Clinical trial results:
A Randomized, Placebo-Controlled, Double-Blind Study to Evaluate the Efficacy, Safety, Tolerability, and Pharmacodynamics of Belimumab in Subjects with Generalized Myasthenia Gravis (MG).

Summary

EudraCT number	2011-002068-26
Trial protocol	DE IT
Global end of trial date	27 October 2015

Results information

Result version number	v3 (current)
This version publication date	01 January 2017
First version publication date	08 April 2016
Version creation reason	• Correction of full data set Corrections required per ctgov changes.

Trial information

Trial identification

Sponsor protocol code	BEL115123

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	GSK Response Center, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343, GlaxoSmithKline, +44 (0)208990 4466, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343, GlaxoSmithKline, +44 (0)208990 4466, 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 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 August 2015
Global end of trial reached?	Yes
Global end of trial date	27 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of belimumab in subjects with MG by testing the hypothesis that belimumab will be more effective than placebo in reducing signs of MG as measured by the Quantitative Myasthenia Gravis (QMG) score.

Protection of trial subjects:

N/A

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 April 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	United States: 19
Worldwide total number of subjects	40
EEA total number of subjects	12

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)	26
From 65 to 84 years	14

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants (par.) with myasthenia gravis (MG) and who were acetylcholine receptor (AChR) or muscle-specific kinase (MuSK) antibody positive, on current standard of care therapy and continued to exhibit signs of MG were eligible for participation in the study.

Pre-assignment

Screening details:

The study was conducted in 3 phases: a 4 week screening period, a 24 week Treatment (trt) Period, and a 12 week Follow-up period. A total of 40 par. were enrolled, however 1 par. withdrew due to MG exacerbation on Day 7 prior to the first efficacy assessment; therefore, 39 par. comprise the Intent-to-Treat (ITT) Population.

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, Monitor, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo IV

Arm description:

Participants received 250 milliliter (ml) of a normal saline placebo administered as intravenous (IV) infusion on Days 0, 14, 28 and then every 28 days through Week 20 of the treatment period. Participants continued with the standard of care therapy throughout the treatment period.

Arm type	Placebo Comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo was given by using normal saline bags without belimumab administered as Intravenous infusion every 4 weeks for 20 weeks (with an additional dose at Week 2).

Arm title	Belimumab 10 mg/kg IV

Arm description:

Participants received 10 milligrams per kilogram (mg/kg) of belimumab administered as IV infusion in 250 mL normal saline on Days 0, 14, 28 and then every 28 days through Week 20 of the treatment period. Participants continued with the standard of care therapy throughout the treatment period.

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

Dosage and administration details:

Belimumab (400 mg in a 20 mL vial) is supplied as a reconstituted solution with a unit dose strength of 10 mg/kg administered as Intravenous infusion every 4 weeks for 20 weeks (with an additional dose at Week 2).

Number of subjects in period 1[1]	Placebo IV	Belimumab 10 mg/kg IV
Started	21	18
Completed	17	16
Not completed	4	2
Adverse event, serious fatal	1	-
Adverse event, non-fatal	2	-
MG exacerbation or change in medication	1	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 40 participants were enrolled, however 1 participant withdrew due to MG exacerbation on Day 7 prior to the first efficacy assessment; therefore, 39 participants comprise the ITT Population which is presented in the subject disposition.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo IV
Reporting group description:	
Participants received 250 milliliter (ml) of a normal saline placebo administered as intravenous (IV) infusion on Days 0, 14, 28 and then every 28 days through Week 20 of the treatment period. Participants continued with the standard of care therapy throughout the treatment period.	
Reporting group title	Belimumab 10 mg/kg IV
Reporting group description:	
Participants received 10 milligrams per kilogram (mg/kg) of belimumab administered as IV infusion in 250 mL normal saline on Days 0, 14, 28 and then every 28 days through Week 20 of the treatment period. Participants continued with the standard of care therapy throughout the treatment period.	

Reporting group values	Placebo IV	Belimumab 10 mg/kg IV	Total
Number of subjects	21	18	39
Age categorical Units: Subjects			
Age continuous			
Data are presented for the ITT Population which includes participants in the Safety Population (defined as all participants with at least one infusion of study agent) who have provided any post treatment efficacy assessment.			
Units: years			
arithmetic mean	59	52.7	
standard deviation	± 13.88	± 17.32	-
Gender categorical			
Data are presented for the ITT Population which includes participants in the Safety Population (defined as all participants with at least one infusion of study agent) who have provided any post treatment efficacy assessment.			
Units: Subjects			
Female	14	10	24
Male	7	8	15
Race			
Data are presented for the ITT Population which includes participants in the Safety Population (defined as all participants with at least one infusion of study agent) who have provided any post treatment efficacy assessment.			
Units: Subjects			
American Indian or Alaskan Native	1	0	1
Asian - East Asian Heritage	1	1	2
White - White/Caucasian/European Heritage	19	17	36

End points

End points reporting groups

Reporting group title	Placebo IV

Reporting group description:

Participants received 250 milliliter (ml) of a normal saline placebo administered as intravenous (IV) infusion on Days 0, 14, 28 and then every 28 days through Week 20 of the treatment period. Participants continued with the standard of care therapy throughout the treatment period.

Reporting group title	Belimumab 10 mg/kg IV

Reporting group description:

Participants received 10 milligrams per kilogram (mg/kg) of belimumab administered as IV infusion in 250 mL normal saline on Days 0, 14, 28 and then every 28 days through Week 20 of the treatment period. Participants continued with the standard of care therapy throughout the treatment period.

Subject analysis set title	Placebo IV
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received 250 ml of a normal saline placebo administered as IV infusion on Days 0, 14, 28 and then every 28 days through Week 20 of the treatment period. Participants continued with the standard of care therapy throughout the treatment period. Intent-to-Treat (ITT) Population includes participants in the Safety Population who has provided any post treatment efficacy assessment.

Subject analysis set title	Belimumab 10 mg/kg IV
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received 10 mg/kg of belimumab administered as IV infusion in 250 mL normal saline on Days 0, 14, 28 and then every 28 days through Week 20 of the treatment period. Participants continued with the standard of care therapy throughout the treatment period. Intent-to-Treat (ITT) Population includes participants in the Safety Population who has provided any post treatment efficacy assessment.

Primary: Mean change from Baseline for quantitative myasthenia gravis (QMG) score at Week 24

End point title	Mean change from Baseline for quantitative myasthenia gravis (QMG) score at Week 24

End point description:

The QMG is a 13 item ordinal scale which measures ocular, bulbar, extremity fatigue and strength, along with respiratory function. The total QMG score was calculated by adding the score of each of the 13 individual QMG questions. Possible scoring on the QMG range from 0 (normal) to 39 (severe). A lower score indicates a better clinical outcome. The QMG score at Baseline is the average of the screening and Week 0 Baseline scores. Change from Baseline was calculated by subtracting the Baseline value from the post-baseline value. The differences in adjusted least square means were presented (Belimumab 10 mg/kg minus Placebo). A negative treatment difference indicates benefit relative to placebo. The analysis method was Mixed-Model Repeated Measures adjusted for Treatment, Visit, Baseline QMG Score, Treatment by Visit, and Baseline QMG Score by Visit.

End point type	Primary

End point timeframe:

Baseline and Week 24

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17[1]	17[2]		
Units: Units on a scale				
least squares mean (standard error)	-2.37 (± 1.099)	-4.21 (± 1.143)		

Notes:

[1] - ITT: includes participants in the Safety Population who has provided any post tx efficacy assessment
[2] - ITT: includes participants in the Safety Population who has provided any post tx efficacy assessment

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Belimumab 10 mg/kg IV v Placebo IV
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.256
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.08
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	1.592

Secondary: Number of participants with improvement by greater than or equal to (>=) 3 points from Baseline through to Week 24 in the QMG score

End point title	Number of participants with improvement by greater than or equal to (>=) 3 points from Baseline through to Week 24 in the QMG score

End point description:

The QMG is a 13 item ordinal scale which measures ocular, bulbar, extremity fatigue and strength, along with respiratory function. The total QMG score was calculated by adding the score of each of the 13 individual QMG questions. Possible scoring on the QMG range from 0 (normal) to 39 (severe). A lower score indicates a better clinical outcome. The QMG score at Baseline is the average of the screening and Week 0 Baseline scores. Proportions compared using exact analyses stratified by the observed median Baseline score (less than or equal to [<=] median, greater than [>] median). Exact odds ratio, double the exact one-sided p-value and exact confidence intervals were presented. Participants with missing data were assumed to have a negative response.

End point type	Secondary

End point timeframe:

Baseline and up to Week 24

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21[3]	18[4]		
Units: Number of participants				
number (not applicable)	6	11		

Notes:

[3] - ITT Population

[4] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo IV v Belimumab 10 mg/kg IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.082
Method	exact methods
Parameter estimate	Odds ratio (OR)
Point estimate	3.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	19.02

Secondary: Number of participants worsening by >=3 points in QMG score from Baseline through to Week 24

End point title	Number of participants worsening by >=3 points in QMG score from Baseline through to Week 24

End point description:

The QMG is a 13 item ordinal scale which measures ocular, bulbar, extremity fatigue and strength, along with respiratory function. The total QMG score was calculated by adding the score of each of the 13 individual QMG questions. Possible scoring on the QMG range from 0 (normal) to 39 (severe). A lower score indicates a better clinical outcome. The QMG score at Baseline is the average of the screening and Week 0 Baseline scores. Proportions compared using exact analyses stratified by the observed median Baseline score (<=median, > median). Exact odds ratio, double the exact one-sided p-value and exact confidence interval were presented. Participants with missing data were assumed to have a worsening response.

End point type	Secondary

End point timeframe:

Baseline and up to Week 24

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21[5]	18[6]		
Units: Number of participants				
number (not applicable)	4	2		

Notes:

[5] - ITT Population

[6] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo IV v Belimumab 10 mg/kg IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.827
Method	exact methods
Parameter estimate	Odds ratio (OR)
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	4.35

Secondary: Number of participants with a sustained response in the QMG score

End point title	Number of participants with a sustained response in the QMG score

End point description:

A sustained response during the treatment phase is when a participant improves by >=3 points from Baseline at Week 12, and the participant maintains at least a 3 point improvement from Baseline through Week 24. The QMG is a 13 item ordinal scale which measures ocular, bulbar, extremity fatigue and strength, along with respiratory function. The total QMG score was calculated by adding the score of each of the 13 individual QMG questions. Possible scoring on the QMG range from 0 (normal) to 39 (severe). A lower score indicates a better clinical outcome. The QMG score at Baseline is the average of the screening and Week 0 Baseline scores. Odds ratios are calculated by Cochran-Mantel-Haenszel method stratified by the observed median baseline score (<= median, > median). Wald confidence intervals and p-values were presented.

End point type	Secondary

End point timeframe:

Baseline and up to Week 24

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21[7]	18[8]		
Units: Number of participants				
number (not applicable)	5	8		

Notes:

[7] - ITT Population

[8] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo IV v Belimumab 10 mg/kg IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.184
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	10.1

Secondary: Mean change from Baseline for QMG score at Week 28, Week 32 and Week 36

End point title	Mean change from Baseline for QMG score at Week 28, Week 32 and Week 36

End point description:

The QMG is a 13 item ordinal scale which measures ocular, bulbar, extremity fatigue and strength, along with respiratory function. Total QMG score was calculated by adding the score of each of the 13 individual QMG questions. Possible scoring on the QMG range from 0 (mild) to 39 (severe). A lower score indicates a better clinical outcome. The QMG score at BL is the average of the screening and Week 0 BL scores. Change from BL was calculated by subtracting the BL value from the post-Baseline value. The differences in adjusted least square means are presented (Belimumab 10 mg/kg minus Placebo). A negative trt difference indicates benefit relative to placebo. Analysis method was Mixed-Model Repeated Measures adjusted for Trt, Visit, BL QMG Score, Trt by Visit and BL QMG Score by Visit. Only follow-up visits are presented but the analysis also includes all trt phase visits. Only those par. available at the indicated time points (represented by n=X, X in the category title) were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 28, Week 32 and Week 36

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21[9]	18[10]		
Units: Units on a scale				
least squares mean (standard error)				
Week 28, n=16, 14	-3.33 (± 0.839)	-5.03 (± 0.889)		
Week 32, n=15, 16	-2.82 (± 0.88)	-4.12 (± 0.904)		
Week 36, n=17, 14	-2.44 (± 0.872)	-4.73 (± 0.921)		

Notes:

[9] - ITT Population

[10] - ITT Population

Statistical analyses

Statistical analysis title	Statisitcal analysis 1
Comparison groups	Belimumab 10 mg/kg IV v Placebo IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.175
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	1.228

Notes:

[11] - Analysis for Week 28. Standard error of mean is for adjusted difference.

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo IV v Belimumab 10 mg/kg IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.31
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.89
upper limit	1.28
Variability estimate	Standard error of the mean
Dispersion value	1.267

Notes:

[12] - Analysis for Week 32. Standard error of mean is for adjusted difference.

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo IV v Belimumab 10 mg/kg IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.081
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.88
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	1.272

Notes:

[13] - Analysis for Week 36. Standard error of mean is for adjusted difference.

Secondary: Mean change from Baseline in Myasthenia Gravis Composite (MGC) scale through to Week 24

End point title	Mean change from Baseline in Myasthenia Gravis Composite (MGC) scale through to Week 24

End point description:

The total MGC score was calculated by adding the score of each of the 10 individual MGC questions. Possible total MGC scores range from 0 (normal) to 50 (severe). A lower score indicates a better clinical outcome. Baseline is defined as the participants last available assessment prior to initiation of study IV infusion. Change from Baseline was calculated by subtracting the Baseline value from the post-baseline value. The differences in adjusted least square means are presented (Belimumab 10 mg/kg minus Placebo). A negative treatment difference indicates benefit relative to placebo. The analysis method was Mixed-Model Repeated Measures adjusted for Treatment, Visit, Baseline MGC Score, Treatment by Visit, and Baseline MGC Score by Visit.

End point type	Secondary

End point timeframe:

Baseline and up to Week 24

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17[14]	17[15]		
Units: Units on a scale				
least squares mean (standard error)	-3.86 (± 1.037)	-3.81 (± 1.064)		

Notes:

[14] - ITT Population

[15] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Standard error of mean is for adjusted difference.	
Comparison groups	Placebo IV v Belimumab 10 mg/kg IV
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.972
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.97
upper limit	3.07
Variability estimate	Standard error of the mean
Dispersion value	1.486

Secondary: Number of participants with improvement by >=3 points from Baseline through to Week 24 in the MGC score

End point title	Number of participants with improvement by >=3 points from Baseline through to Week 24 in the MGC score
End point description:	
The total MGC score was calculated by adding the score of each of the 10 individual MGC questions. Possible total MGC scores range from 0 (normal) to 50 (severe). A lower score indicates a better clinical outcome. Baseline is defined as the participants last available assessment prior to initiation of study IV infusion. Proportions compared using exact analyses stratified by the observed median baseline score (<= median, > median). Exact odds ratios, double the exact one-sided p-values and exact confidence intervals were presented. Participants with missing data were assumed to have a negative response.	
End point type	Secondary
End point timeframe:	
Baseline and up to Week 24	

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21[16]	18[17]		
Units: Number of participants				
number (not applicable)	10	9		

Notes:

[16] - ITT Population

[17] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo IV v Belimumab 10 mg/kg IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	exact methods
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	5.48

Secondary: Number of participants worsening by >=3 points from Baseline through to Week 24 in the MGC score

End point title	Number of participants worsening by >=3 points from Baseline through to Week 24 in the MGC score

End point description:

The total MGC score was calculated by adding the score of each of the 10 individual MGC questions. Possible total MGC scores range from 0 (normal) to 50 (severe). A lower score indicates a better clinical outcome. Baseline is defined as the participants last available assessment prior to initiation of study IV infusion. Proportions compared using exact analyses stratified by the observed median baseline score (<= median, > median). Exact odds ratios, double the exact one-sided p-values and exact confidence intervals were presented. Participants with missing data were assumed to have a worsening response.

End point type	Secondary

End point timeframe:

Baseline and up to Week 24

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21[18]	18[19]		
Units: Number of participants				
number (not applicable)	5	2		

Notes:

[18] - ITT Population.

[19] - ITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo IV v Belimumab 10 mg/kg IV

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.53
Method	exact methods
Parameter estimate	Odds ratio (OR)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	2.89

Secondary: Number of participants with a sustained response in the MGC score

End point title	Number of participants with a sustained response in the MGC score

End point description:

A sustained response during the treatment phase is when a participant improves by >=3 points from Baseline at Week 12, and the participant maintains at least a 3 point improvement from Baseline through Week 24. The total MGC score was calculated by adding the score of each of the 10 individual MGC questions. Possible total MGC scores range from 0 (normal) to 50 (severe). A lower score indicates a better clinical outcome. Baseline is defined as the participants last available assessment prior to initiation of study IV infusion. Odds ratios are calculated by Cochran-Mantel-Haenszel method without adjusting for any strata. Wald confidence intervals and p-values were presented.

End point type	Secondary

End point timeframe:

Baseline and up to Week 24

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21[20]	18[21]		
Units: Number of participants				
number (not applicable)	4	7		

Notes:

[20] - ITT Population

[21] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo IV v Belimumab 10 mg/kg IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.175
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	11.46

Secondary: Mean change from Baseline in the Myasthenia Gravis Activities of Daily Living Scale (MG-ADL) at Week 12 and Week 24

End point title	Mean change from Baseline in the Myasthenia Gravis Activities of Daily Living Scale (MG-ADL) at Week 12 and Week 24

End point description:

The total MG-ADL score was calculated by adding the score of each of the 8 individual MG-ADL questions. Possible total MG-ADL scores ranges from 0 (normal) to 24 (severe). A lower score indicates a better clinical outcome. Baseline is defined as the participants last available assessment prior to initiation of study IV infusion. Change from Baseline was calculated by subtracting the Baseline value from the post-baseline value. The differences in adjusted least square means are presented (Belimumab 10 mg/kg minus Placebo). A negative treatment difference indicates benefit relative to placebo. The analysis method was Mixed-Model Repeated Measures adjusted for Treatment, Visit, Baseline MG-ADL Score, Treatment by Visit, and Baseline MG-ADL Score by Visit.

End point type	Secondary

End point timeframe:

Baseline, Week 12 and Week 24

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21[22]	18[23]		
Units: Units on a scale				
least squares mean (standard error)				
Week 12, n=19, 18	-1.33 (± 0.489)	-1.83 (± 0.511)		
Week 24, n=17, 17	-2.01 (± 0.589)	-2.32 (± 0.603)		

Notes:

[22] - ITT Population

[23] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Statistical analysis is presented for Week 12. Standard error of mean is for adjusted mean difference.

Comparison groups	Placebo IV v Belimumab 10 mg/kg IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.483
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.94
upper limit	0.93
Variability estimate	Standard error of the mean
Dispersion value	0.707

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Statistical analysis is presented for Week 24. Standard error of mean is for adjusted mean difference.	
Comparison groups	Placebo IV v Belimumab 10 mg/kg IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.711
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.03
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.844

Secondary: Median time to QMG response which is sustained from earliest time point at which improvement by >=3 points from Baseline is observed and maintained through Week 24

End point title	Median time to QMG response which is sustained from earliest time point at which improvement by >=3 points from Baseline is observed and maintained through Week 24

End point description:

A sustained response during the treatment phase is when a participant improves by >=3 points from Baseline at Week 12, and the participant maintains at least a 3 point improvement from Baseline through Week 24. The QMG is a 13 item ordinal scale which measures ocular, bulbar, extremity fatigue and strength, along with respiratory function. The total QMG score was calculated by adding the score of each of the 13 individual QMG questions. Possible scoring on the QMG range from 0 (normal) to 39 (severe). A lower score indicates a better clinical outcome. The QMG score at Baseline is the average of the screening and Week 0 Baseline scores. As per the criteria documented in the Reporting and Analysis Plan, these analyses were not conducted since <50% of subjects met the criteria (i.e. had the event in question).

End point type	Secondary

End point timeframe:

Baseline and up to Week 24

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[24]	0[25]		
Units: weeks				
median (full range (min-max))	(to)	(to)		

Notes:

[24] - Greater than 50% of the participants did not had a response. Hence, the analysis was not performed.
[25] - Greater than 50% of the participants did not had a response. Hence, the analysis was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Median time to MGC response which is sustained from earliest time point at which improvement by >=3 points from Baseline is observed and maintained through Week 24

End point title	Median time to MGC response which is sustained from earliest time point at which improvement by >=3 points from Baseline is observed and maintained through Week 24

End point description:

A sustained response during the treatment phase is when a participant improves by >=3 points from Baseline at Week 12, and the participant maintains at least a 3 point improvement from Baseline through Week 24. The total MGC score was calculated by adding the score of each of the 10 individual MGC questions. Possible total MGC scores range from 0 (normal) to 50 (severe). A lower score indicates a better clinical outcome. Baseline is defined as the participants' last available assessment prior to initiation of study intravenous (IV) infusion. As per the criteria documented in the Reporting and Analysis Plan these analyses were not conducted since <50% of subjects met the criteria (i.e. had the event in question).

End point type	Secondary

End point timeframe:

Baseline and up to Week 24

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[26]	0[27]		
Units: Weeks				
median (full range (min-max))	(to)	(to)		

Notes:

[26] - Greater than 50% of the participants did not had a response. Hence, the analysis was not performed.
[27] - Greater than 50% of the participants did not had a response. Hence, the analysis was not performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline for MGC score at Week 28, Week 32 and Week 36

End point title	Mean change from Baseline for MGC score at Week 28, Week 32 and Week 36

End point description:

The total MGC score was calculated by adding the score of each of the 10 individual MGC questions. Possible total MGC scores range from 0 (normal) to 50 (severe). A lower score indicates a better clinical outcome. Baseline is defined as the participant's last available assessment prior to initiation of study IV infusion. Change from Baseline was calculated by subtracting the Baseline value from the post-Baseline value. The differences in adjusted least square means are presented (Belimumab 10 mg/kg minus Placebo). A negative treatment difference indicates benefit relative to placebo. The analysis method was Mixed-Model Repeated Measures adjusted for Treatment, Visit, Baseline MGC Score, Treatment by Visit, and Baseline MGC Score by Visit. Only follow-up visits are presented but the analysis also includes all treatment phase visits. Only those participants available at the indicated time points (represented by n=X, X in the category titles) were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 28, Week 32 and Week 36

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21[28]	18[29]		
Units: Units on a scale				
least squares mean (standard error)				
Week 28, n=16, 14	-4.63 (± 0.856)	-5.64 (± 0.905)		
Week 32, n=15, 16	-5.46 (± 0.975)	-5.44 (± 0.948)		
Week 36, n=17, 14	-4.77 (± 0.97)	-5.04 (± 1.052)		

Notes:

[28] - ITT Population

[29] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Belimumab 10 mg/kg IV v Placebo IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority[30]
P-value	= 0.423
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.56
upper limit	1.53
Variability estimate	Standard error of the mean
Dispersion value	1.245

Notes:

[30] - Analysis for Week 28. Standard error of mean is for adjusted difference.

Statistical analysis title	Statistical analysis 2
Comparison groups	Belimumab 10 mg/kg IV v Placebo IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority[31]
P-value	= 0.986
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.76
upper limit	2.8
Variability estimate	Standard error of the mean
Dispersion value	1.361

Notes:

[31] - Analysis for Week 32. Standard error of mean is for adjusted difference.

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo IV v Belimumab 10 mg/kg IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority[32]
P-value	= 0.848
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.21
upper limit	2.65
Variability estimate	Standard error of the mean
Dispersion value	1.43

Notes:

[32] - Analysis for Week 36. Standard error of mean is for adjusted difference.

Secondary: Number of participants with a MGFA-PIS of minimal manifestation or better at Week 24 and Week 36

End point title	Number of participants with a MGFA-PIS of minimal manifestation or better at Week 24 and Week 36

End point description:

Myasthenia Foundation of America (MGFA) post intervention status (PIS) assesses whether subjects can be categorized as being in a status of Minimal Manifestation (MM), Pharmacologic Remission (PR) or Complete Remission (CR). Only MM and PR were assessed in this study as CR is not achievable based on the definition. The Reporting and Analysis Plan pre-specified that these analyses would not be conducted since during a review of blinded data it was identified that the MGFA scale had been inconsistently performed across sites and any statistical analyses would not be interpretable.

End point type	Secondary

End point timeframe:

Week 24 and Week 36

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[33]	0[34]		
Units: Number of participants				
number (not applicable)				

Notes:

[33] - ITT Population. Analysis would not be conducted.

[34] - ITT Population. Analysis would not be conducted.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with MGFA-PIS of minimal manifestation sustained response (MM at Week 12 and maintained the response through Week 24)

End point title	Number of participants with MGFA-PIS of minimal manifestation sustained response (MM at Week 12 and maintained the response through Week 24)

End point description:

Myasthenia Foundation of America (MGFA) post intervention status (PIS) assesses whether subjects can be categorized as being in a status of Minimal Manifestation (MM), Pharmacologic Remission (PR) or Complete Remission (CR). Only MM and PR were assessed in this study as CR is not achievable based on the definition. The Reporting and Analysis Plan pre-specified that these analyses would not be conducted since during a review of blinded data it was identified that the MGFA scale had been inconsistently performed across sites and any statistical analyses would not be interpretable.

End point type	Secondary

End point timeframe:

Week 12 through Week 24

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[35]	0[36]		
Units: Number of participants				
number (not applicable)				

Notes:

[35] - ITT Population. Analysis would not be conducted.

[36] - ITT Population. Analysis would not be conducted.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with MGFA-PIS of pharmacologic remission or better at Week 24 and Week 36

End point title	Number of participants with MGFA-PIS of pharmacologic remission or better at Week 24 and Week 36

End point description:

Myasthenia Foundation of America (MGFA) post intervention status (PIS) assesses whether subjects can be categorized as being in a status of Minimal Manifestation (MM), Pharmacologic Remission (PR) or Complete Remission (CR). Only MM and PR were assessed in this study as CR is not achievable based on the definition. The Reporting and Analysis Plan pre-specified that these analyses would not be conducted since during a review of blinded data it was identified that the MGFA scale had been inconsistently performed across sites and any statistical analyses would not be interpretable.

End point type	Secondary

End point timeframe:

Week 24 and Week 36

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[37]	0[38]		
Units: Number of participants				
number (not applicable)				

Notes:

[37] - ITT Population. Analysis would not be conducted.

[38] - ITT Population. Analysis would not be conducted.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with MGFA-PIS of pharmacologic response sustained response (PR at week 12 and maintained the response through Week 24)

End point title	Number of participants with MGFA-PIS of pharmacologic response sustained response (PR at week 12 and maintained the response through Week 24)

End point description:

Myasthenia Foundation of America (MGFA) post intervention status (PIS) assesses whether subjects can be categorized as being in a status of Minimal Manifestation (MM), Pharmacologic Remission (PR) or Complete Remission (CR). Only MM and PR were assessed in this study as CR is not achievable based on the definition. The Reporting and Analysis Plan pre-specified that these analyses would not be conducted since during a review of blinded data it was identified that the MGFA scale had been inconsistently performed across sites and any statistical analyses would not be interpretable.

End point type	Secondary

End point timeframe:

Week 12 through Week 24

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[39]	0[40]		
Units: Number of participants				
number (not applicable)				

Notes:

[39] - ITT Population. Analysis would not be conducted.

[40] - ITT Population. Analysis would not be conducted.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with MGFA-PIS (Unchanged, Improved, Worsened) at Week 24 and Week 36

End point title	Number of participants with MGFA-PIS (Unchanged, Improved, Worsened) at Week 24 and Week 36

End point description:

Myasthenia Foundation of America (MGFA) post intervention status (PIS) assesses whether subjects can be categorized as being unchanged, improved or worsened. The Reporting and Analysis Plan pre-specified that these analyses would not be conducted since during a review of blinded data it was identified that the MGFA scale had been inconsistently performed across sites and any statistical analyses would not be interpretable.

End point type	Secondary

End point timeframe:

Week 24 and Week 36

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[41]	0[42]		
Units: Number of participants				
number (not applicable)				

Notes:

[41] - ITT Population. Analysis would not be conducted.

[42] - ITT Population. Analysis would not be conducted.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in the Myasthenia Gravis Activities of Daily Living Scale (MG-ADL) at Week 28, Week 32 and Week 36

End point title	Mean change from Baseline in the Myasthenia Gravis Activities of Daily Living Scale (MG-ADL) at Week 28, Week 32 and Week 36

End point description:

The total MG-ADL score was calculated by adding the score of each of the 8 individual MG-ADL questions. Possible total MG-ADL scores range from 0 (normal) to 24 (severe). A lower score indicates a better clinical outcome. Baseline is defined as the participant's last available assessment prior to initiation of study IV infusion. Change from Baseline was calculated by subtracting the Baseline value from the post-Baseline value. The differences in adjusted least square means are presented (Belimumab 10 mg/kg minus Placebo). A negative treatment difference indicates benefit relative to placebo. The analysis method was Mixed-Model Repeated Measures adjusted for Treatment, Visit, Baseline MG-ADL Score, Treatment by Visit, and Baseline MG-ADL Score by Visit. Only follow-up visits are presented but the analysis also includes all treatment phase visits. Only those participants available at the indicated time points (represented by n=X, X in the category titles) were analyzed.

End point type	Secondary

End point timeframe:

Baseline, Week 28, Week 32 and Week 36

End point values	Placebo IV	Belimumab 10 mg/kg IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21[43]	18[44]		
Units: Units on a scale				
least squares mean (standard error)				
Week 28, n=16, 14	-1.21 (± 0.522)	-2.96 (± 0.546)		
Week 32, n=15, 16	-1.52 (± 0.632)	-1.8 (± 0.619)		
Week 36, n=17, 14	-1.51 (± 0.621)	-1.78 (± 0.663)		

Notes:

[43] - ITT Population

[44] - ITT Population

Statistical analyses

Statistical analysis title	Statisitcal analysis 1
Comparison groups	Belimumab 10 mg/kg IV v Placebo IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority[45]
P-value	= 0.028
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.757

Notes:

[45] - Analysis for Week 28. Standard error of mean is for adjusted difference.

Statistical analysis title	Statistical analysis 2
Comparison groups	Belimumab 10 mg/kg IV v Placebo IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority[46]
P-value	= 0.756
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.28

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	1.55
Variability estimate	Standard error of the mean
Dispersion value	0.887

Notes:

[46] - Analysis for Week 32. Standard error of mean is for adjusted difference.

Statistical analysis title	Statistical analysis 3
Comparison groups	Belimumab 10 mg/kg IV v Placebo IV
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority[47]
P-value	= 0.775
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.12
upper limit	1.59
Variability estimate	Standard error of the mean
Dispersion value	0.909

Notes:

[47] - Analysis for Week 36. Standard error of mean is for adjusted difference.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment serious adverse events (SAEs) and non-serious AEs were collected from the date first infusion of investigational product up to the Week 24 visit.

Adverse event reporting additional description:

AEs and SAEs are reported for the safety population which is comprised of participants who had at least one infusion of study agent.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Placebo IV

Reporting group description:

Participants received 250 ml of a normal saline placebo administered as IV infusion on Days 0, 14, 28 and then every 28 days through Week 20 of the treatment period. Participants continued with the standard of care therapy throughout the treatment period.

Reporting group title	Belimumab 10 mg/kg IV

Reporting group description:

Participants received 10 mg/kg of belimumab administered as IV infusion in 250 mL normal saline on Days 0, 14, 28 and then every 28 days through Week 20 of the treatment period. Participants continued with the standard of care therapy throughout the treatment period.

Serious adverse events	Placebo IV	Belimumab 10 mg/kg IV	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 22 (18.18%)	0 / 18 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Vascular disorders			
Aortic dissection rupture			
subjects affected / exposed	1 / 22 (4.55%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Myasthenia gravis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	1 / 22 (4.55%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	

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

Non-serious adverse events	Placebo IV	Belimumab 10 mg/kg IV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 22 (72.73%)	14 / 18 (77.78%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 22 (9.09%)	1 / 18 (5.56%)	
occurrences (all)	3	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 22 (4.55%)	2 / 18 (11.11%)	
occurrences (all)	1	2	
Fatigue			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Feeling hot			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Peripheral swelling			

subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Productive cough			
subjects affected / exposed	2 / 22 (9.09%)	1 / 18 (5.56%)	
occurrences (all)	3	1	
Dyspnoea			
subjects affected / exposed	1 / 22 (4.55%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Oropharyngeal pain			
subjects affected / exposed	2 / 22 (9.09%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
Epistaxis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Throat tightness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 22 (9.09%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
Depression			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Investigations			
Neutrophil count increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
White blood cell count increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			

Wound			
subjects affected / exposed	1 / 22 (4.55%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Tooth fracture			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 22 (13.64%)	1 / 18 (5.56%)	
occurrences (all)	6	1	
Dizziness			
subjects affected / exposed	1 / 22 (4.55%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Sciatica			
subjects affected / exposed	1 / 22 (4.55%)	1 / 18 (5.56%)	
occurrences (all)	1	2	
Hypoaesthesia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Lethargy			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 22 (4.55%)	1 / 18 (5.56%)	
occurrences (all)	2	2	
Eye pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Photopsia			

subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 22 (18.18%)	1 / 18 (5.56%)	
occurrences (all)	5	1	
Nausea			
subjects affected / exposed	0 / 22 (0.00%)	3 / 18 (16.67%)	
occurrences (all)	0	6	
Abdominal pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Dental caries			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	3	
Photosensitivity reaction			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	2 / 22 (9.09%)	2 / 18 (11.11%)	
occurrences (all)	2	2	
Back pain			
subjects affected / exposed	3 / 22 (13.64%)	0 / 18 (0.00%)	
occurrences (all)	6	0	
Muscle spasms			

subjects affected / exposed	2 / 22 (9.09%)	1 / 18 (5.56%)	
occurrences (all)	3	1	
Groin pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	2	
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 22 (0.00%)	3 / 18 (16.67%)	
occurrences (all)	0	3	
Nasopharyngitis			
subjects affected / exposed	2 / 22 (9.09%)	1 / 18 (5.56%)	
occurrences (all)	2	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 22 (4.55%)	2 / 18 (11.11%)	
occurrences (all)	2	2	
Cystitis			
subjects affected / exposed	2 / 22 (9.09%)	0 / 18 (0.00%)	
occurrences (all)	3	0	
Urinary tract infection			
subjects affected / exposed	1 / 22 (4.55%)	1 / 18 (5.56%)	
occurrences (all)	2	1	
Conjunctivitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Ear infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Herpes zoster			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	

Tooth infection subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 18 (5.56%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 August 2011	This amendment provides clarity for the conduct of the study and corrects typographical errors.
11 June 2012	Addition of a 3-hour clinical supervision period after subjects receive the first 2 infusions. Removal of the week 24 IP infusion (all efficacy and safety endpoints remain unchanged). Widen inclusion criteria to allow enrollment of MuSK antibody positive subjects. Enrollment to be stratified by MuSK antibody status. Revision to the timing of pharmacodynamic and pharmacokinetic endpoints.
08 August 2013	Safety sections updated to reflect new information on possible delayed hypersensitivity reactions. Amended timing such that analysis of data to be conducted twice – once when all subjects have reached week 24 (pre-specified primary endpoint) and again at week 36 when all subjects have completed post-treatment follow up). Criteria updated to exclude subjects positive for Hepatitis B surface antigen (HBsAg) and/or Hepatitis B core antibody (HBcAb). Patients who are positive for hepatitis C antibody but negative for a confirmatory RNA assay will be eligible to participate. Criteria updated to specify that doses of cholinesterase inhibitor which exceed 300 mg/day may be allowed after discussion with the GSK Medical Monitor. Removal of MGFA Post-Intervention status at Week 4, 8, 16, 20, 28 and 32. MG Composite Score (MGC) updated to include Mean change from baseline in MGC at Week 24. Mean change from baseline in MGC at Week 24 added as secondary endpoint under Multiple Comparisons Adjustments. Removed secondary endpoints from the Multiple Comparisons Adjustments section for Minimal Manifestation (MM) and Pharmacologic Response (PR). Footnotes in the Time and Events Table corrected.
05 March 2014	Progressive multifocal leukoencephalopathy (PML) has been reported in SLE patients receiving immunosuppressant pharmacotherapy, including belimumab. Section 6.3.8 updated to include this information.
15 April 2014	Allow enrollment of subjects taking methotrexate; reduce the time prior to screening for use of IVIg and/or plasmapheresis; and allow prior treatment with rituximab provided treatment was more than 12 months prior to screening.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported