



## 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          | v1            |
| This version publication date  | 08 April 2016 |
| First version publication date | 08 April 2016 |

#### 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,<br>GlaxoSmithKline, +44 (0)208990 4466,<br>GSKClinicalSupportHD@gsk.com |
| Scientific contact           | GSK Response Center, GlaxoSmithKline, 1 866-435-7343,<br>GlaxoSmithKline, +44 (0)208990 4466,<br>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 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 ITT population which is presented in the subject disposition.

### 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                | Subject, Investigator, Monitor, Carer, Assessor |

### Arms

|                              |            |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes        |
| <b>Arm title</b>             | 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).

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | 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).

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

---

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:<br>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:<br>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:<br>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:<br>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:<br>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. The total QMG score ranged from 0 to 39. 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:<br>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 <sup>[1]</sup>    | 17 <sup>[2]</sup>     |  |  |
| 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

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 1             |
| 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                                 | = 0.256                            |
| 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:   |   |
| <p>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. The total QMG score ranged from 0 to 39. 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 [<math>\leq</math>] median, greater than [<math>&gt;</math>] 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.</p> |   |
| 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 <sup>[3]</sup>    | 18 <sup>[4]</sup>     |  |  |
| 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                                  | Cochran-Mantel-Haenszel            |
| 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 $\geq 3$ points in QMG score from Baseline through to Week 24

|                 |   |
|-----------------|---|
| End point title | Number of participants worsening by $\geq 3$ 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. The total QMG score ranged from 0 to 39. 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 ( $\leq$  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 <sup>[5]</sup>    | 18 <sup>[6]</sup>     |  |  |
| 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                                  | Cochran-Mantel-Haenszel            |
| 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  $\geq 3$  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. The total QMG score ranged from 0 to 39. 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 ( $\leq$  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 <sup>[7]</sup>    | 18 <sup>[8]</sup>     |  |  |
| 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. The total QMG score was calculated by adding the score of each of the 13 individual QMG questions. The total QMG score ranged from 0 to 39. 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 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 QMG Score, Treatment by Visit, and Baseline QMG Score by Visit. Only follow-up visits are presented but the analysis also includes all treatment phase visits.

|                |           |
|----------------|-----------|
| 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         | 0 <sup>[9]</sup>     | 0 <sup>[10]</sup>     |  |  |
| Units: Units on a scale             |                      |                       |  |  |
| least squares mean (standard error) | ( )                  | ( )                   |  |  |

Notes:

[9] - ITT population. Data has not been analyzed. Probably the data will be available by June 2016.

[10] - ITT population. Data has not been analyzed. Probably the data will be available by June 2016.

## Statistical analyses

No statistical analyses for this end point

## 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. The total MGC score ranged from 0 to 50. 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 <sup>[11]</sup>   | 17 <sup>[12]</sup>    |  |  |
| Units: Units on a scale             |                      |                       |  |  |
| least squares mean (standard error) | -3.86 (± 1.037)      | -3.81 (± 1.064)       |  |  |

Notes:

[11] - ITT Population

[12] - 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 $\geq 3$ points from Baseline through to Week 24 in the MGC score

|   |  |
|---|--|
| End point title   | Number of participants with improvement by $\geq 3$ 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. The total MGC score ranged from 0 to 50. 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 ( $\leq$ 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 <sup>[13]</sup>   | 18 <sup>[14]</sup>    |  |  |
| Units: Number of participants |                      |                       |  |  |
| number (not applicable)       | 10                   | 9                     |  |  |

Notes:

[13] - ITT Population

[14] - 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                                  | Cochran-Mantel-Haenszel |
| 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 $\geq 3$ points from Baseline through to Week 24 in the MGC score

|                 |   |
|-----------------|---|
| End point title | Number of participants worsening by $\geq 3$ 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. The total MGC score ranged from 0 to 50. 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 ( $\leq$  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 <sup>[15]</sup>   | 18 <sup>[16]</sup>    |  |  |
| Units: Number of participants |                      |                       |  |  |
| number (not applicable)       | 5                    | 2                     |  |  |

Notes:

[15] - ITT Population.

[16] - ITT Population.

### Statistical analyses

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>       | 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                                  | Cochran-Mantel-Haenszel            |
| 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  $\geq 3$  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. The total MGC score ranged from 0 to 50. 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 <sup>[17]</sup>   | 18 <sup>[18]</sup>    |  |  |
| Units: Number of participants |                      |                       |  |  |
| number (not applicable)       | 4                    | 7                     |  |  |

Notes:

[17] - ITT Population

[18] - 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. The total MG-ADL score ranged from 0 to 24. 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 <sup>[19]</sup>   | 18 <sup>[20]</sup>    |  |  |
| 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:

[19] - ITT Population

[20] - 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                      |

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>   | Statistical analysis 2             |
| Statistical analysis description:<br>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  $\geq 3$  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 $\geq 3$ 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  $\geq 3$  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. The total QMG score ranged from 0 to 39. 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 <sup>[21]</sup>    | 0 <sup>[22]</sup>     |  |  |
| Units: weeks                  |                      |                       |  |  |
| median (full range (min-max)) | ( to )               | ( to )                |  |  |

Notes:

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

[22] - 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 $\geq 3$ 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 $\geq 3$ 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  $\geq 3$  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. The total MGC score ranged from 0 to 50. 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 <sup>[23]</sup>    | 0 <sup>[24]</sup>     |  |  |
| Units: Weeks                  |                      |                       |  |  |
| median (full range (min-max)) | ( to )               | ( to )                |  |  |

Notes:

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

[24] - 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. The total MGC score ranged from 0 to 50. 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. Only follow-up visits are presented but the analysis also includes all treatment phase visits.

---

|                |           |
|----------------|-----------|
| 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         | 0 <sup>[25]</sup>    | 0 <sup>[26]</sup>     |  |  |
| Units: Units on a scale             |                      |                       |  |  |
| least squares mean (standard error) | ( )                  | ( )                   |  |  |

**Notes:**

[25] - ITT Population. Data has not been analyzed. Probably the data will be available by June 2016

[26] - ITT Population. Data has not been analyzed. Probably the data will be available by June 2016

---

**Statistical analyses**

No statistical analyses for this end point

---

---

**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 <sup>[27]</sup>    | 0 <sup>[28]</sup>     |  |  |
| Units: Number of participants |                      |                       |  |  |
| number (not applicable)       |                      |                       |  |  |

Notes:

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

[28] - 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 <sup>[29]</sup>    | 0 <sup>[30]</sup>     |  |  |
| Units: Number of participants |                      |                       |  |  |
| number (not applicable)       |                      |                       |  |  |

Notes:

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

[30] - 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 <sup>[31]</sup>    | 0 <sup>[32]</sup>     |  |  |
| Units: Number of participants |                      |                       |  |  |
| number (not applicable)       |                      |                       |  |  |

Notes:

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

[32] - 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 <sup>[33]</sup>    | 0 <sup>[34]</sup>     |  |  |
| 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 (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:<br>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:<br>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 <sup>[35]</sup>    | 0 <sup>[36]</sup>     |  |  |
| 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: 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:<br>The total MG-ADL score was calculated by adding the score of each of the 8 individual MG-ADL questions. The total MG-ADL score ranged from 0 to 24. 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. Only follow-up visits are presented but the analysis also includes all treatment phase visits. |  |
| End point type   | Secondary  |
| End point timeframe:<br>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          | 0 <sup>[37]</sup>    | 0 <sup>[38]</sup>     |  |  |
| Units: Units on a scale              |                      |                       |  |  |
| arithmetic mean (standard deviation) | ( )                  | ( )                   |  |  |

---

Notes:

[37] - ITT Population. Data has not been analyzed. Probably the data will be available by June 2016.

[38] - ITT Population. Data has not been analyzed. Probably the data will be available by June 2016.

---

## **Statistical analyses**

No statistical analyses for this end point

## 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 have 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 %

| <b>Non-serious adverse events</b>                     | 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<br>occurrences (all) | 0 / 22 (0.00%)<br>0 | 1 / 18 (5.56%)<br>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<br>subjects affected / exposed<br>occurrences (all)                                    | 1 / 22 (4.55%)<br>1  | 1 / 18 (5.56%)<br>1 |  |
| Tooth fracture<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 22 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1 |  |
| Cardiac disorders<br>Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all) | 0 / 22 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1 |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)     | 3 / 22 (13.64%)<br>6 | 1 / 18 (5.56%)<br>1 |  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 22 (4.55%)<br>1  | 1 / 18 (5.56%)<br>1 |  |
| Sciatica<br>subjects affected / exposed<br>occurrences (all)                                 | 1 / 22 (4.55%)<br>1  | 1 / 18 (5.56%)<br>2 |  |
| Hypoaesthesia<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 22 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1 |  |
| Lethargy<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 22 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1 |  |
| Somnolence<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 22 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1 |  |
| Eye disorders<br>Cataract<br>subjects affected / exposed<br>occurrences (all)                | 1 / 22 (4.55%)<br>2  | 1 / 18 (5.56%)<br>2 |  |
| Eye pain<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 22 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1 |  |
| Photopsia  |                      |                     |  |

|  |                     |                     |  |
|--|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 22 (0.00%)<br>0 | 1 / 18 (5.56%)<br>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<br>subjects affected / exposed<br>occurrences (all) | 0 / 22 (0.00%)<br>0 | 1 / 18 (5.56%)<br>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