants and including anti-malarials, non-steroidal anti-inflammatory drugs (NSAIDs), and/or corticosteroids tapered down to prednisone equivalent of less than or equal to (<=) 5 mg/day until Week 104. Participants did not receive treatment after 52 weeks and were in observation until Week 104.

Reporting group title	Belimumab + Rituximab

Reporting group description:

Participants received Belimumab 200 mg administered SC on Day 1 and then weekly (i.e., every 7 days) through Week 52. Participants also received rituximab 1000 mg administered by IV infusions at Weeks 4 and 6 in double blind manner. Participants received standard therapy excluding Immunosuppressants and including anti-malarials, NSAIDs, and/or corticosteroids tapered down to prednisone equivalent of <= 5 mg/day until Week 104. Participants did not receive treatment after 52 weeks and were in observation until Week 104.

Reporting group title	Belimumab + Standard therapy

Reporting group description:

Participants received open-label Belimumab 200 mg administered SC on Day 1 and then weekly (i.e., every 7 days) until Week 104. Participants also received standard therapy including immunosuppressant, anti-malarials, NSAIDs, and/or corticosteroids tapered down to prednisone equivalent of <= 5 mg/day until Week 104.

Primary: Percentage of participants with a state of disease control at week 52

End point title	Percentage of participants with a state of disease control at week 52

End point description:

Percentage of participants with a state of disease control (Independent blinded assessor [IBA]) was defined as the percentage of participants with a Systemic Lupus Erythematosus Disease Activity Index 2000(SLEDAI-2K)score less than or equal to(<=)2 achieved without immunosuppressants and with corticosteroids at a prednisone equivalent dose of <=5 mg/day at Week 52. SLEDAI-2K consisting 24 individual items within 9 organ systems. The SLEDAI-2K score was sum of all 24 individual items from the SLEDAI-2K, ranges from 0(no symptoms) to 105(presence of all defined symptoms) with higher scores representing increased disease activity .Modified Intent-to-Treat (MITT) Population comprised of all randomized participants who received at least one dose of study treatment (Belimumab or Rituximab or Placebo) and excluding participants from Arm 3 (Belimumab + Standard therapy) who were randomized prior to 07-Sep-2018.

End point type	Primary

End point timeframe:

Week 52

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[1]	144[2]	47[3]	
Units: Percentage of participants				
number (confidence interval 95%)	16.7 (8.1 to 25.3)	19.4 (13.0 to 25.9)	25.5 (13.1 to 38.0)	

Notes:

[1] - Modified Intent-to-Treat (MITT) Population

[2] - Modified Intent-to-Treat (MITT) Population

[3] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

Statistical analysis title	Stastistical Analysis 2

Statistical analysis description:

Odds ratio was calculated using logistic regression model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, and Baseline prednisone equivalent dose. Belimumab + Placebo arm excluded from model.

Comparison groups	Belimumab + Rituximab v Belimumab + Standard therapy
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	1.54

Statistical analysis title	Stastistical Analysis 1

Statistical analysis description:

Odds ratio was calculated using logistic regression model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose. Belimumab + Standard therapy arm was excluded from model.

Comparison groups	Belimumab + Rituximab v Belimumab + Placebo
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5342
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	2.71

Secondary: Percentage of participants with a state of clinical remission at Week 64

End point title	Percentage of participants with a state of clinical remission at Week 64

End point description:

Percentage of participants with a state of clinical remission (IBA) was defined as percentage of participants with a clinical SLEDAI-2K score =0 (does not include anti-double stranded deoxyribonucleic [dsDNA] and complement activity scores), achieved without immunosuppressants and with corticosteroids at a prednisone equivalent dose of 0 mg/day at Week 64. SLEDAI-2K was a weighted, cumulative index for measuring SLE disease activity in previous 10 days, consisting 24 individual items in which signs and symptoms, laboratory tests, and physician's assessment for each item within each of 9 organ systems were given a weighted score (1 to 8 with higher score indicating increased activity) and summed if present at the time of the visit or in the preceding 10 days. The clinical SLEDAI-2K score was sum of 22 out of all 24 individual items from the SLEDAI-2K and ranges from 0 (no symptoms) to 101 (presence of all defined symptoms) with higher scores representing increased disease activity.

End point type	Secondary

End point timeframe:

Week 64

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[4]	144[5]	47[6]	
Units: Percentage of participants				
number (confidence interval 95%)	5.6 (0.3 to 10.8)	6.3 (2.3 to 10.2)	10.6 (1.8 to 19.5)	

Notes:

[4] - Modified Intent-to-Treat (MITT) Population

[5] - Modified Intent-to-Treat (MITT) Population

[6] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

Statistical analysis title	Stastistical Analysis 1

Statistical analysis description:

Odds ratio was calculated using logistic regression model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Standard therapy arm was excluded from model.

Comparison groups	Belimumab + Placebo v Belimumab + Rituximab
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8582
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	3.78

Statistical analysis title	Stastistical Analysis 2

Statistical analysis description:

Odds ratio was calculated using logistic regression model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Placebo arm was excluded from model.

Comparison groups	Belimumab + Rituximab v Belimumab + Standard therapy
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	1.7

Secondary: Percentage of participants with a state of disease control at Week 104

End point title	Percentage of participants with a state of disease control at Week 104

End point description:

Percentage of participants with a state of disease control (IBA) was defined as the percentage of participants with a SLEDAI-2K score <=2, achieved without immunosuppressants and with corticosteroids at a prednisone equivalent dose of <=5 mg/day at Week 104. SLEDAI-2K was a weighted, cumulative index for measuring SLE disease activity in previous 10 days which consisted of 24 individual items in which signs and symptoms, laboratory tests, and physician's assessment for each item within each of 9 organ systems were given a weighted score (1 to 8 with higher score indicating increased activity) and summed if present at the time of the visit or in the preceding 10 days. The SLEDAI-2K score was the sum of all 24 individual items from the SLEDAI-2K which ranges from 0 (no symptoms) to 105 (presence of all defined symptoms) with higher scores representing increased disease activity.

End point type	Secondary

End point timeframe:

Week 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[7]	144[8]	47[9]	
Units: Percentage of participants				
number (confidence interval 95%)	6.9 (1.1 to 12.8)	11.1 (6.0 to 16.2)	21.3 (9.6 to 33.0)	

Notes:

[7] - Modified Intent-to-Treat (MITT) Population

[8] - Modified Intent-to-Treat (MITT) Population

[9] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

Statistical analysis title	Stastistical Analysis 2

Statistical analysis description:

Odds ratio was calculated using logistic regression model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Placebo arm excluded from model.

Comparison groups	Belimumab + Rituximab v Belimumab + Standard therapy
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	1.09

Statistical analysis title	Stastistical Analysis 1

Statistical analysis description:

Odds ratio was calculated using logistic regression model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Standard therapy arm was excluded from model.

Comparison groups	Belimumab + Placebo v Belimumab + Rituximab
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3613
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	4.72

Secondary: Percentage of participants with a state of disease control by visits

End point title	Percentage of participants with a state of disease control by visits

End point description:

Percentage of participants with a state of disease control (IBA) was defined as the percentage of participants with a SLEDAI-2K score <=2, achieved without immunosuppressants and with corticosteroids at a prednisone equivalent dose of <=5 mg/day. SLEDAI-2K was a weighted, cumulative index for measuring SLE disease activity in previous 10 days which consisted of 24 individual items in which signs and symptoms, laboratory tests, and physician’s assessment for each item within each of 9 organ systems were given a weighted score (1 to 8 with higher score indicating increased activity) and summed if present at the time of the visit or in the preceding 10 days. The SLEDAI-2K score was the sum of all 24 individual items from the SLEDAI-2K which ranges from 0 (no symptoms) to 105 (presence of all defined symptoms) with higher scores representing increased disease activity.

End point type	Secondary

End point timeframe:

Weeks 12, 26, 40, 52, 64, 80 and 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[10]	144[11]	47[12]	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 12	8.3 (1.9 to 14.7)	12.5 (7.1 to 17.9)	21.3 (9.6 to 33.0)	
Week 26	16.7 (8.1 to 25.3)	21.5 (14.8 to 28.2)	25.5 (13.1 to 38.0)	
Week 40	13.9 (5.9 to 21.9)	20.8 (14.2 to 27.5)	23.4 (11.3 to 35.5)	
Week 52	16.7 (8.1 to 25.3)	19.4 (13.0 to 25.9)	25.5 (13.1 to 38.0)	
Week 64	11.1 (3.9 to 18.4)	18.1 (11.8 to 24.3)	25.5 (13.1 to 38.0)	
Week 80	6.9 (1.1 to 12.8)	13.2 (7.7 to 18.7)	27.7 (14.9 to 40.4)	
Week 104	6.9 (1.1 to 12.8)	11.1 (6.0 to 16.2)	21.3 (9.6 to 33.0)	

Notes:

[10] - Modified Intent-to-Treat (MITT) Population

[11] - Modified Intent-to-Treat (MITT) Population

[12] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a state of clinical remission by visits

End point title	Percentage of participants with a state of clinical remission by visits

End point description:

Percentage of participants with a state of clinical remission (IBA) was defined as percentage of participants with a clinical SLEDAI-2K score =0 (does not include anti-dsDNA and complement activity scores), achieved without immunosuppressants and with corticosteroids at a prednisone equivalent dose of 0 mg/day. SLEDAI-2K was a weighted, cumulative index for measuring SLE disease activity in previous 10 days, consisting 24 individual items in which signs and symptoms, laboratory tests, and physician’s assessment for each item within each of 9 organ systems were given a weighted score (1 to 8 with higher score indicating increased activity) and summed if present at the time of the visit or in the preceding 10 days. The clinical SLEDAI-2K score was sum of 22 out of all 24 individual items from the SLEDAI-2K and ranges from 0 (no symptoms) to 101 (presence of all defined symptoms) with higher scores representing increased disease activity

End point type	Secondary

End point timeframe:

Weeks 64, 80 and 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[13]	144[14]	47[15]	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 64	5.6 (0.3 to 10.8)	6.3 (2.3 to 10.2)	10.6 (1.8 to 19.5)	
Week 80	4.2 (0 to 8.8)	4.2 (0.9 to 7.4)	12.8 (3.2 to 22.3)	
Week 104	1.4 (0 to 4.1)	4.2 (0.9 to 7.4)	6.4 (0 to 13.4)	

Notes:

[13] - Modified Intent-to-Treat (MITT) Population

[14] - Modified Intent-to-Treat (MITT) Population

[15] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a state of complete remission (CR) sustained for at least 24 weeks during Week 52 to Week 104

End point title	Percentage of participants with a state of complete remission (CR) sustained for at least 24 weeks during Week 52 to Week 104

End point description:

Percentage of participants with a state of CR (Principal Investigator [PI] assessed) was defined as percentage of participants with a SLEDAI-2K=0 achieved without immunosuppressants and with corticosteroids at prednisone equivalent dose of 0 mg/day,sustained for at least 24 weeks. Sustained CR was longest period a participant maintains CR without break calculated as last consecutive CR date minus first consecutive CR date plus 1. SLEDAI-2K consisted of 24 individual items within each 9 organ systems. Each item was given a weighted score (1 to 8,higher score indicates increased activity) and summed if present at time of visit or in preceding 10 days. SLEDAI-2K score was sum of all 24 individual items from SLEDAI-2K, ranges from 0(no symptoms) to 105(presence of all defined symptoms),higher scores indicates increased disease activity. 99999 indicates that data was not available as confidence interval could not be calculated as there was no participant with a state of complete remission

End point type	Secondary

End point timeframe:

Week 52 to Week 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[16]	144[17]	47[18]	
Units: Percentage of participants				
number (confidence interval 95%)	2.8 (0 to 6.6)	0 (-99999 to 99999)	6.4 (0 to 13.4)	

Notes:

[16] - Modified Intent-to-Treat (MITT) Population

[17] - Modified Intent-to-Treat (MITT) Population

[18] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a state of clinical remission (CLR) sustained for at least 24 weeks from Week 80 to Week 104

End point title	Percentage of participants with a state of clinical remission (CLR) sustained for at least 24 weeks from Week 80 to Week 104

End point description:

Percentage of participants with a state of CLR (PI assessed) at Week 104 was defined as percentage of participants with a clinical SLEDAI-2K score=0 (does not include anti-dsDNA and complement activity scores) achieved without immunosuppressants and with corticosteroids at a prednisone equivalent dose of 0 mg/day, sustained for at least 24 weeks(from Week 80 to Week 104). Sustained CLR is longest period a participant maintains CLR without a break, calculated as last consecutive CLR date minus first consecutive CLR date plus 1. SLEDAI-2K consisted of 24 individual items within each of 9 organ systems. Each item was given a weighted score(1 to 8 with higher score indicating increased activity) and summed if present at the time of visit or in preceding 10 days. The clinical SLEDAI-2K score was sum of 22 out of all 24 individual items from the SLEDAI-2K and ranges from 0 (no symptoms) to 101 (presence of all defined symptoms) with higher scores representing increased disease activity.

End point type	Secondary

End point timeframe:

From Week 80 to Week 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[19]	144[20]	47[21]	
Units: Percentage of participants				
number (confidence interval 95%)	2.8 (0 to 6.6)	2.1 (0 to 4.4)	4.3 (0 to 10.0)	

Notes:

[19] - Modified Intent-to-Treat (MITT) Population

[20] - Modified Intent-to-Treat (MITT) Population

[21] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a state of complete remission by visits

End point title	Percentage of participants with a state of complete remission by visits

End point description:

Percentage of participants with a state of complete remission (PI assessed) was defined as the percentage of participants with a SLEDAI-2K score =0, achieved without immunosuppressants and with corticosteroids at a prednisone equivalent dose of 0 mg/day. SLEDAI-2K was a weighted, cumulative index which consisted of 24 individual items in which signs and symptoms, laboratory tests, and physician’s assessment for each item within for each of 9 organ systems were given a weighted score (1 to 8 with higher score indicating increased activity) and summed if present at the time of the visit or in the preceding 10 days. The SLEDAI-2K score was the sum of all 24 individual items from the SLEDAI-2K which ranges from 0 (no symptoms) to 105 (presence of all defined symptoms) with higher scores representing increased disease activity. 99999 indicates that data was not available as confidence interval could not be calculated as there was no participant with a state of complete remission.

End point type	Secondary

End point timeframe:

Weeks 60, 64, 72, 80, 88, 96 and 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[22]	144[23]	47[24]	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 60	5.6 (0.3 to 10.8)	0.7 (0 to 2.1)	6.4 (0 to 13.4)	
Week 64	5.6 (0.3 to 10.8)	0.7 (0 to 2.1)	6.4 (0 to 13.4)	
Week 72	4.2 (0 to 8.8)	0.7 (0 to 2.1)	6.4 (0 to 13.4)	
Week 80	2.8 (0 to 6.6)	1.4 (0 to 3.3)	8.5 (0.5 to 16.5)	
Week 88	2.8 (0 to 6.6)	0 (-99999 to 99999)	4.3 (0 to 10.0)	
Week 96	1.4 (0 to 4.1)	0.7 (0 to 2.1)	6.4 (0 to 13.4)	
Week 104	1.4 (0 to 4.1)	0.7 (0 to 2.1)	4.3 (0 to 10.0)	

Notes:

[22] - Modified Intent-to-Treat (MITT) Population

[23] - Modified Intent-to-Treat (MITT) Population

[24] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first severe flare

End point title	Time to first severe flare

End point description:

Time to first severe SLE flare was the number of days from treatment start date until the participant met an event. Time to first severe flare was defined as event date minus treatment start date plus 1. Time to first severe flare was measured by Modified SLE flare index which identifies whether a participant had experienced a mild/moderate or severe flare. Analysis of first severe flare was performed on the modified SLE Flare index that excludes severe flares that were triggered only by an increase is SLEDAI-2K score to greater than 12. 99999 indicates that data was not available as only <75% of participants experienced the event within the treatment arm. Hence, third-quartile could not be derived

End point type	Secondary

End point timeframe:

Up to Week 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[25]	144[26]	47[27]	
Units: Days				
median (inter-quartile range (Q1-Q3))	372.0 (202.0 to 485.0)	379.0 (198.0 to 99999)	730.0 (210.0 to 99999)	

Notes:

[25] - Modified Intent-to-Treat (MITT) Population

[26] - Modified Intent-to-Treat (MITT) Population

[27] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

Statistical analysis title	Stastistical Analysis 2

Statistical analysis description:

Hazard ratio was calculated using Cox proportional hazards model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Placebo arm excluded from model.

Comparison groups	Belimumab + Rituximab v Belimumab + Standard therapy
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	2.63

Statistical analysis title	Stastistical Analysis 1

Statistical analysis description:

Hazard ratio was calculated using Cox proportional hazards model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Standard therapy arm was excluded from model.

Comparison groups	Belimumab + Placebo v Belimumab + Rituximab
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.215
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.13

Secondary: Time to first flare

End point title	Time to first flare

End point description:

Time to first SLE flare was the number of days from treatment start date until the participant met an event. Time to first flare was defined as event date minus treatment start date plus 1. Time to first flare was measured by modified SLE flare index which identifies whether a participant had experienced a mild/moderate or severe flare.

End point type	Secondary

End point timeframe:

Up to Week 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[28]	144[29]	47[30]	
Units: Days				
median (inter-quartile range (Q1-Q3))	168.0 (92.0 to 257.0)	170.0 (57.0 to 365.0)	168.0 (91.0 to 337.0)	

Notes:

[28] - Modified Intent-to-Treat (MITT) Population

[29] - Modified Intent-to-Treat (MITT) Population

[30] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

Statistical analysis title	Stastistical Analysis 2

Statistical analysis description:

Hazard ratio was calculated using Cox proportional hazards model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Placebo arm excluded from model.

Comparison groups	Belimumab + Rituximab v Belimumab + Standard therapy
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.49

Statistical analysis title	Stastistical Analysis 1

Statistical analysis description:

Hazard ratio was calculated using Cox proportional hazards model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Standard therapy arm was excluded from model.

Comparison groups	Belimumab + Placebo v Belimumab + Rituximab
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3757
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.19

Secondary: Time to disease control sustained for at least 24 weeks and maintained through Week 104

End point title	Time to disease control sustained for at least 24 weeks and maintained through Week 104

End point description:

Disease control sustained for at least 24 weeks and maintained through Week 104 was defined as SLEDAI-2K score <=2, achieved without immunosuppressants and with corticosteroids at a prednisone equivalent dose of <=5 mg/day. Time to disease control (PI assessed) was defined as the first visit of sustained disease control until Week 104 on or before Week 80 minus treatment start date (Day 1) plus 1. Sustained disease control was longest period a participant maintained disease control without a break. SLEDAI-2K consisted of 24 individual items within each of 9 organ systems. SLEDAI-2K score was the sum of all 24 individual items from SLEDAI-2K , ranges from 0 (no symptoms) to 105 (presence of all defined symptoms),higher scores representing increased disease activity. 99999 indicates that data was not available as only <25% of participants experienced the event within the treatment arm. Hence, median and inter-quartile range could not be derived.

End point type	Secondary

End point timeframe:

Up to Week 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[31]	144[32]	47[33]	
Units: Days				
median (inter-quartile range (Q1-Q3))	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Notes:

[31] - Modified Intent-to-Treat (MITT) Population

[32] - Modified Intent-to-Treat (MITT) Population

[33] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

Statistical analysis title	Stastistical Analysis 1

Statistical analysis description:

Hazard ratio was calculated using Cox proportional hazards model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Standard therapy arm was excluded from model.

Comparison groups	Belimumab + Placebo v Belimumab + Rituximab
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5127
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	5.78

Statistical analysis title	Stastistical Analysis 2

Statistical analysis description:

Hazard ratio was calculated using Cox proportional hazards model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Placebo arm excluded from model.

Comparison groups	Belimumab + Rituximab v Belimumab + Standard therapy
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	2.1

Secondary: Time to clinical remission sustained for at least 24 weeks and maintained through Week 104

End point title	Time to clinical remission sustained for at least 24 weeks and maintained through Week 104

End point description:

Clinical remission sustained for at least 24 weeks and maintained through Week 104 was defined as clinical SLEDAI-2K score=0 (does not include anti-dsDNA and complement activity scores), achieved without immunosuppressants and with corticosteroids at a prednisone equivalent dose of 0 mg/day. Time to CLR (PI assessed) was defined as first visit of sustained CLR until Week 104 on or before Week 80 minus treatment start date (Day 1) plus 1. Sustained CLR was longest period a participant maintained clinical remission without a break. SLEDAI-2K consisted of 24 individual items within each of 9 organ systems. Clinical SLEDAI-2K score was sum of 22 out of all 24 individual items from the

SLEDAI-2K and ranges from 0 (no symptoms) to 101 (presence of all defined symptoms) with higher scores representing increased disease activity. 99999 indicates that data was not available as only <25% of participants experienced the event within the treatment arm.

End point type	Secondary

End point timeframe:

Up to Week 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[34]	144[35]	47[36]	
Units: Days				
median (inter-quartile range (Q1-Q3))	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Notes:

[34] - Modified Intent-to-Treat (MITT) Population

[35] - Modified Intent-to-Treat (MITT) Population

[36] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

Statistical analysis title	Stastistical Analysis 2

Statistical analysis description:

Hazard ratio was calculated using Cox proportional hazards model with covariates: Baseline SLEDAI-2K, Baseline prednisone equivalent dose and treatment group. Belimumab + Placebo arm excluded from model.

Comparison groups	Belimumab + Rituximab v Belimumab + Standard therapy
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Hazard ratio (HR)
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	3.14

Statistical analysis title	Stastistical Analysis 1

Statistical analysis description:

Hazard ratio was calculated using Cox proportional hazards model with covariates: Baseline SLEDAI-2K, Baseline prednisone equivalent dose and treatment group. Belimumab + Standard therapy arm was excluded from model.

Comparison groups	Belimumab + Placebo v Belimumab + Rituximab

Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8436
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	5.05

Secondary: Duration of disease control

End point title	Duration of disease control

End point description:

Duration of disease control was defined as SLEDAI-2K score <=2, achieved without immunosuppressants and with corticosteroids at a prednisone equivalent dose of <=5 mg/day. The duration of disease control (PI assessed) was the longest period between 2 visits that the participant was a disease control responder at all visits and calculated as the first visit of disease control minus last visit of disease control plus 1. SLEDAI-2K consisted of 24 individual items within each of 9 organ systems. Each item was given a weighted score (1 to 8, higher score indicates increased activity) and summed if present at the time of visit or in preceding 10 days. SLEDAI-2K score was the sum of all 24 individual items from SLEDAI-2K, ranges from 0(no symptoms) to 105 (presence of all defined symptoms),higher scores representing increased disease activity. Only those participants with at least one assessment where disease control was met were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34[37]	77[38]	31[39]	
Units: Days				
median (inter-quartile range (Q1-Q3))	49.5 (1.0 to 172.0)	116.0 (21.0 to 265.0)	116.0 (23.0 to 351.0)	

Notes:

[37] - Modified Intent-to-Treat (MITT) Population

[38] - Modified Intent-to-Treat (MITT) Population

[39] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of clinical remission

End point title	Duration of clinical remission

End point description:

Clinical remission was defined as clinical SLEDAI-2K score =0 (does not include anti-dsDNA and complement activity scores), achieved without immunosuppressants and with corticosteroids at a prednisone equivalent dose of 0 mg/day. The duration of clinical remission (PI assessed) was the longest period between 2 visits that the participant was a clinical remission responder at all visits and was calculated as the first visit of clinical remission minus last visit of clinical remission plus 1. SLEDAI-2K consisted of 24 individual items within each of 9 organ systems. The clinical SLEDAI-2K score was sum of 22 out of all 24 individual items from the SLEDAI-2K and ranges from 0 (no symptoms) to 101 (presence of all defined symptoms) with higher scores representing increased disease activity. Only those participants with at least one assessment where clinical remission was met were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13[40]	22[41]	11[42]	
Units: Days				
median (inter-quartile range (Q1-Q3))	31.0 (1.0 to 253.0)	73.0 (29.0 to 225.0)	176.0 (85.0 to 279.0)	

Notes:

[40] - Modified Intent-to-Treat (MITT) Population

[41] - Modified Intent-to-Treat (MITT) Population

[42] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score by visit (PI assessed)

End point title	Change from Baseline in systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score by visit (PI assessed)

End point description:

The SLEDAI-2K consisted of 24 individual items within 9 organ systems. Each item was given a weighted score (1 to 8 with higher score indicating increased activity) and summed if present at the time of visit or in the preceding 10 days. Weighted scores for central nervous system (CNS) (7 items) was 8; for vascular (1 item) was 8; for Musculoskeletal (2 items) was 4; for Renal (4 items) was 4; for Mucocutaneous (3 items) was 2; for Cardiovascular and Respiratory (2 items) was 2; for Immunologic (2 items) was 2;for Constitutional (1 item) was 1 and for Hematologic (2 items) was 1. SLEDAI-2K score was the sum of all 24 individual items from the SLEDAI-2K which ranges from 0 (no symptoms) to 105 (presence of all defined symptoms) with higher scores representing increased disease activity. Change from Baseline was defined as post-dose visit value minus Baseline value. Only those participants with data available at specified time points were analyzed (represented by n=X in category titles)

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 4, 8, 12, 16, 20, 24, 26, 28, 32, 36, 40, 44, 48, 52, 60, 64, 72, 80, 88, 96, 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[43]	144[44]	47[45]	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 4; n=69, 137, 43	-1.4 (± 2.75)	-0.8 (± 3.39)	-1.3 (± 3.15)	
Week 8; n=63, 132, 43	-3.2 (± 3.59)	-2.9 (± 4.09)	-2.9 (± 3.43)	
Week 12; n=63, 131, 43	-2.8 (± 3.50)	-3.6 (± 4.32)	-2.9 (± 3.68)	
Week 16; n=65, 129, 43	-3.4 (± 4.12)	-4.4 (± 4.62)	-4.1 (± 3.29)	
Week 20; n=63, 127, 44	-3.8 (± 4.06)	-5.0 (± 4.44)	-3.8 (± 3.98)	
Week 24; n=61, 128, 43	-4.0 (± 3.71)	-5.0 (± 4.45)	-5.0 (± 4.00)	
Week 26; n=61, 118, 40	-4.1 (± 3.61)	-5.4 (± 4.79)	-5.0 (± 3.18)	
Week 28; n=62, 125, 43	-3.7 (± 3.79)	-5.1 (± 4.74)	-5.2 (± 4.31)	
Week 32; n=61, 125, 43	-4.7 (± 3.87)	-5.7 (± 5.03)	-5.3 (± 3.90)	
Week 36; n=61, 125, 43	-5.0 (± 4.43)	-5.6 (± 5.21)	-5.0 (± 3.68)	
Week 40; n=62, 125, 43	-4.6 (± 4.14)	-5.8 (± 4.83)	-5.0 (± 3.78)	
Week 44; n=62, 122, 43	-4.7 (± 4.71)	-6.1 (± 4.47)	-5.2 (± 4.06)	
Week 48; n=59, 122, 40	-4.5 (± 4.16)	-6.2 (± 4.59)	-5.3 (± 4.08)	
Week 52; n=62, 119, 39	-5.3 (± 4.62)	-6.1 (± 4.42)	-5.6 (± 4.02)	
Week 60; n=57, 114, 37	-5.0 (± 4.15)	-5.8 (± 5.17)	-6.0 (± 3.94)	
Week 64; n=60, 117, 36	-5.1 (± 4.16)	-6.2 (± 4.96)	-5.5 (± 4.40)	
Week 72; n=49, 103, 30	-5.2 (± 4.32)	-6.6 (± 4.50)	-5.3 (± 4.63)	
Week 80; n=46, 102, 36	-5.4 (± 4.58)	-6.5 (± 4.79)	-6.0 (± 4.08)	
Week 88; n=49, 101, 34	-5.3 (± 4.61)	-6.5 (± 4.29)	-6.1 (± 3.80)	
Week 96; n=49, 100, 34	-5.6 (± 4.35)	-7.0 (± 4.44)	-6.1 (± 3.80)	
Week 104; n=50, 104, 34	-5.1 (± 3.69)	-7.2 (± 4.22)	-6.3 (± 3.76)	

Notes:

[43] - Modified Intent-to-Treat (MITT) Population

[44] - Modified Intent-to-Treat (MITT) Population

[45] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with SLEDAI-2K organ improvement compared to Baseline by visits (PI assessed)

End point title	Percentage of participants with SLEDAI-2K organ improvement compared to Baseline by visits (PI assessed)

End point description:

SLEDAI-2K assessments consisted of 24 individual items with 9 organ systems. SLEDAI-2K score was sum of all 24 individual items from SLEDAI-2K ranges from 0(no symptoms) to 105(presence of all defined symptoms). Higher scores indicates increased disease activity. An improvement was defined as a decrease(compared to Baseline) in SLEDAI-2K score within same organ system at a post-Baseline visit. Data for following organ systems was reported: CNS total, Vascular total, Musculoskeletal total, Renal total, Mucocutaneous total, Cardiovascular (Cardio) and Respiratory (Resp) total, Immunologic total and Hematologic total. Constitutional organ system was removed from analysis and its one item (fever)moved to hematologic organ system. 99999 indicates data was not available. Only those participants with data available at specified time points were analyzed (represented by n=X in category titles). Only participants with organ system involvement at Baseline were included.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 4, 8, 12, 16, 20, 24, 26, 28, 32, 36, 40, 44, 48, 52, 60, 64, 72, 80, 88, 96, 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[46]	144[47]	47[48]	
Units: Percentage of participants				
number (not applicable)				
CNS Total; Week 4; n= 2,3,2	0	33.3	0	
CNS Total; Week 8; n= 2,3,2	50.0	66.7	0	
CNS Total; Week 12; n= 2,3,2	50.0	66.7	50.0	
CNS Total; Week 16; n= 2,3,2	50.0	66.7	0	
CNS Total; Week 20; n= 2,3,2	100	66.7	0	
CNS Total; Week 24; n= 2,3,2	100	66.7	100	
CNS Total; Week 26; n= 2,3,2	50.0	66.7	0	
CNS Total; Week 28; n= 2,3,2	100	66.7	100	
CNS Total; Week 32; n= 2,3,2	100	66.7	100	
CNS Total; Week 36; n= 2,3,2	100	66.7	50.0	
CNS Total; Week 40; n= 2,3,2	100	66.7	100	
CNS Total; Week 44; n= 2,3,2	100	66.7	100	
CNS Total; Week 48; n= 2,3,2	100	66.7	50.0	
CNS Total; Week 52; n= 2,3,2	100	66.7	100	
CNS Total; Week 60; n= 2,3,2	100	66.7	100	
CNS Total; Week 64; n= 2,3,2	100	66.7	100	
CNS Total; Week 72; n= 2,3,2	100	33.3	50.0	
CNS Total; Week 80; n= 2,3,2	100	33.3	50.0	
CNS Total; Week 88; n= 2,3,2	100	33.3	100	
CNS Total; Week 96; n= 2,3,2	100	33.3	100	
CNS Total; Week 104; n=2,3,2	100	33.3	100	
Vascular Total; Week 4; n= 6,11,0	50.0	9.1	99999	
Vascular Total; Week 8; n= 6,11,0	33.3	36.4	99999	
Vascular Total; Week 12; n= 6,11,0	50.0	54.5	99999	
Vascular Total; Week 16; n= 6,11,0	50.0	54.5	99999	
Vascular Total; Week 20; n=6,11,0	50.0	72.7	99999	
Vascular Total; Week 24; n= 6,11,0	50.0	72.7	99999	
Vascular Total; Week 26; n= 6, 11, 0	50.0	63.6	99999	
Vascular Total; Week 28; n= 6, 11,0	33.3	72.7	99999	
Vascular Total; Week 32; n= 6,11, 0	50.0	72.7	99999	
Vascular Total; Week 36; n= 6, 11,0	50.0	63.6	99999	
Vascular Total; Week 40; n= 6, 11,0	33.3	72.7	99999	
Vascular Total; Week 44; n= 6, 11, 0	33.3	72.7	99999	
Vascular Total; Week 48; n= 6, 11, 0	33.3	63.6	99999	
Vascular Total; Week 52; n= 6, 11, 0	66.7	63.6	99999	
Vascular Total; Week 60; n= 6, 11, 0	50.0	63.6	99999	
Vascular Total; Week 64; n= 6, 11, 0	50.0	90.9	99999	
Vascular Total; Week 72; n= 6, 11, 0	33.3	81.8	99999	
Vascular Total; Week 80; n= 6, 11, 0	50.0	72.7	99999	
Vascular Total; Week 88; n= 6, 11, 0	50.0	45.5	99999	
Vascular Total; Week 96; n= 6, 11, 0	50.0	63.6	99999	

Vascular Total; Week 104; n= 6, 11, 0	33.3	72.7	99999	
Musculoskeletal Total; Week 4; n= 57, 110, 34	22.8	13.6	23.5	
Musculoskeletal Total; Week 8; n=57,110, 34	40.4	40.0	50.0	
Musculoskeletal Total; Week 12; n= 57,110,34	36.8	44.5	47.1	
Musculoskeletal Total; Week 16; n= 57,110,34	42.1	56.4	67.6	
Musculoskeletal Total; Week 20; n= 57,110,34	47.4	58.2	64.7	
Musculoskeletal Total; Week 24; n= 57,110,34	42.1	54.5	70.6	
Musculoskeletal Total; Week 26; n=57,110,34	43.9	46.4	73.5	
Musculoskeletal Total; Week 28; n= 57,110,34	49.1	53.6	76.5	
Musculoskeletal Total; Week 32; n= 57,110,34	54.4	63.6	76.5	
Musculoskeletal Total; Week 36; n= 57,110,34	61.4	61.8	76.5	
Musculoskeletal Total; Week 40; n= 57,110,34	54.4	58.2	73.5	
Musculoskeletal Total; Week 44; n= 57,110,34	50.9	60.0	76.5	
Musculoskeletal Total; Week 48; n= 57,110,34	57.9	60.9	73.5	
Musculoskeletal Total; Week 52; n= 57,110,34	59.6	59.1	73.5	
Musculoskeletal Total; Week 60; n= 57,110,34	54.4	54.5	67.6	
Musculoskeletal Total; Week 64; n= 57,110,34	56.1	55.5	67.6	
Musculoskeletal Total; Week 72; n= 57,110,34	47.4	58.2	58.8	
Musculoskeletal Total; Week 80; n= 57,110,34	47.4	58.2	76.5	
Musculoskeletal Total; Week 88; n= 57,110,34	57.9	59.1	67.6	
Musculoskeletal Total; Week 96; n= 57,110,34	50.9	60.9	70.6	
Musculoskeletal Total; Week 104; n= 57,110,34	47.4	64.5	67.6	
Renal Total; Week 4; n= 14,23,8	21.4	30.4	12.5	
Renal Total; Week 8; n= 14, 23, 8	50.0	43.5	12.5	
Renal Total; Week 12; n= 14, 23, 8	28.6	52.2	12.5	
Renal Total; Week 16; n= 14, 23, 8	35.7	52.2	12.5	
Renal Total; Week 20; n= 14, 23, 8	57.1	60.9	12.5	
Renal Total; Week 24; n= 14, 23, 8	35.7	60.9	12.5	
Renal Total; Week 26; n= 14, 23, 8	28.6	65.2	25.0	
Renal Total; Week 28; n= 14, 23, 8	21.4	56.5	37.5	
Renal Total; Week 32; n= 14, 23, 8	35.7	65.2	25.0	
Renal Total; Week 36; n= 14, 23, 8	42.9	65.2	50.0	
Renal Total; Week 40; n=14, 23, 8	42.9	69.6	25.0	
Renal Total; Week 44; n= 14, 23, 8	50.0	69.6	12.5	
Renal Total; Week 48; n=14, 23, 8	42.9	69.6	50.0	
Renal Total; Week 52; n= 14, 23, 8	64.3	69.6	25.0	
Renal Total; Week 60; n= 14, 23, 8	50.0	65.2	25.0	
Renal Total; Week 64; n= 14, 23, 8	50.0	69.6	12.5	

Renal Total; Week 72; n= 14, 23, 8	50.0	65.2	12.5	
Renal Total; Week 80; n= 14, 23, 8	42.9	65.2	50.0	
Renal Total; Week 88; n= 14, 23, 8	50.0	73.9	25.0	
Renal Total; Week 96; n= 14, 23, 8	35.7	78.3	37.5	
Renal Total; Week 104; n= 14, 23, 8	35.7	69.6	50.0	
Mucocutaneous Total; Week 4; n= 59, 126,43	30.5	28.6	32.6	
Mucocutaneous Total; Week 8; n= 59,126,43	54.2	45.2	51.2	
Mucocutaneous Total; Week 12; n= 59, 126, 43	55.9	57.1	55.8	
Mucocutaneous Total; Week 16; n= 59, 126, 43	57.6	58.7	67.4	
Mucocutaneous Total; Week 20; n= 59, 126, 43	50.8	62.7	69.8	
Mucocutaneous Total; Week 24; n= 59, 126, 43	59.3	61.9	69.8	
Mucocutaneous Total; Week 26; n=59, 126, 43	59.3	60.3	65.1	
Mucocutaneous Total; Week 28; n= 59, 126, 43	62.7	62.7	69.8	
Mucocutaneous Total; Week 32; n= 59, 126, 43	62.7	65.1	74.4	
Mucocutaneous Total; Week 36; n= 59, 126, 43	66.1	65.9	69.8	
Mucocutaneous Total; Week 40; n= 59, 126, 43	62.7	66.7	67.4	
Mucocutaneous Total; Week 44; n= 59, 126, 43	61.0	61.1	69.8	
Mucocutaneous Total; Week 48; n= 59, 126, 43	50.8	66.7	69.8	
Mucocutaneous Total; Week 52; n=59, 126, 43	64.4	64.3	69.8	
Mucocutaneous Total; Week 60; n=59, 126, 43	55.9	65.1	67.4	
Mucocutaneous Total; Week 64; n=59, 126, 43	64.4	65.9	62.8	
Mucocutaneous Total; Week 72; n=59, 126, 43	57.6	60.3	58.1	
Mucocutaneous Total; Week 80; n= 59, 126, 43	62.7	61.9	62.8	
Mucocutaneous Total; Week 88; n= 59, 126, 43	59.3	62.7	67.4	
Mucocutaneous Total; Week 96; n= 59, 126, 43	52.5	62.7	62.7	
Mucocutaneous Total; Week 104; n= 59, 126, 43	61.0	69.0	60.5	
Cardio and Resp Total; Week 4; n= 3, 7, 0	0	42.9	99999	
Cardio and Resp Total; Week 8; n= 3, 7, 0	0	71.4	99999	
Cardio and Resp Total; Week 12; n= 3, 7, 0	0	71.4	99999	
Cardio and Resp Total; Week 16; n= 3, 7, 0	0	85.7	99999	
Cardio and Resp Total; Week 20; n= 3,7, 0	33.3	71.4	99999	
Cardio and Resp Total; Week 24; n= 3, 7, 0	66.7	100	99999	
Cardio and Resp Total; Week 26; n=3, 7, 0	0	85.7	99999	

Cardio and Resp Total; Week 28; n= 3,7, 0	0	85.7	99999	
Cardio and Resp Total; Week 32; n= 3, 7, 0	33.3	100	99999	
Cardio and Resp Total; Week 36; n= 3, 7, 0	66.7	85.7	99999	
Cardio and Resp Total; Week 40; n=3,7, 0	33.3	71.4	99999	
Cardio and Resp Total; Week 44; n= 3,7, 0	66.7	57.1	99999	
Cardio and Resp Total; Week 48; n= 3, 7, 0	33.3	85.7	99999	
Cardio and Resp Total; Week 52; n= 3, 7, 0	66.7	85.7	99999	
Cardio and Resp Total; Week 60; n= 3,7,0	100	71.4	99999	
Cardio and Resp Total; Week 64; n=3,7,0	100	85.7	99999	
Cardio and Resp Total; Week 72; n= 3,7,0	66.7	71.4	99999	
Cardio and Resp Total; Week 80; n=3,7,0	66.7	85.7	99999	
Cardio and Resp Total; Week 88; n= 3,7,0	66.7	71.4	99999	
Cardio and Resp Total; Week 96; n= 3,7,0	66.7	71.4	99999	
Cardio and Resp Total; Week 104; n= 3,7,0	66.7	71.4	99999	
Immunologic Total; Week 4; n=48, 104, 34	12.5	10.6	17.6	
Immunologic Total; Week 8; n= 48, 104, 34	16.7	17.3	17.6	
Immunologic Total; Week 12; n= 48, 104, 34	22.9	24.0	17.6	
Immunologic Total; Week 16; n= 48, 104, 34	20.8	30.8	11.8	
Immunologic Total; Week 20; n= 48, 104, 34	20.8	36.5	23.5	
Immunologic Total; Week 24; n= 48, 104, 34	22.9	34.6	20.6	
Immunologic Total; Week 26; n= 48, 104, 34	18.8	39.4	11.8	
Immunologic Total; Week 28; n= 48, 104, 34	18.8	34.6	20.6	
Immunologic Total; Week 32; n= 48, 104, 34	25.0	40.4	23.5	
Immunologic Total; Week 36; n= 48, 104, 34	20.8	41.3	17.6	
Immunologic Total; Week 40; n= 48, 104, 34	14.6	44.2	23.5	
Immunologic Total; Week 44; n= 48, 104, 34	25.0	39.4	38.2	
Immunologic Total; Week 48; n= 48, 104, 34	20.8	41.3	29.4	
Immunologic Total; Week 52; n= 48, 104, 34	20.8	37.5	26.5	
Immunologic Total; Week 60; n= 48, 104, 34	25.0	45.2	20.6	
Immunologic Total; Week 64; n= 48, 104, 34	20.8	43.3	26.5	
Immunologic Total; Week 72; n=48, 104, 34	29.2	36.5	17.6	

Immunologic Total; Week 80; n=48, 104, 34	22.9	31.7	23.5	
Immunologic Total; Week 88; n=48, 104, 34	31.3	29.8	14.7	
Immunologic Total; Week 96; n=48, 104, 34	20.8	33.7	20.6	
Immunologic Total; Week 104; n=48, 104, 34	27.1	40.4	20.6	
Hematologic Total; Week 4; n= 8, 19, 3	50.0	42.1	0	
Hematologic Total; Week 8; n= 8, 19, 3	62.5	63.2	66.7	
Hematologic Total; Week 12; n= 8, 19, 3	62.5	52.6	33.3	
Hematologic Total; Week 16; n= 8, 19, 3	75.0	63.2	66.7	
Hematologic Total; Week 20; n= 8, 19, 3	87.5	57.9	100	
Hematologic Total; Week 24; n= 8, 19, 3	62.5	52.6	100	
Hematologic Total; Week 26; n= 8, 19, 3	75.0	36.8	100	
Hematologic Total; Week 28; n= 8, 19, 3	62.5	57.9	66.7	
Hematologic Total; Week 32; n= 8, 19, 3	62.5	57.9	66.7	
Hematologic Total; Week 36; n= 8, 19, 3	87.5	63.2	66.7	
Hematologic Total; Week 40; n= 8, 19, 3	62.5	52.6	66.7	
Hematologic Total; Week 44; n= 8, 19, 3	87.5	57.9	66.7	
Hematologic Total; Week 48; n= 8, 19, 3	37.5	63.2	66.7	
Hematologic Total; Week 52; n= 8, 19, 3	75.0	52.6	33.3	
Hematologic Total; Week 60; n= 8, 19, 3	50.0	57.9	33.3	
Hematologic Total; Week 64; n= 8, 19, 3	62.5	68.4	33.3	
Hematologic Total; Week 72; n= 8, 19, 3	62.5	47.4	0	
Hematologic Total; Week 80; n= 8, 19, 3	50.0	52.6	33.3	
Hematologic Total; Week 88; n= 8, 19, 3	37.5	57.9	33.3	
Hematologic Total; Week 96; n= 8, 19, 3	50.0	52.6	33.3	
Hematologic Total; Week 104; n= 8, 19, 3	50.0	63.2	33.3	

Notes:

[46] - Modified Intent-to-Treat (MITT) Population

[47] - Modified Intent-to-Treat (MITT) Population

[48] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with SLEDAI-2K organ worsening compared to Baseline by visits (PI assessed)

End point title	Percentage of participants with SLEDAI-2K organ worsening

	compared to Baseline by visits (PI assessed)

End point description:

SLEDAI-2K assessments consisted of 24 individual items with 9 organ systems. SLEDAI-2K score was sum of all 24 individual items from SLEDAI-2K, ranges from 0(no symptoms) to 105(presence of all defined symptoms). Higher scores indicates increased disease activity. A worsening was defined as an increase(compared to Baseline) in SLEDAI-2K score within same organ system at a post-Baseline visit. Percentage of participants with SLEDAI-2K organ worsening for following organ systems were reported;CNS total,Vascular total,Musculoskeletal total,Renal total,Mucocutaneous total,Cardio and Resp total,Immunologic total and Hematologic total. Constitutional organ system was removed from analysis and its one item (fever)moved to hematologic organ system. Only those participants with data available at specified time points were analyzed (represented by n=X in category titles). Only participants with no organ system involvement at Baseline were included.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 4, 8, 12, 16, 20, 24, 26, 28, 32, 36, 40, 44, 48, 52, 60, 64, 72, 80, 88, 96, 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[49]	144[50]	47[51]	
Units: Percentage of participants				
number (not applicable)				
CNS Total; Week 4; n= 69, 136, 43	0	0	0	
CNS Total; Week 8; n= 64,132, 42	0	0	0	
CNS Total; Week 12; n= 65, 134, 42	0	0	0	
CNS Total; Week 16; n= 65, 130, 42	0	0.8	0	
CNS Total; Week 20; n= 63, 128, 42	0	0	0	
CNS Total; Week 24; n= 61, 127, 41	0	0.8	0	
CNS Total; Week 26; n=61, 116, 38	0	0.9	0	
CNS Total; Week 28; n=62, 124, 41	0	0	0	
CNS Total; Week 32; n= 61, 124, 41	0	0.8	0	
CNS Total; Week 36; n= 61, 124, 41	0	1.6	0	
CNS Total; Week 40; n= 61, 123, 41	0	0	0	
CNS Total; Week 44; n= 61, 121, 41	0	0	0	
CNS Total; Week 48; n= 58, 120,39	0	0	0	
CNS Total; Week 52; n= 62, 120, 38	0	0	0	
CNS Total; Week 60; n=59, 117, 35	0	0	0	
CNS Total; Week 64; n=60, 117, 34	0	0	0	
CNS Total; Week 72; n= 56, 109, 31	0	0	0	
CNS Total; Week 80; n=55, 111, 35	0	0	0	
CNS Total; Week 88; n= 57, 107, 34	0	0	0	
CNS Total; Week 96; n=52, 107, 33	0	0	0	
CNS Total; Week 104; n= 53, 112, 34	0	0	0	
Vascular Total;Week 4; n= 65, 128, 45	0	3.9	0	
Vascular Total;Week 8; n= 61, 124, 44	0	2.4	0	
Vascular Total; Week 12; n= 62, 126, 44	1.6	1.6	0	
Vascular Total; Week 16; n=62, 122, 44	0	1.6	0	
Vascular Total; Week 20; n=60, 120, 44	0	0.8	0	
Vascular Total; Week 24; n= 59, 119, 43	0	0	0	

Vascular Total; Week 26; n=58, 109, 40	0	0.9	0	
Vascular Total;Week 28; n= 61, 116, 43	0	1.7	0	
Vascular Total;Week 32; n=59, 116, 43	0	2.6	0	
Vascular Total;Week 36; n= 59, 116, 43	0	1.7	0	
Vascular Total;Week 40; n=59, 115, 43	0	1.7	0	
Vascular Total;Week 44; n= 59, 113, 43	0	0	0	
Vascular Total;Week 48; n= 57, 112, 40	0	0	0	
Vascular Total;Week 52; n=60, 112, 40	0	0.9	0	
Vascular Total;Week 60; n= 58, 109, 37	0	0	0	
Vascular Total;Week 64; n=59, 109, 36	0	1.8	0	
Vascular Total;Week 72; n=55, 101, 33	0	0	0	
Vascular Total;Week 80; n= 54, 104, 37	0	1.0	0	
Vascular Total;Week 88; n=56, 102, 36	0	0	0	
Vascular Total;Week 96; n=51, 101, 35	0	0	0	
Vascular Total;Week 104; n=53, 105, 36	0	0	0	
Musculoskeletal Total; Week 4; n=15, 33, 12	0	12.1	0	
Musculoskeletal Total; Week 8; n= 15, 33, 12	6.7	6.1	0	
Musculoskeletal Total; Week 12; n= 15, 33, 12	13.3	6.1	0	
Musculoskeletal Total; Week 16; n= 15, 32, 12	6.7	3.1	8.3	
Musculoskeletal Total; Week 20; n= 15, 32, 12	6.7	6.3	0	
Musculoskeletal Total; Week 24; n= 15, 31, 11	0	6.5	0	
Musculoskeletal Total; Week 26; n= 15, 31, 11	0	3.2	0	
Musculoskeletal Total; Week 28; n= 14, 31, 11	0	3.2	9.1	
Musculoskeletal Total; Week 32; n= 15, 30, 11	0	6.7	9.1	
Musculoskeletal Total; Week 36; n= 14, 30, 11	7.1	3.3	9.1	
Musculoskeletal Total; Week 40; n=15, 30, 11	0	3.3	9.1	
Musculoskeletal Total; Week 44; n=15, 29, 11	0	6.9	9.1	
Musculoskeletal Total; Week 48; n= 14, 30, 10	7.1	3.3	10.0	
Musculoskeletal Total; Week 52; n= 15, 30, 11	6.7	6.7	9.1	
Musculoskeletal Total; Week 60; n= 14, 28, 11	0	0	9.1	
Musculoskeletal Total; Week 64; n=14, 29, 10	0	3.4	10.0	
Musculoskeletal Total; Week 72; n= 14, 27, 10	0	11.1	10.0	
Musculoskeletal Total; Week 80; n= 13, 26, 9	0	0	11.1	
Musculoskeletal Total; Week 88; n= 13, 25, 9	15.4	4.0	0	
Musculoskeletal Total; Week 96; n= 12, 26, 9	0	3.8	0	
Musculoskeletal Total; Week 104; n= 13, 27, 9	0	0	0	
Renal Total; Week 4; n= 57, 117, 36	5.3	6.0	11.1	

Renal Total; Week 8; n=51, 110, 36	2.0	3.6	5.6	
Renal Total; Week 12; n=53, 115, 35	1.9	3.5	8.6	
Renal Total; Week 16; n=53, 112, 35	7.5	4.5	2.9	
Renal Total; Week 20; n= 49, 108, 36	8.2	3.7	8.3	
Renal Total; Week 24; n= 49, 111, 35	10.2	3.6	2.9	
Renal Total; Week 26; n= 49, 99, 33	6.1	0	0	
Renal Total; Week 28; n= 50, 106, 36	10.0	1.9	2.8	
Renal Total; Week 32; n= 50,107, 36	6.0	2.8	2.8	
Renal Total; Week 36; n= 50, 107, 36	8.0	2.8	5.6	
Renal Total; Week 40; n= 47, 106, 34	6.4	4.7	0	
Renal Total; Week 44; n= 49, 103, 35	6.1	1.0	2.9	
Renal Total; Week 48; n= 47, 101, 32	10.6	5.9	6.3	
Renal Total; Week 52; n= 49, 103, 32	8.2	3.9	3.1	
Renal Total; Week 60; n=47, 96, 30	6.4	4.2	0	
Renal Total; Week 64; n= 50, 99, 29	2.0	2.0	0	
Renal Total; Week 72; n= 40, 89, 26	5.0	4.5	0	
Renal Total; Week 80; n= 41, 90, 29	14.6	3.3	6.9	
Renal Total; Week 88; n= 44, 85, 29	13.6	1.2	0	
Renal Total; Week 96; n= 43, 85, 29	4.7	1.2	0	
Renal Total; Week 104; n= 44, 90, 30	6.8	2.2	0	
Mucocutaneous Total; Week 4; n= 13, 18, 4	15.4	5.6	0	
Mucocutaneous Total; Week 8; n= 12, 18, 4	8.3	11.1	0	
Mucocutaneous Total; Week 12; n= 12, 18, 4	8.3	16.7	0	
Mucocutaneous Total; Week 16; n= 12, 18, 4	0	5.6	0	
Mucocutaneous Total; Week 20; n= 12, 18, 4	25.0	5.6	0	
Mucocutaneous Total; Week 24; n= 11, 17, 4	18.2	5.9	0	
Mucocutaneous Total; Week 26; n= 10, 17, 4	20.0	11.8	0	
Mucocutaneous Total; Week 28; n= 10, 17, 4	0	11.8	0	
Mucocutaneous Total; Week 32; n= 10, 17, 4	10.0	5.9	0	
Mucocutaneous Total; Week 36; n= 10, 17, 4	0	5.9	0	
Mucocutaneous Total; Week 40; n= 10, 17, 4	20.0	11.8	0	
Mucocutaneous Total; Week 44; n= 10, 17, 4	10.0	0	0	
Mucocutaneous Total; Week 48; n=10, 16, 3	0	6.3	0	
Mucocutaneous Total; Week 52; n= 10, 17, 4	0	5.9	25.0	
Mucocutaneous Total; Week 60; n= 9, 17, 4	11.1	11.8	0	
Mucocutaneous Total; Week 64; n= 10, 16, 4	0	6.3	25.0	
Mucocutaneous Total; Week 72; n=10, 16, 4	20	6.3	25.0	
Mucocutaneous Total; Week 80; n= 9, 17, 4	0	0	25.0	
Mucocutaneous Total; Week 88; n= 9, 16, 4	0	6.3	25.0	

Mucocutaneous Total; Week 96; n= 9, 15, 4	11.1	0	25.0	
Mucocutaneous Total; Week 104; n= 9, 17, 4	11.1	5.9	0	
Cardio and Resp Total; Week 4; n= 68, 132, 45	2.9	0.8	0	
Cardio and Resp Total; Week 8; n= 63, 128, 44	0	0.8	0	
Cardio and Resp Total; Week 12; n= 64, 130, 44	0	0.8	0	
Cardio and Resp Total; Week 16; n= 64, 126, 44	3.1	0	0	
Cardio and Resp Total; Week 20; n= 63, 124, 44	1.6	0.8	0	
Cardio and Resp Total; Week 24; n= 60, 123, 43	0	0	0	
Cardio and Resp Total; Week 26; n=59, 112, 40	0	0	0	
Cardio and Resp Total; Week 28; n= 61, 120, 43	3.3	0.8	0	
Cardio and Resp Total; Week 32; n= 60, 120, 43	1.7	0	0	
Cardio and Resp Total; Week 36; n= 60, 120, 43	1.7	0	0	
Cardio and Resp Total; Week 40; n=60, 119, 43	0	0	0	
Cardio and Resp Total; Week 44; n= 60, 117, 43	1.7	0	0	
Cardio and Resp Total; Week 48; n= 57, 116, 40	0	0	2.5	
Cardio and Resp Total; Week 52; n=61, 116, 40	0	0	0	
Cardio and Resp Total; Week 60; n= 58, 114, 37	0	0	0	
Cardio and Resp Total; Week 64; n= 59, 114, 36	0	0.9	0	
Cardio and Resp Total; Week 72; n= 55, 106, 33	0	0	0	
Cardio and Resp Total; Week 80; n= 54, 107, 37	1.9	0	0	
Cardio and Resp Total; Week 88; n= 56, 104, 36	1.8	0	0	
Cardio and Resp Total; Week 96; n=51, 104, 35	0	1.0	0	
Cardio and Resp Total; Week 104; n= 52, 109, 36	0	0	0	
Immunologic Total; Week 4; n=23, 37, 13	17.4	0	7.7	
Immunologic Total; Week 8; n=20, 37, 12	20.0	10.8	0	
Immunologic Total; Week 12; n=21, 37,12	23.8	8.1	16.7	
Immunologic Total; Week 16; n= 21, 35, 12	9.5	11.4	0	
Immunologic Total; Week 20; n= 19, 35, 12	15.8	11.4	0	
Immunologic Total; Week 24; n= 18, 35, 12	5.6	5.7	0	
Immunologic Total; Week 26; n= 18, 30, 12	5.6	6.7	8.3	
Immunologic Total; Week 28; n= 19, 35, 12	15.8	8.6	16.7	

Immunologic Total; Week 32; n= 19, 33, 12	10.5	12.1	8.3	
Immunologic Total; Week 36; n= 19, 34, 12	15.8	8.8	16.7	
Immunologic Total; Week 40; n= 19, 33, 12	21.1	6.1	8.3	
Immunologic Total; Week 44; n= 18, 33, 12	22.2	0	0	
Immunologic Total; Week 48; n= 18, 33, 11	22.2	3.0	27.3	
Immunologic Total; Week 52; n= 19, 32, 12	21.1	3.1	8.3	
Immunologic Total; Week 60; n= 18, 32, 10	16.7	6.3	0	
Immunologic Total; Week 64; n= 19, 33, 10	21.1	6.1	20.0	
Immunologic Total; Week 72; n= 17, 28, 9	23.5	7.1	11.1	
Immunologic Total; Week 80; n= 18, 29, 11	5.6	6.9	18.2	
Immunologic Total; Week 88; n= 19, 29, 11	10.5	6.9	18.2	
Immunologic Total; Week 96; n= 16, 30, 11	12.5	13.3	18.2	
Immunologic Total; Week 104; n= 17, 28, 12	11.8	17.9	16.7	
Hematologic Total; Week 4; n= 59, 115, 40	5.1	3.5	5.0	
Hematologic Total; Week 8; n= 52, 109, 38	3.8	5.5	0	
Hematologic Total; Week 12; n= 55, 110, 38	1.8	4.5	10.5	
Hematologic Total; Week 16; n=54, 107, 34	1.9	2.8	2.9	
Hematologic Total; Week 20; n= 54, 108, 40	5.6	5.6	5.0	
Hematologic Total; Week 24; n= 53, 111, 37	3.8	2.7	2.7	
Hematologic Total; Week 26; n= 53, 101, 37	9.4	5.0	10.8	
Hematologic Total; Week 28; n= 52, 106, 39	7.7	3.8	5.1	
Hematologic Total; Week 32; n=52, 110, 38	0	4.5	7.9	
Hematologic Total; Week 36; n= 53, 109, 40	5.7	6.4	2.5	
Hematologic Total; Week 40; n= 51, 108, 37	0	10.2	5.4	
Hematologic Total; Week 44; n=53, 107, 38	7.5	6.5	5.3	
Hematologic Total; Week 48; n=51, 105, 35	5.9	4.8	0	
Hematologic Total; Week 52; n= 53, 103, 37	3.8	3.9	2.7	
Hematologic Total; Week 60; n=53, 101, 35	9.4	5.0	5.7	
Hematologic Total; Week 64; n=54, 98, 32	11.1	5.1	6.3	
Hematologic Total; Week 72; n= 47,96, 29	10.6	5.2	3.4	
Hematologic Total; Week 80; n= 45, 94, 35	0	4.3	5.7	

Hematologic Total; Week 88; n= 46, 88, 32	10.9	9.1	3.1	
Hematologic Total; Week 96; n= 45, 90, 32	4.4	4.4	3.1	
Hematologic Total; Week 104; n= 46, 94, 32	4.3	6.4	6.3	

Notes:

[49] - Modified Intent-to-Treat (MITT) Population

[50] - Modified Intent-to-Treat (MITT) Population

[51] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Physician Global Assessment (PGA) by visits

End point title	Change from Baseline in Physician Global Assessment (PGA) by visits

End point description:

The Physician's Global Assessment (PGA) was a physician-reported visual analogue scale that provides an overall measure of the participant's current disease activity. Physician's Global Assessment was collected on a 10 centimeter (cm) visual analogue scale (VAS) by placing a mark on the scale between 0 (no disease activity) to 10 (maximum disease activity). The PGA score was then rescaled for reporting by multiplying the collected score by 3 divided by 10. Hence, the PGA score ranges from 0 to 3 with higher scores indicating greater disease activity. Baseline value was the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was defined as the post-dose visit value minus Baseline value. Only those participants with data available at specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 4, 8, 12, 16, 20, 24, 26, 28, 32, 36, 40, 44, 48, 52, 60, 64, 72, 80, 88, 96, 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[52]	144[53]	47[54]	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 4; n=72, 142, 45	-0.285 (± 0.4816)	-0.247 (± 0.4640)	-0.303 (± 0.5464)	
Week 8; n=66, 135, 44	-0.535 (± 0.5134)	-0.520 (± 0.5243)	-0.585 (± 0.5793)	
Week 12; n=66, 137, 44	-0.592 (± 0.5265)	-0.660 (± 0.5776)	-0.654 (± 0.5450)	
Week 16; n=68, 132, 44	-0.619 (± 0.5475)	-0.717 (± 0.5802)	-0.759 (± 0.6072)	
Week 20; n=66, 130, 44	-0.697 (± 0.6157)	-0.787 (± 0.5445)	-0.786 (± 0.6772)	
Week 24; n=62, 130, 43	-0.770 (± 0.5888)	-0.766 (± 0.5059)	-0.965 (± 0.6413)	
Week 26; n=62, 120, 40	-0.786 (± 0.5727)	-0.811 (± 0.5445)	-0.929 (± 0.6631)	
Week 28; n=63, 127, 43	-0.781 (± 0.5395)	-0.817 (± 0.5360)	-0.980 (± 0.6286)	

Week 32; n=62, 124, 43	-0.851 (± 0.5989)	-0.864 (± 0.5519)	-1.005 (± 0.6723)	
Week 36; n=64, 126, 43	-0.916 (± 0.6141)	-0.927 (± 0.5400)	-0.917 (± 0.5504)	
Week 40; n=63, 126, 43	-0.893 (± 0.6157)	-0.925 (± 0.5621)	-0.993 (± 0.6711)	
Week 44; n=63, 124, 43	-0.800 (± 0.6764)	-0.905 (± 0.5289)	-0.970 (± 0.6065)	
Week 48; n=59, 121, 40	-0.885 (± 0.6178)	-0.928 (± 0.5627)	-0.956 (± 0.5175)	
Week 52; n=64, 122, 41	-0.947 (± 0.6918)	-0.938 (± 0.6125)	-1.004 (± 0.5527)	
Week 60; n=61, 120, 37	-0.836 (± 0.6982)	-0.848 (± 0.6085)	-1.206 (± 0.5917)	
Week 64; n=62, 120, 36	-0.876 (± 0.6971)	-0.943 (± 0.5711)	-1.095 (± 0.6365)	
Week 72; n=58, 110, 33	-0.928 (± 0.6838)	-0.944 (± 0.5708)	-1.047 (± 0.6088)	
Week 80; n=57, 112, 37	-0.949 (± 0.6909)	-0.954 (± 0.6221)	-1.138 (± 0.5574)	
Week 88; n=59, 109, 36	-1.060 (± 0.6307)	-0.993 (± 0.5733)	-1.140 (± 0.5514)	
Week 96; n=54, 109, 35	-1.016 (± 0.6093)	-0.994 (± 0.5669)	-1.214 (± 0.5580)	
Week 104; n=55, 114, 36	-1.052 (± 0.5095)	-1.074 (± 0.5166)	-1.085 (± 0.5987)	

Notes:

[52] - Modified Intent-to-Treat (MITT) Population

[53] - Modified Intent-to-Treat (MITT) Population

[54] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Systemic Lupus International Collaborating Clinics (SLICC) -American College of Rheumatology (ACR) damage index worsening compared with Baseline at Week 52 and Week 104

End point title	Percentage of participants with Systemic Lupus International Collaborating Clinics (SLICC) -American College of Rheumatology (ACR) damage index worsening compared with Baseline at Week 52 and Week 104

End point description:

The SLICC-ACR Damage Index measures irreversible (not related to active inflammation) changes occurring since the diagnosis of SLE ascertained by clinical assessment and present for at least 6 months. The questionnaire contains 39 items covering 12 different organ systems which were scored on a numerical scale between 0 (no damage) to 7 (increasing disease damage). Individual ranges for organ systems were; ocular: 0-2, neuropsychiatric: 0-6, renal: 0-3, pulmonary: 0-5, cardiovascular:0-6, peripheral vascular: 0-5, gastrointestinal:0-5, musculoskeletal: 0-6, skin: 0-3, endocrine (diabetes): 0-1, gonadal:0-1 and malignancies: 0-2. The SLICC-ACR score was calculated by taking sum of the individual scores for 12 organ systems which ranges from 0 (no damage) to 45 (increasing disease damage) where higher score indicates increasing disease damage severity. Baseline value was the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 52 and Week 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[55]	144[56]	47[57]	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 52	1.4 (0 to 4.1)	2.1 (0 to 4.4)	2.1 (0 to 6.3)	
Week 104	5.6 (0.3 to 10.8)	5.6 (1.8 to 9.3)	6.4 (0 to 13.4)	

Notes:

[55] - Modified Intent-to-Treat (MITT) Population

[56] - Modified Intent-to-Treat (MITT) Population

[57] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

Statistical analysis title	Stastistical Analysis 1

Statistical analysis description:

Odds ratio at Week 52 was calculated using Logistic regression model with covariates:Baseline SLEDAI-2K,Baseline immunosuppressant,Baseline prednisone equivalent dose and treatment group. Belimumab+ Standard therapy arm was excluded from the model.

Comparison groups	Belimumab + Placebo v Belimumab + Rituximab
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7102 [58]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	15.7

Notes:

[58] - Week 52

Statistical analysis title	Stastistical Analysis 2

Statistical analysis description:

Odds ratio at Week 52 was calculated using Logistic regression model with covariates:Baseline SLEDAI-2K,Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Placebo arm was excluded from the model.

Comparison groups	Belimumab + Rituximab v Belimumab + Standard therapy
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	10.71

Statistical analysis title	Stastistical Analysis 3

Statistical analysis description:

Odds ratio at Week 104 was calculated using Logistic regression model with covariates:Baseline SLEDAI-2K,Baseline immunosuppressant,Baseline prednisone equivalent dose and treatment group. Belimumab + Standard therapy arm was excluded from the model.

Comparison groups	Belimumab + Placebo v Belimumab + Rituximab
Number of subjects included in analysis	216
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8641 [59]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	3.15

Notes:

[59] - Week 104

Statistical analysis title	Stastistical Analysis 4

Statistical analysis description:

Odds ratio at Week 104 was calculated using Logistic regression model with covariates:Baseline SLEDAI-2K,Baseline immunosuppressant,Baseline prednisone equivalent dose and treatment group. Belimumab + Placebo arm was excluded from the model.

Comparison groups	Belimumab + Rituximab v Belimumab + Standard therapy
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	5.64

Secondary: Percentage of participants that met the Lupus Low Disease Activity State (LLDAS) response criteria by visits (PI assessed)

End point title	Percentage of participants that met the Lupus Low Disease Activity State (LLDAS) response criteria by visits (PI assessed)

End point description:

Lupus low disease activity state (LLDAS) was defined as a state which, if sustained, was associated with a low likelihood of adverse outcome, considering disease activity and medication safety. The LLDAS response criteria were: (1) SLEDAI-2K <=4, with no activity in major organ systems (renal, CNS, cardiopulmonary, vasculitis, fever) and no hemolytic anemia or gastrointestinal activity; (2) no new

features of lupus disease activity compared with the previous assessment; (3) PGA (scale 0-3), <=1; (4) current prednisolone (or equivalent) dose <=7.5 mg daily; and (5) well tolerated standard maintenance doses of immunosuppressive drugs and approved biological agents, excluding investigational drugs. Percentage of participants that met the LLDAS response criteria were reported. 99999 indicates that data was not available as there was no participant who met the LLDAS response criteria. Hence, 95% CI could not be calculated.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 16, 20, 24, 26, 28, 32, 36, 40, 44, 48, 52, 60, 64, 72, 80, 88, 96 and 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[60]	144[61]	47[62]	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	0 (-9999 to 9999)	2.1 (0 to 4.4)	2.1 (0 to 6.3)	
Week 8	9.7 (2.9 to 16.6)	1.4 (0 to 3.3)	10.6 (1.8 to 19.5)	
Week 12	8.3 (1.9 to 14.7)	9.7 (4.9 to 14.6)	6.4 (0 to 13.4)	
Week 16	11.1 (3.9 to 18.4)	16.7 (10.6 to 22.8)	19.1 (7.9 to 30.4)	
Week 20	11.1 (3.9 to 18.4)	25.7 (18.6 to 32.8)	19.1 (7.9 to 30.4)	
Week 24	12.5 (4.9 to 20.1)	22.2 (15.4 to 29.0)	36.2 (22.4 to 49.9)	
Week 26	22.2 (12.6 to 31.8)	25.7 (18.6 to 32.8)	34.0 (20.5 to 47.6)	
Week 28	20.8 (11.5 to 30.2)	25.0 (17.9 to 32.1)	34.0 (20.5 to 47.6)	
Week 32	29.2 (18.7 to 39.7)	31.9 (24.3 to 39.6)	36.2 (22.4 to 49.9)	
Week 36	30.6 (19.9 to 41.2)	34.0 (26.3 to 41.8)	29.8 (16.7 to 42.9)	
Week 40	22.2 (12.6 to 31.8)	33.3 (25.6 to 41.0)	38.3 (24.4 to 52.2)	
Week 44	30.6 (19.9 to 41.2)	37.5 (29.6 to 45.4)	31.9 (18.6 to 45.2)	
Week 48	26.4 (16.2 to 36.6)	37.5 (29.6 to 45.4)	31.9 (18.6 to 45.2)	
Week 52	27.8 (17.4 to 38.1)	34.0 (26.3 to 41.8)	29.8 (16.7 to 42.9)	
Week 60	26.4 (16.2 to 36.6)	23.6 (16.7 to 30.5)	36.2 (22.4 to 49.9)	
Week 64	20.8 (11.5 to 30.2)	30.6 (23.0 to 38.1)	31.9 (18.6 to 45.2)	
Week 72	22.2 (12.6 to 31.8)	31.3 (23.7 to 38.8)	31.9 (18.6 to 45.2)	
Week 80	18.1 (9.2 to 26.9)	26.4 (19.2 to 33.6)	34.0 (20.5 to 47.6)	
Week 88	23.6 (13.8 to 33.4)	24.3 (17.3 to 31.3)	29.8 (16.7 to 42.9)	
Week 96	20.8 (11.5 to 30.2)	30.6 (23.0 to 38.1)	36.2 (22.4 to 49.9)	

Week 104	20.8 (11.5 to 30.2)	32.6 (25.0 to 40.3)	38.3 (24.4 to 52.2)	

Notes:

[60] - Modified Intent-to-Treat (MITT) Population

[61] - Modified Intent-to-Treat (MITT) Population

[62] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a state of disease control using the PI assessment of SLEDAI-2K by visit

End point title	Percentage of participants with a state of disease control using the PI assessment of SLEDAI-2K by visit

End point description:

Percentage of participants with a state of disease control was defined as the percentage of participants with a SLEDAI-2K score <=2, achieved without immunosuppressants and with corticosteroids at a prednisone equivalent dose of <=5 mg/day, using the PI assessment of SLEDAI-2K. SLEDAI-2K consisted of 24 individual items within each of 9 organ systems. Each item was given a weighted score (1 to 8, higher score indicates increased activity) and summed if present at the time of visit or in preceding 10 days. SLEDAI-2K score was the sum of all 24 individual items from SLEDAI-2K, ranges from 0 (no symptoms) to 105 (presence of all defined symptoms), higher scores representing increased disease activity. Percentage of participants with a state of disease control using the PI assessment of SLEDAI-2K were summarized.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 16, 20, 24, 26, 28, 32, 36, 40, 44, 48, 52, 60, 64, 72, 80, 88, 96, 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[63]	144[64]	47[65]	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	2.8 (0 to 6.6)	3.5 (0.5 to 6.5)	8.5 (0.5 to 16.5)	
Week 8	13.9 (5.9 to 21.9)	9.0 (4.3 to 13.7)	21.3 (9.6 to 33.0)	
Week 12	11.1 (3.9 to 18.4)	12.5 (7.1 to 17.9)	19.1 (7.9 to 30.4)	
Week 16	15.3 (7.0 to 23.6)	22.2 (15.4 to 29.0)	29.8 (16.7 to 42.9)	
Week 20	13.9 (5.9 to 21.9)	24.3 (17.3 to 31.3)	31.9 (18.6 to 45.2)	
Week 24	18.1 (9.2 to 26.9)	25.0 (17.9 to 32.1)	34.0 (20.5 to 47.6)	
Week 26	15.3 (7.0 to 23.6)	25.7 (18.6 to 32.8)	25.5 (13.1 to 38.0)	
Week 28	11.1 (3.9 to 18.4)	25.7 (18.6 to 32.8)	36.2 (22.4 to 49.9)	
Week 32	15.3 (7.0 to 23.6)	28.5 (21.1 to 35.8)	31.9 (18.6 to 45.2)	
Week 36	19.4 (10.3 to 28.6)	27.8 (20.5 to 35.1)	27.7 (14.9 to 40.4)	

Week 40	16.7 (8.1 to 25.3)	24.3 (17.3 to 31.3)	23.4 (11.3 to 35.5)	
Week 44	18.1 (9.2 to 26.9)	26.4 (19.2 to 33.6)	27.7 (14.9 to 40.4)	
Week 48	18.1 (9.2 to 26.9)	26.4 (19.2 to 33.6)	27.7 (14.9 to 40.4)	
Week 52	19.4 (10.3 to 28.6)	20.1 (13.6 to 26.7)	27.7 (14.9 to 40.4)	
Week 60	18.1 (9.2 to 26.9)	20.8 (14.2 to 27.5)	23.4 (11.3 to 35.5)	
Week 64	11.1 (3.9 to 18.4)	18.1 (11.8 to 24.3)	27.7 (14.9 to 40.4)	
Week 72	9.7 (2.9 to 16.6)	12.5 (7.1 to 17.9)	23.4 (11.3 to 35.5)	
Week 80	8.3 (1.9 to 14.7)	13.2 (7.7 to 18.7)	31.9 (18.6 to 45.2)	
Week 88	11.1 (3.9 to 18.4)	9.7 (4.9 to 14.6)	21.3 (9.6 to 33.0)	
Week 96	8.3 (1.9 to 14.7)	12.5 (7.1 to 17.9)	31.9 (18.6 to 45.2)	
Week 104	8.3 (1.9 to 14.7)	11.8 (6.5 to 17.1)	23.4 (11.3 to 35.5)	

Notes:

[63] - Modified Intent-to-Treat (MITT) Population

[64] - Modified Intent-to-Treat (MITT) Population

[65] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a state of clinical remission using the PI assessment of SLEDAI-2K by visit

End point title	Percentage of participants with a state of clinical remission using the PI assessment of SLEDAI-2K by visit

End point description:

Percentage of participants with a state of clinical remission was defined as the percentage of participants with a clinical SLEDAI-2K score =0 (does not include anti-dsDNA and complement activity scores), achieved without immunosuppressants (which was allowed in Belimumab+ Standard therapy arm only) and with corticosteroids at a prednisone equivalent dose of 0 mg/day using the PI assessment of SLEDAI-2K. SLEDAI-2K consisted of 24 individual items within each of 9 organ systems. Each item was given a weighted score (1 to 8, higher score indicates increased activity) and summed if present at the time of visit or in preceding 10 days. The clinical SLEDAI-2K score was sum of 22 out of all 24 individual items from the SLEDAI-2K and ranges from 0 (no symptoms) to 101 (presence of all defined symptoms) with higher scores representing increased disease activity. Percentage of participants with a state of clinical remission using the PI assessment of SLEDAI-2K were summarized.

End point type	Secondary

End point timeframe:

Weeks 60, 64, 72, 80, 88, 96 and 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[66]	144[67]	47[68]	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 60	6.9 (1.1 to 12.8)	3.5 (0.5 to 6.5)	10.6 (1.8 to 19.5)	
Week 64	6.9 (1.1 to 12.8)	5.6 (1.8 to 9.3)	10.6 (1.8 to 19.5)	
Week 72	6.9 (1.1 to 12.8)	3.5 (0.5 to 6.5)	14.9 (4.7 to 25.1)	
Week 80	6.9 (1.1 to 12.8)	4.2 (0.9 to 7.4)	14.9 (4.7 to 25.1)	
Week 88	6.9 (1.1 to 12.8)	2.1 (0 to 4.4)	14.9 (4.7 to 25.1)	
Week 96	4.2 (0 to 8.8)	4.2 (0.9 to 7.4)	12.8 (3.2 to 22.3)	
Week 104	2.8 (0 to 6.6)	3.5 (0.5 to 6.5)	6.4 (0 to 13.4)	

Notes:

[66] - Modified Intent-to-Treat (MITT) Population

[67] - Modified Intent-to-Treat (MITT) Population

[68] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with serious adverse events (SAE) and non-serious AE (non-SAE)

End point title	Number of participants with serious adverse events (SAE) and non-serious AE (non-SAE)

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study treatment, whether or not considered related to the study treatment. A SAE is defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, is a congenital anomaly/birth defect or any other situations as per medical or scientific judgment. Data for number of participants with SAE and non-SAE (>=5 %) has been summarized. Intent-to-Treat Population comprised of all randomized participants who received at least one dose of study treatment (Belimumab or Rituximab or Placebo).

End point type	Secondary

End point timeframe:

Up to Week 111 (including 8 weeks of safety follow-up)

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[69]	144[70]	76[71]	
Units: Participants				
SAE	10	32	15	
non-SAE	48	109	53	

Notes:

[69] - Intent-to-Treat Population

[70] - Intent-to-Treat Population

[71] - Intent-to-Treat Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events of special interest (AESIs)

End point title	Number of participants with adverse events of special interest (AESIs)

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study treatment, whether or not considered related to the study treatment. AESIs were Malignant Neoplasms, Post-Injection Systemic Reactions (PISR), All Infections of Special Interest (Opportunistic Infections (OI), Herpes Zoster (HZ), Tuberculosis (TB), and Sepsis), Depression (including mood disorders and anxiety)/suicide/self-injury and Deaths. Data for number of participants with AESIs has been summarized.

End point type	Secondary

End point timeframe:

Up to Week 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[72]	144[73]	76[74]	
Units: Participants				
Malignant Neoplasms	1	1	1	
PISR	7	19	4	
All Infections of Special Interest	5	12	5	
Depression/suicide/self-injury	9	16	5	
Deaths	1	2	0	

Notes:

[72] - InIntent-to-Treat Population

[73] - Intent-to-Treat Population

[74] - Intent-to-Treat Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient Global Assessment (PtGA) by visits

End point title	Change from Baseline in Patient Global Assessment (PtGA) by visits

End point description:

The Patient's Global Assessment (PtGA) of Disease Activity is a single-item, participant reported scale developed for the assessment of the participant’s overall rating of their disease activity due to SLE. The scale measures disease activity ranging from 0 (Very Well) to 10 (Very Poor) and the higher score indicates severe disease activity. Baseline value was the latest pre-dose assessment with a non-missing

value, including those from unscheduled visits. Change from Baseline was defined as the post-dose visit value minus Baseline value. Only those participants with data available at specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 8, 12, 26, 40, 52, 64, 72 and 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[75]	144[76]	47[77]	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 8; n=66, 132, 44	-0.96 (± 2.751)	-1.06 (± 2.141)	-0.91 (± 2.848)	
Week 12; n=66, 133, 44	-0.69 (± 2.237)	-1.07 (± 2.290)	-1.57 (± 2.756)	
Week 26; n=61, 115, 40	-0.95 (± 2.765)	-1.50 (± 2.596)	-1.57 (± 2.450)	
Week 40; n=63, 123, 43	-1.77 (± 2.624)	-1.60 (± 2.809)	-1.67 (± 2.962)	
Week 52; n=64, 120, 41	-1.74 (± 2.752)	-1.82 (± 2.631)	-1.84 (± 3.228)	
Week 64; n=62, 117, 36	-1.41 (± 2.985)	-1.96 (± 2.595)	-1.96 (± 3.034)	
Week 72; n=59, 107, 33	-1.46 (± 3.209)	-1.81 (± 2.609)	-1.43 (± 3.487)	
Week 104; n=55, 111, 36	-1.61 (± 2.589)	-2.00 (± 2.739)	-1.98 (± 2.895)	

Notes:

[75] - Modified Intent-to-Treat (MITT) Population

[76] - Modified Intent-to-Treat (MITT) Population

[77] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Lupus Quality of Life (LupusQoL) domain scores by visit

End point title	Change from Baseline in Lupus Quality of Life (LupusQoL) domain scores by visit

End point description:

LupusQoL is a SLE-specific health related qualify of life (HRQOL) instrument with 34 questions across 8 domains:Physical health(8 items),Pain(3 items),Planning(3 items),Intimate relationship(2 items),Burden to others(3 items),Emotional health(6 items),Body image(5 items),Fatigue(4 items)..A 5-point Likert response format was used, ranging from 0(all of the time) to 4(never) for each question. Individual domain scores were reported which were calculated by taking sum of responses to all items within each domain. Individual domain scores range:Physical health(0-32),Pain(0-12),Planning(0-12),Intimate relationship(0-8),Burden to others(0-12),Emotional health(0-24),Body image(0-20),Fatigue(0-16).Higher score indicates better HRQOL. Change from Baseline was defined as post-dose visit value minus Baseline value. Only those participants with data available at specified time points were analyzed(represented by n=X in category titles).

End point type	Secondary

End point timeframe:
Baseline (Day 1) and Weeks 8, 12, 26, 40, 52, 64, 72 and 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[78]	144[79]	47[80]	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Physical health; Week 8; n=66, 132, 44	3.0 (± 15.20)	6.0 (± 15.08)	6.3 (± 18.79)	
Physical health; Week 12; n=66, 133, 44	3.5 (± 16.60)	5.8 (± 17.15)	6.4 (± 20.06)	
Physical health; Week 26; n=61, 115, 40	3.3 (± 18.74)	10.5 (± 17.27)	11.6 (± 19.19)	
Physical health; Week 40; n=63, 122, 43	8.5 (± 19.53)	9.5 (± 19.29)	8.2 (± 19.46)	
Physical health; Week 52; n=64, 120, 41	8.1 (± 19.90)	10.0 (± 20.16)	11.6 (± 19.53)	
Physical health; Week 64; n=62, 117, 36	5.8 (± 18.66)	10.2 (± 18.60)	9.5 (± 21.74)	
Physical health; Week 72; n=59, 107, 33	7.0 (± 21.13)	9.1 (± 18.84)	8.5 (± 22.59)	
Physical health; Week 104; n=55, 111, 36	6.2 (± 20.19)	10.6 (± 19.96)	7.2 (± 23.33)	
Pain; Week 8; n=66, 132, 44	5.8 (± 19.67)	11.4 (± 18.55)	10.4 (± 21.87)	
Pain; Week 12; n=66, 133, 44	7.5 (± 19.78)	13.0 (± 20.81)	6.1 (± 28.44)	
Pain; Week 26; n=61, 115, 40	7.0 (± 22.42)	17.2 (± 21.54)	13.1 (± 22.79)	
Pain; Week 40; n=63, 122, 43	12.3 (± 23.18)	18.0 (± 22.70)	12.6 (± 29.17)	
Pain; Week 52; n=64, 120, 41	13.9 (± 24.26)	17.6 (± 23.62)	15.7 (± 27.34)	
Pain; Week 64; n=62, 117, 36	10.2 (± 21.89)	17.4 (± 23.59)	13.2 (± 26.90)	
Pain; Week 72; n=59, 107, 33	13.1 (± 24.91)	17.0 (± 22.66)	11.9 (± 29.02)	
Pain; Week 104; n=55, 111, 36	13.8 (± 25.82)	19.0 (± 22.59)	12.5 (± 27.92)	
Planning; Week 8; n=66, 132, 44	3.4 (± 19.77)	8.0 (± 18.21)	10.0 (± 27.88)	
Planning; Week 12; n=66, 133, 44	4.5 (± 23.03)	7.6 (± 20.15)	7.8 (± 27.81)	
Planning; Week 26; n=61, 115, 40	3.4 (± 25.20)	9.9 (± 21.28)	12.1 (± 27.86)	
Planning; Week 40; n=63, 122, 43	11.6 (± 29.08)	12.2 (± 22.30)	10.7 (± 26.62)	
Planning; Week 52; n=64, 120, 41	11.6 (± 28.66)	12.6 (± 23.89)	14.0 (± 28.35)	
Planning; Week 64; n=62, 117, 36	7.8 (± 24.42)	14.5 (± 23.65)	7.2 (± 30.55)	
Planning; Week 72; n=59, 107, 33	9.2 (± 30.78)	11.4 (± 20.97)	6.6 (± 31.02)	
Planning; Week 104; n=55, 111, 36	12.1 (± 30.76)	14.2 (± 20.77)	8.8 (± 34.96)	
Intimate relationship; Week 8; n=51, 110, 36	-1.2 (± 21.83)	5.2 (± 20.63)	7.6 (± 19.66)	
Intimate relationship; Week 12; n=52, 106, 36	-2.6 (± 25.16)	4.6 (± 23.42)	7.6 (± 27.10)	
Intimate relationship; Week 26; n=48, 86, 30	-1.3 (± 29.20)	8.9 (± 24.32)	14.2 (± 28.38)	
Intimate relationship; Week 40; n=50, 94, 30	4.3 (± 28.75)	7.7 (± 25.01)	15.8 (± 30.43)	
Intimate relationship; Week 52; n=51, 91, 30	4.7 (± 29.36)	6.6 (± 22.54)	15.8 (± 30.78)	
Intimate relationship; Week 64; n=47, 90, 25	-4.5 (± 28.00)	11.0 (± 25.41)	12.5 (± 29.76)	

Intimate relationship; Week 72; n=42, 83, 21	0.0 (± 31.60)	8.6 (± 23.82)	5.4 (± 39.44)	
Intimate relationship; Week 104; n=40, 85,27	-0.3 (± 23.93)	11.2 (± 25.59)	4.6 (± 35.21)	
Burden to others; Week 8; n=66, 132, 44	7.3 (± 22.95)	6.8 (± 20.56)	10.6 (± 23.46)	
Burden to others; Week 12; n=66, 133, 44	11.4 (± 27.91)	8.4 (± 23.65)	6.4 (± 29.90)	
Burden to others; Week 26; n=61, 115, 40	8.7 (± 26.68)	10.5 (± 27.42)	7.5 (± 27.66)	
Burden to others; Week 40; n=63, 122, 43	13.9 (± 27.23)	12.6 (± 26.94)	12.0 (± 27.66)	
Burden to others; Week 52; n=64, 120, 41	16.5 (± 29.15)	14.9 (± 27.03)	15.0 (± 33.40)	
Burden to others; Week 64; n=62, 117, 36	14.4 (± 28.83)	17.0 (± 26.67)	12.3 (± 28.21)	
Burden to others; Week 72; n=59, 107, 33	17.1 (± 28.68)	14.4 (± 28.77)	11.1 (± 27.85)	
Burden to others; Week 104; n=55, 111, 36	18.9 (± 25.93)	15.0 (± 29.25)	12.7 (± 33.42)	
Emotional health; Week 8; n=66, 132, 44	5.2 (± 18.33)	6.4 (± 16.87)	11.6 (± 20.55)	
Emotional health; Week 12; n=66, 133, 44	8.1 (± 17.32)	4.5 (± 19.67)	9.1 (± 23.87)	
Emotional health; Week 26; n=61,115, 40	7.7 (± 19.84)	6.7 (± 17.35)	10.1 (± 18.12)	
Emotional health; Week 40; n=63, 122, 43	9.7 (± 21.44)	6.7 (± 20.85)	9.4 (± 22.20)	
Emotional health; Week 52; n=64, 120, 41	10.2 (± 21.48)	7.8 (± 20.63)	11.4 (± 21.99)	
Emotional health; Week 64; n=62, 117, 36	8.1 (± 20.75)	9.3 (± 20.73)	8.1 (± 22.11)	
Emotional health; Week 72; n=59, 107, 33	8.8 (± 21.39)	6.2 (± 19.05)	6.6 (± 21.80)	
Emotional health; Week 104; n=55, 111, 36	6.8 (± 20.20)	9.3 (± 19.67)	10.5 (± 23.00)	
Body image; Week 8; n=60, 114, 37	5.7 (± 19.57)	8.9 (± 19.26)	5.7 (± 25.05)	
Body image; Week 12; n=58, 118, 39	1.9 (± 23.23)	10.1 (± 20.73)	5.9 (± 26.89)	
Body image; Week 26; n=56, 96, 33	5.8 (± 20.62)	9.0 (± 25.03)	5.7 (± 23.07)	
Body image; Week 40; n=54, 103, 35	8.9 (± 25.42)	8.2 (± 24.82)	5.1 (± 22.07)	
Body image; Week 52; n=55, 101, 33	7.9 (± 25.77)	9.1 (± 24.07)	10.3 (± 25.24)	
Body image; Week 64; n=52, 98, 27	6.0 (± 22.51)	11.3 (± 23.08)	7.7 (± 23.98)	
Body image; Week 72; n=44, 93, 25	7.8 (± 26.74)	8.7 (± 24.91)	2.5 (± 29.28)	
Body image; Week 104; n=48, 94, 28	4.4 (± 26.62)	11.4 (± 25.65)	3.5 (± 27.40)	
Fatigue; Week 8; n=66,132, 44	9.8 (± 17.02)	9.2 (± 18.40)	8.5 (± 24.30)	
Fatigue; Week 12; n=66, 133, 44	8.2 (± 18.48)	7.0 (± 17.96)	10.4 (± 28.11)	
Fatigue; Week 26; n=61, 115, 40	8.6 (± 20.23)	11.4 (± 20.12)	11.9 (± 20.21)	
Fatigue; Week 40; n=63, 122, 43	11.9 (± 22.33)	10.3 (± 22.41)	11.3 (± 24.75)	
Fatigue; Week 52; n=64, 120, 41	14.2 (± 21.17)	12.0 (± 20.95)	16.6 (± 25.30)	
Fatigue; Week 64; n=62, 117, 36	10.5 (± 21.94)	14.0 (± 20.35)	10.8 (± 25.21)	
Fatigue; Week 72; n=59, 107, 33	12.1 (± 22.74)	13.1 (± 18.31)	11.6 (± 25.87)	
Fatigue; Week 104; n=55, 111, 36	9.4 (± 20.41)	14.3 (± 20.18)	9.7 (± 24.25)	

Notes:

[78] - Modified Intent-to-Treat (MITT) Population

[79] - Modified Intent-to-Treat (MITT) Population

[80] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score by visit

End point title	Change from Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score by visit

End point description:

The FACIT-Fatigue scale was a 13-item questionnaire completed by the participant, which provides a measure of fatigue/quality of life, with a 7-day recall period. The participant scored each item on a 5-point scale: 0 (Not at all) to 4 (Very much). The higher score for the questions, the greater the fatigue. The total score was the sum of the responses from all questions (inverted for reversed items) multiplied by 13, then divided by the number of questions answered, ranging from 0 (worse fatigue) to 52 (no fatigue) where a higher score indicates an improvement in the participant's health status and decrease in the score indicates worse fatigue/quality of life. Baseline value was the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was defined as the post-dose visit value minus Baseline value. Only those participants with data available at specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 8, 12, 26, 40, 52, 64, 72 and 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[81]	144[82]	47[83]	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 8; n=66, 132, 44	4.2 (± 9.84)	4.6 (± 8.84)	4.8 (± 8.25)	
Week 12; n=66, 133, 44	4.7 (± 9.50)	4.0 (± 9.86)	3.8 (± 10.94)	
Week 26; n=61, 115, 40	3.1 (± 10.08)	5.4 (± 9.17)	4.1 (± 8.54)	
Week 40; n=63, 122, 43	6.0 (± 10.18)	5.2 (± 10.80)	5.2 (± 10.14)	
Week 52; n=64, 120, 41	6.5 (± 10.12)	6.1 (± 10.84)	5.1 (± 10.51)	
Week 64;n=62, 117, 36	4.9 (± 10.61)	6.2 (± 9.72)	4.6 (± 10.32)	
Week 72; n=59, 107, 33	5.6 (± 10.21)	5.2 (± 10.31)	2.9 (± 12.75)	
Week 104; n=55, 111, 36	5.7 (± 9.07)	7.1 (± 11.50)	3.1 (± 10.30)	

Notes:

[81] - Modified Intent-to-Treat (MITT) Population

[82] - Modified Intent-to-Treat (MITT) Population

[83] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with improvement in FACIT-Fatigue score exceeding the Minimal Clinically Important Difference (MCID, greater than or equal to [>=]4)

End point title	Percentage of participants with improvement in FACIT-Fatigue score exceeding the Minimal Clinically Important Difference (MCID, greater than or equal to [>=]4)

End point description:

The FACIT-Fatigue scale was a 13-item questionnaire completed by the participant, which provides a measure of fatigue/quality of life, with a 7-day recall period. The participant scored each item on a 5-point scale: 0 (Not at all) to 4 (Very much). The larger the participant's response to the questions, the greater the fatigue. The total score was the sum of the responses (inverted for reversed items) multiplied by 13, then divided by the number of questions answered, ranging from 0 (worse fatigue) to 52 (no fatigue) where a higher score indicates an improvement in the participant's health status and decrease in the score indicates worse fatigue/quality of life. A participant was considered to had an improvement exceeding the minimal clinically important difference if they had >=4 points improvement in their FACIT-Fatigue Scale score from Baseline. Only those participants with data available at specified time points were analyzed (represented by n=X in category titles).

End point type	Secondary

End point timeframe:

Weeks 8, 12, 26, 40, 52, 64, 72 and 104

End point values	Belimumab + Placebo	Belimumab + Rituximab	Belimumab + Standard therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	72[84]	144[85]	47[86]	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 8; n=66, 132, 44	47.0 (34.9 to 59.0)	51.5 (43.0 to 60.0)	59.1 (44.6 to 73.6)	
Week 12; n=66, 133, 44	56.1 (44.1 to 68.0)	50.4 (41.9 to 58.9)	52.3 (37.5 to 67.0)	
Week 26; n=61, 115, 40	47.5 (35.0 to 60.1)	56.5 (47.5 to 65.6)	45.0 (29.6 to 60.4)	
Week 40; n=63, 122, 43	54.0 (41.7 to 66.3)	54.1 (45.3 to 62.9)	53.5 (38.6 to 68.4)	
Week 52; n=64, 120, 41	60.9 (49.0 to 72.9)	58.3 (49.5 to 67.2)	56.1 (40.9 to 71.3)	
Week 64; n=62, 117, 36	51.6 (39.2 to 64.1)	59.8 (50.9 to 68.7)	52.8 (36.5 to 69.1)	
Week 72; n=59, 107, 33	57.6 (45.0 to 70.2)	57.0 (47.6 to 66.4)	42.4 (25.6 to 59.3)	
Week 104; n=55, 111, 36	56.4 (43.3 to 69.5)	62.2 (53.1 to 71.2)	44.4 (28.2 to 60.7)	

Notes:

[84] - Modified Intent-to-Treat (MITT) Population

[85] - Modified Intent-to-Treat (MITT) Population

[86] - Modified Intent-to-Treat (MITT) Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality, serious adverse events (SAEs) and non-SAEs were collected up to Week 111 (including 8 weeks of safety follow-up).

Adverse event reporting additional description:

Intent-To-Treat (ITT) Population was used to assess the all-cause mortality, SAEs and non-SAEs which comprised of all randomized participants who received at least one dose of study treatment (Belimumab or Rituximab or placebo) .

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Belimumab + Placebo

Reporting group description:

Participants received Belimumab 200 milligrams (mg) administered subcutaneously (SC) on Day 1 and then weekly (i.e., every 7 days) through Week 52. Participants also received rituximab-placebo administered by intravenous (IV) infusions at Weeks 4 and 6 in double blind manner. Participants received standard therapy excluding Immunosuppressants and including anti-malarials, non-steroidal anti-inflammatory drugs (NSAIDs), and/or corticosteroids tapered down to prednisone equivalent of less than or equal to (<= 5) mg/day until Week 104. Participants did not receive treatment after 52 weeks and were in observation until Week 104.

Reporting group title	Belimumab + Standard therapy

Reporting group description:

Participants received open-label Belimumab 200 mg administered SC on Day 1 and then weekly (i.e., every 7 days) until Week 104. Participants also received standard therapy including immunosuppressant, anti-malarials, NSAIDs, and/or corticosteroids tapered down to prednisone equivalent of <= 5 mg/day until Week 104.

Reporting group title	Belimumab + Rituximab

Reporting group description:

Participants received Belimumab 200 mg administered SC on Day 1 and then weekly (i.e., every 7 days) through Week 52. Participants also received rituximab 1000 mg administered by IV infusions at Weeks 4 and 6 in double blind manner. Participants received standard therapy excluding Immunosuppressants and including anti-malarials, NSAIDs, and/or corticosteroids tapered down to prednisone equivalent of <= 5 mg/day until Week 104.Participants did not receive treatment after 52 weeks and were in observation until Week 104.

Serious adverse events	Belimumab + Placebo	Belimumab + Standard therapy	Belimumab + Rituximab
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 72 (13.89%)	15 / 76 (19.74%)	32 / 144 (22.22%)
number of deaths (all causes)	1	0	2
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma stage 0			

subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangiocarcinoma			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vascular disorders			
Vasculitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	2 / 144 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jugular vein thrombosis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis superficial			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitis necrotising			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Immune system disorders			
Allergy to vaccine			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic reaction			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			

subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shrinking lung syndrome			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal behaviour			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adjustment disorder			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Poisoning deliberate			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuropericarditis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Hemiparesis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropsychiatric lupus			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperplasia of thymic epithelium			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenic purpura			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Ocular myasthenia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Volvulus			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pemphigoid			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurogenic bladder			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			

subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma muscle			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Urinary tract infection			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	2 / 144 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute sinusitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bartholinitis			

subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis viral			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Latent tuberculosis			

subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 76 (1.32%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 76 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord abscess			
subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			

subjects affected / exposed	0 / 72 (0.00%)	0 / 76 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Belimumab + Placebo	Belimumab + Standard therapy	Belimumab + Rituximab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 72 (66.67%)	53 / 76 (69.74%)	109 / 144 (75.69%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 72 (1.39%)	4 / 76 (5.26%)	7 / 144 (4.86%)
occurrences (all)	1	5	8
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 72 (18.06%)	8 / 76 (10.53%)	30 / 144 (20.83%)
occurrences (all)	13	14	44
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 72 (1.39%)	3 / 76 (3.95%)	10 / 144 (6.94%)
occurrences (all)	1	9	11
Chest pain			
subjects affected / exposed	1 / 72 (1.39%)	4 / 76 (5.26%)	6 / 144 (4.17%)
occurrences (all)	1	5	8
Fatigue			
subjects affected / exposed	5 / 72 (6.94%)	1 / 76 (1.32%)	5 / 144 (3.47%)
occurrences (all)	7	2	7
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 72 (2.78%)	4 / 76 (5.26%)	7 / 144 (4.86%)
occurrences (all)	2	4	9
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 72 (2.78%)	2 / 76 (2.63%)	18 / 144 (12.50%)
occurrences (all)	3	5	22
Diarrhoea			

subjects affected / exposed	6 / 72 (8.33%)	5 / 76 (6.58%)	6 / 144 (4.17%)
occurrences (all)	6	9	6
Vomiting			
subjects affected / exposed	2 / 72 (2.78%)	2 / 76 (2.63%)	11 / 144 (7.64%)
occurrences (all)	2	4	12
Abdominal pain upper			
subjects affected / exposed	5 / 72 (6.94%)	1 / 76 (1.32%)	7 / 144 (4.86%)
occurrences (all)	7	1	7
Abdominal pain			
subjects affected / exposed	2 / 72 (2.78%)	1 / 76 (1.32%)	9 / 144 (6.25%)
occurrences (all)	2	1	9
Dyspepsia			
subjects affected / exposed	0 / 72 (0.00%)	4 / 76 (5.26%)	4 / 144 (2.78%)
occurrences (all)	0	4	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 72 (5.56%)	4 / 76 (5.26%)	9 / 144 (6.25%)
occurrences (all)	4	4	9
Psychiatric disorders			
Depression			
subjects affected / exposed	2 / 72 (2.78%)	4 / 76 (5.26%)	6 / 144 (4.17%)
occurrences (all)	2	4	6
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 72 (6.94%)	10 / 76 (13.16%)	12 / 144 (8.33%)
occurrences (all)	5	13	13
Back pain			
subjects affected / exposed	4 / 72 (5.56%)	4 / 76 (5.26%)	8 / 144 (5.56%)
occurrences (all)	5	7	8
Systemic lupus erythematosus			
subjects affected / exposed	6 / 72 (8.33%)	2 / 76 (2.63%)	3 / 144 (2.08%)
occurrences (all)	9	2	3
Musculoskeletal chest pain			
subjects affected / exposed	1 / 72 (1.39%)	4 / 76 (5.26%)	2 / 144 (1.39%)
occurrences (all)	1	4	3
Infections and infestations			

Urinary tract infection			
subjects affected / exposed	12 / 72 (16.67%)	10 / 76 (13.16%)	23 / 144 (15.97%)
occurrences (all)	16	27	27
Nasopharyngitis			
subjects affected / exposed	9 / 72 (12.50%)	11 / 76 (14.47%)	23 / 144 (15.97%)
occurrences (all)	13	18	32
Upper respiratory tract infection			
subjects affected / exposed	5 / 72 (6.94%)	9 / 76 (11.84%)	22 / 144 (15.28%)
occurrences (all)	6	12	31
Bronchitis			
subjects affected / exposed	6 / 72 (8.33%)	7 / 76 (9.21%)	10 / 144 (6.94%)
occurrences (all)	6	7	10
Influenza			
subjects affected / exposed	9 / 72 (12.50%)	4 / 76 (5.26%)	4 / 144 (2.78%)
occurrences (all)	12	4	4
Oral herpes			
subjects affected / exposed	3 / 72 (4.17%)	3 / 76 (3.95%)	9 / 144 (6.25%)
occurrences (all)	6	7	13
Sinusitis			
subjects affected / exposed	4 / 72 (5.56%)	2 / 76 (2.63%)	7 / 144 (4.86%)
occurrences (all)	4	2	8
Pharyngitis			
subjects affected / exposed	1 / 72 (1.39%)	4 / 76 (5.26%)	4 / 144 (2.78%)
occurrences (all)	1	4	7

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 April 2017	Protocol Amendment 01: GlaxoSmithKline (GSK) received additional comments and feedback from European Medicines Agency (EMA) and Food and Drug Administration (FDA) and incorporated the recommendations in Amendment 1. In addition, further changes and updates were identified by the study team and incorporated in Amendment 1.
17 November 2018	Protocol Amendment 02: 1) To change the timing of the initial analysis from Study Week 64 to Study Week 52 to support an earlier submission to regulatory authorities, 2) Recruit additional 80 participants into the study to ensure adequate number of evaluable participants, and 3) provide clarification of changes and updates on wording related to study conduct.
15 August 2019	Protocol Amendment 03: 1) To define dosing interruptions based on neutrophil count, 2) Incorporate country-specific changes for South Korea, Germany and Argentina into Global Amendment 03 protocol, 3) define an modified Intent to Treat (MITT) Population for analysis, and 4) provide clarification of changes and updates on wording related to study conduct.
30 April 2020	Protocol Amendment 04: In response to the Coronavirus disease-2019 (COVID-19) pandemic, changes are being made in order to protect participant safety and data integrity. 1) Visit windows are being conditionally extended for all participant visits for the study. 2) Clarification that the independent blinded assessor can be called upon to perform the SLEDAI-2K (S2K) efficacy assessment at an unscheduled visit. 3) In the event that participants are unable to visit the site, it is acceptable for sites to supply investigational product (belimumab) to participants by shipment to the participant. 4) Clarification regarding acceptable use and dosage of antimalarial treatments (e.g. hydroxychloroquine). 5) Change to the language describing the timing of the primary analysis. 6) Recommendations for safety contact with participants in the event they cannot attend clinic visits. 7) Guidance for study treatment discontinuation if a participant has suspected or confirmed COVID-19 infection.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported