



## Clinical trial results:

### **A Multi-center, Randomized Parallel Group, Placebo-Controlled Double-Blind Trial to Evaluate the Safety, Efficacy, and Pharmacokinetics of Belimumab, a Human Monoclonal Anti-BLyS Antibody, Plus Standard Therapy in Pediatric Patients with Systemic Lupus Erythematosus (SLE)** **Summary**

|                          |                               |
|--------------------------|-------------------------------|
| EudraCT number           | 2011-000368-88                |
| Trial protocol           | GB ES PL NL IT Outside EU/EEA |
| Global end of trial date |                               |

#### **Results information**

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 08 August 2018 |
| First version publication date | 08 August 2018 |

#### **Trial information**

##### **Trial identification**

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 114055 |
|-----------------------|--------|

##### **Additional study identifiers**

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

Notes:

##### **Sponsors**

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | GlaxoSmithKline  |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, |
| Public contact               | GSK Response Center, GlaxoSmithKline, 1 866-435-7343,      |
| Scientific contact           | GSK Response Center, GlaxoSmithKline, 1 866-435-7343,      |

Notes:

##### **Paediatric regulatory details**

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-000520-PIP01-08 |
| 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? | Yes                 |

Notes:

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Interim         |
| Date of interim/final analysis                       | 16 April 2018   |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 24 January 2018 |
| Global end of trial reached?                         | No              |

Notes:

## General information about the trial

Main objective of the trial:

Evaluate the safety, tolerability, pharmacokinetics, efficacy of belimumab and to evaluate the effects of belimumab on the quality of life in the pediatric SLE population.

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 07 September 2012 |
| Long term follow-up planned                               | Yes               |
| Long term follow-up rationale                             | Safety            |
| Long term follow-up duration                              | 10 Years          |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Argentina: 12          |
| Country: Number of subjects enrolled | Canada: 5              |
| Country: Number of subjects enrolled | Japan: 6               |
| Country: Number of subjects enrolled | Mexico: 12             |
| Country: Number of subjects enrolled | Peru: 14               |
| Country: Number of subjects enrolled | Poland: 2              |
| Country: Number of subjects enrolled | Russian Federation: 11 |
| Country: Number of subjects enrolled | Spain: 14              |
| Country: Number of subjects enrolled | United Kingdom: 5      |
| Country: Number of subjects enrolled | United States: 12      |
| Worldwide total number of subjects   | 93                     |
| EEA total number of subjects         | 21                     |

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          | 0 |

|                           |    |
|---------------------------|----|
| months)                   |    |
| Children (2-11 years)     | 13 |
| Adolescents (12-17 years) | 80 |
| Adults (18-64 years)      | 0  |
| From 65 to 84 years       | 0  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

A total of 93 pediatric participants with Systemic Lupus Erythematosus (SLE) were enrolled at 29 study centers in 10 different countries. This was a multi-center study to evaluate the safety, efficacy and pharmacokinetics of belimumab plus background standard therapy. The results presented are based on Part A (double blind).

### Pre-assignment

Screening details:

The study consisted of three separate phases: Randomized, placebo-controlled, double-blind 52-week treatment phase (Part A), Long term belimumab open label safety follow up for participants who completed Part A (Part B) and Long term safety follow-up phase for participants who were withdrawn from Part A or Part B at any time (Part C).

### 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          |

### Arms

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

Arm description:

Participants received saline infusion (placebo) intravenously monthly for 48 weeks on a background of standard of care

|  |                       |
|--|-----------------------|
| Arm type                               | Placebo               |
| Investigational medicinal product name | Placebo               |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

Normal Saline intravenously.

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Belimumab 10 mg/kg |
|------------------|--------------------|

Arm description:

Participants received 10 milligrams per kilograms (mg/kg) reconstituted solution intravenously monthly for 48 weeks on a background of standard of care.

|  |                                  |
|--|----------------------------------|
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Benlysta (belimumab)             |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

Belimumab (10 mg/kg or adjusted dose) intravenously.

| <b>Number of subjects in period 1</b> | Placebo | Belimumab 10 mg/kg |
|---------------------------------------|---------|--------------------|
| Started                               | 40      | 53                 |
| Completed                             | 31      | 45                 |
| Not completed                         | 9       | 8                  |
| Adverse event, serious fatal          | 1       | -                  |
| Consent withdrawn by subject          | 2       | 1                  |
| Physician decision                    | -       | 3                  |
| Adverse event, non-fatal              | 4       | 3                  |
| Lack of efficacy                      | 1       | 1                  |
| Protocol deviation                    | 1       | -                  |

## Baseline characteristics

### Reporting groups

|  |                    |
|--|--------------------|
| Reporting group title  | Placebo            |
| Reporting group description:<br>Participants received saline infusion (placebo) intravenously monthly for 48 weeks on a background of standard of care                                   |                    |
| Reporting group title  | Belimumab 10 mg/kg |
| Reporting group description:<br>Participants received 10 milligrams per kilograms (mg/kg) reconstituted solution intravenously monthly for 48 weeks on a background of standard of care. |                    |

| Reporting group values | Placebo | Belimumab 10 mg/kg | Total |
|------------------------|---------|--------------------|-------|
| Number of subjects     | 40      | 53                 | 93    |
| Age categorical        |         |                    |       |
| Units: Subjects        |         |                    |       |

|  |        |        |    |
|--|--------|--------|----|
| Age continuous                                 |        |        |    |
| Units: years                                   |        |        |    |
| arithmetic mean                                | 14.8   | 13.5   |    |
| standard deviation                             | ± 2.17 | ± 2.59 | -  |
| Gender categorical                             |        |        |    |
| Units: Subjects                                |        |        |    |
| Female   | 39     | 49     | 88 |
| Male   | 1      | 4      | 5  |
| Race/Ethnicity, Customized                     |        |        |    |
| Units: Subjects                                |        |        |    |
| Race White - White/Caucasian/European Heritage | 21     | 27     | 48 |
| Race Asian                                     | 6      | 8      | 14 |
| Race African American/African Heritage         | 2      | 3      | 5  |
| Race American Indian or Alaskan Native         | 11     | 15     | 26 |

## End points

### End points reporting groups

|  |                    |
|--|--------------------|
| Reporting group title  | Placebo            |
| Reporting group description:   |                    |
| Participants received saline infusion (placebo) intravenously monthly for 48 weeks on a background of standard of care                                   |                    |
| Reporting group title  | Belimumab 10 mg/kg |
| Reporting group description:   |                    |
| Participants received 10 milligrams per kilograms (mg/kg) reconstituted solution intravenously monthly for 48 weeks on a background of standard of care. |                    |

### Primary: Percentage of participants with SLE Responder Index (SRI) response at Week 52

|   |   |
|---|---|
| End point title   | Percentage of participants with SLE Responder Index (SRI) response at Week 52 |
| End point description:  |   |
| SRI response is defined as $\geq 4$ point reduction, from Baseline in safety of estrogen in lupus national assessment (SELENA) systemic lupus erythematosus disease activity index (SLEDAI) score, no worsening (increase of $<0.30$ points from Baseline) in physician's global assessment (PGA) and no new British Isles Lupus Assessment Group of SLE clinics (BILAG) A organ domain score or 2 new BILAG B organ domain scores compared with Baseline. Analysis was performed using a logistic regression model for the comparison between belimumab and placebo with covariates treatment group, Baseline SELENA SLEDAI score ( $\leq 12$ vs. $\geq 13$ ). Percentage of participants with SRI response at Week 52 of Part A were reported. Intent-to-Treat Population comprised of all participants who were randomized and treated with at least one dose of study agent in Part A. One participant had missing data at Baseline and therefore, could not be included in the analysis. |   |
| End point type  | Primary   |
| End point timeframe:  |   |
| Week 52   |   |

| End point values                  | Placebo           | Belimumab 10 mg/kg |  |  |
|-----------------------------------|-------------------|--------------------|--|--|
| Subject group type                | Reporting group   | Reporting group    |  |  |
| Number of subjects analysed       | 39 <sup>[1]</sup> | 53 <sup>[2]</sup>  |  |  |
| Units: Percentage of participants |                   |                    |  |  |
| number (not applicable)           |                   |                    |  |  |
| Percentage of participants        | 43.6              | 52.8               |  |  |

Notes:

[1] - Intent-to-Treat Population

[2] - Intent-to-Treat Population

### Statistical analyses

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

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 92              |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority     |
| Parameter estimate                      | Odds ratio (OR) |
| Point estimate                          | 1.49            |
| Confidence interval                     |                 |
| level                                   | 95 %            |
| sides                                   | 2-sided         |
| lower limit                             | 0.64            |
| upper limit                             | 3.46            |

**Secondary: Percentage of participants meeting Pediatric Rheumatology International Trials Organization (PRINTO)/ American College of Rheumatology (ACR) Juvenile SLE Response Evaluation criteria for improvement in juvenile SLE at Week 52 using definition 1 and 2**

|                 |  |
|-----------------|--|
| End point title | Percentage of participants meeting Pediatric Rheumatology International Trials Organization (PRINTO)/ American College of Rheumatology (ACR) Juvenile SLE Response Evaluation criteria for improvement in juvenile SLE at Week 52 using definition 1 and 2 |
|-----------------|--|

End point description:

Percentage of participants meeting PRINTO/ACR Juvenile SLE Response Evaluation criteria for improvement in juvenile SLE using two different PRINTO/ACR Juvenile SLE Response Evaluation definitions of improvement that is Definition 1: At least 50% improvement in any 2 of 5 endpoints below and no more than 1 of the remaining worsening by more than 30% and Definition 2: At least 30% improvement in 3 of 5 endpoints below and no more than 1 of the remaining worsening more than 30%. Endpoints were: 1. Percent change in Parent's Global Assessment (ParentGA) at Week 52, 2. Percent change in PGA at Week 52, 3. Percent change in SELENA SLEDAI score at Week 52, 4. Percent change in Pediatric Quality of Life Inventory (PedsQL) physical functioning domain at Week 52, 5. Percent change in 24 hour proteinuria at Week 52 (gram/24hour equivalent by spot urine protein to creatinine ratio).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 52

| End point values                  | Placebo           | Belimumab 10 mg/kg |  |  |
|-----------------------------------|-------------------|--------------------|--|--|
| Subject group type                | Reporting group   | Reporting group    |  |  |
| Number of subjects analysed       | 40 <sup>[3]</sup> | 53 <sup>[4]</sup>  |  |  |
| Units: Percentage of participants |                   |                    |  |  |
| number (not applicable)           |                   |                    |  |  |
| Definition 1                      | 35.0              | 60.4               |  |  |
| Definition 2                      | 27.5              | 52.8               |  |  |

Notes:

[3] - Intent-to-Treat Population

[4] - Intent-to-Treat Population

**Statistical analyses**

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Definition 1



|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Belimumab 10 mg/kg |
| Number of subjects included in analysis | 93                           |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | superiority                  |
| Parameter estimate                      | Odds ratio (OR)              |
| Point estimate                          | 2.74                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 1.15                         |
| upper limit                             | 6.54                         |

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2       |
| Statistical analysis description:       |                              |
| Definition 2                            |                              |
| Comparison groups                       | Placebo v Belimumab 10 mg/kg |
| Number of subjects included in analysis | 93                           |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | superiority                  |
| Parameter estimate                      | Odds ratio (OR)              |
| Point estimate                          | 2.92                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 1.19                         |
| upper limit                             | 7.17                         |

## Secondary: Percent change from Baseline in ParentGA at Week 52

|   |   |
|---|---|
| End point title   | Percent change from Baseline in ParentGA at Week 52 |
| End point description:  |   |
| ParentGA assesses the participant's overall well-being at the moment rated on a 21-numbered circle visual analog scale (VAS; 0 - very well, 10 - very poorly). Baseline was defined as measurements at Day 0. Percent change from Baseline was calculated by subtracting the Baseline value from value at Week 52 divided by the Baseline value X 100. Last Observation Carried Forward (LOCF) was used. Eight participants had a score of zero at Baseline and therefore, could not be included in the analysis. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Baseline (Day 0) and Week 52  |   |

| End point values              | Placebo                 | Belimumab 10 mg/kg       |  |  |
|-------------------------------|-------------------------|--------------------------|--|--|
| Subject group type            | Reporting group         | Reporting group          |  |  |
| Number of subjects analysed   | 38 <sup>[5]</sup>       | 47 <sup>[6]</sup>        |  |  |
| Units: Percent change         |                         |                          |  |  |
| median (full range (min-max)) |                         |                          |  |  |
| Percent change                | -23.61 (-95.0 to 600.0) | -53.85 (-100.0 to 900.0) |  |  |

Notes:

[5] - Intent-to-Treat Population

[6] - Intent-to-Treat Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent change from Baseline in PGA at Week 52

|                 |  |
|-----------------|--|
| End point title | Percent change from Baseline in PGA at Week 52 |
|-----------------|--|

End point description:

The PGA is a 10 centimeter (cm) visual analogue scale (VAS), anchored at 0 (none) and 3 (severe), designed for the physician to indicate the participant's overall disease activity at a particular visit as part of the validated SELENA SLEDAI index. Primary investigator or a subinvestigator scored the PGA for the participant, and same person evaluated the participant each time. Baseline was defined as measurements at Day 0. Percent change from Baseline was calculated by subtracting the Baseline value from value at Week 52 divided by the Baseline value X 100. LOCF was used.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 0) and Week 52

| End point values                     | Placebo             | Belimumab 10 mg/kg  |  |  |
|--------------------------------------|---------------------|---------------------|--|--|
| Subject group type                   | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed          | 40 <sup>[7]</sup>   | 53 <sup>[8]</sup>   |  |  |
| Units: Percent change                |                     |                     |  |  |
| arithmetic mean (standard deviation) |                     |                     |  |  |
| Percent change                       | -48.802 (± 42.0423) | -56.525 (± 43.7939) |  |  |

Notes:

[7] - Intent-to-Treat Population

[8] - Intent-to-Treat Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent change from Baseline in SELENA SLEDAI at Week 52

|                 |  |
|-----------------|--|
| End point title | Percent change from Baseline in SELENA SLEDAI at Week 52 |
|-----------------|--|

End point description:

The SELENA SLEDAI score is a weighted index for assessing SLE disease activity in which signs and symptoms, laboratory tests and physician's assessment for each of 9 organ system were given a weighted score and summed if present at the time of the visit or in the preceding 10 days. A SELENA SLEDAI score of 0 would suggest no lupus activity; while a score of 105 is the maximum calculable if all items were scored as being present from active lupus. A decrease of 4 points or more equates to a

clinically meaningful improvement. Baseline was defined as measurements at Day 0. Percent change from Baseline was calculated by subtracting the Baseline value from value at Week 52 divided by the Baseline value X 100. One participant had missing data at Baseline and therefore, could not be included in the analysis.

|                              |           |
|------------------------------|-----------|
| End point type               | Secondary |
| End point timeframe:         |           |
| Baseline (Day 0) and Week 52 |           |

| End point values                     | Placebo           | Belimumab 10 mg/kg |  |  |
|--------------------------------------|-------------------|--------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group    |  |  |
| Number of subjects analysed          | 39 <sup>[9]</sup> | 53 <sup>[10]</sup> |  |  |
| Units: Percent change                |                   |                    |  |  |
| arithmetic mean (standard deviation) |                   |                    |  |  |
| Percent change                       | -38.0 (± 39.50)   | -43.3 (± 43.73)    |  |  |

Notes:

[9] - Intent-to-Treat Population

[10] - Intent-to-Treat Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent change from Baseline in PedsQL Physical Functioning Domain Score at Week 52

|                 |   |
|-----------------|---|
| End point title | Percent change from Baseline in PedsQL Physical Functioning Domain Score at Week 52 |
|-----------------|---|

End point description:

The PedsQL is a generic quality of life scale validated for the pediatric population which consists of 23 items, encompassing 4 health domains: Physical Functioning (8 items), Emotional Functioning (5 items), Social Functioning (5 items), and School Functioning (5 items). From the raw scores of the 23 items, a total summary score and individual domain scores can be calculated. The total and domain scores are each transformed on a 0 to 100 score with higher scores indicating higher quality of life. For Physical Functioning Domain scale, score was from 0 to 100 where, 0 indicates lower quality of life and 100 indicates greater quality of life. Baseline was defined as measurements at Day 0. Percent change from Baseline was calculated by subtracting the Baseline value from value at Week 52 divided by the Baseline Value X 100. LOCF was used.

|                              |           |
|------------------------------|-----------|
| End point type               | Secondary |
| End point timeframe:         |           |
| Baseline (Day 0) and Week 52 |           |

| End point values              | Placebo            | Belimumab 10 mg/kg |  |  |
|-------------------------------|--------------------|--------------------|--|--|
| Subject group type            | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed   | 40 <sup>[11]</sup> | 53 <sup>[12]</sup> |  |  |
| Units: Percent change         |                    |                    |  |  |
| median (full range (min-max)) |                    |                    |  |  |
| Percent change                | 12.5 (-53 to 575)  | 10.5 (-100 to 280) |  |  |

Notes:

[11] - Intent-to-Treat Population

[12] - Intent-to-Treat Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percent change from Baseline in proteinuria at Week 52

|                 |  |
|-----------------|--|
| End point title | Percent change from Baseline in proteinuria at Week 52 |
|-----------------|--|

End point description:

Percent change from Baseline in proteinuria was calculated. The percent change from baseline to Week 52 in 24 hour proteinuria was analyzed using summary statistics and 95% confidence intervals, without any adjustment for covariates. Baseline was defined as measurements at Day 0. Percent change from Baseline was calculated by subtracting the Baseline value from value at Week 52 divided by the Baseline Value X 100. LOCF was used.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 0) and Week 52

| End point values              | Placebo                     | Belimumab 10 mg/kg            |  |  |
|-------------------------------|-----------------------------|-------------------------------|--|--|
| Subject group type            | Reporting group             | Reporting group               |  |  |
| Number of subjects analysed   | 40 <sup>[13]</sup>          | 53 <sup>[14]</sup>            |  |  |
| Units: Percent Change         |                             |                               |  |  |
| median (full range (min-max)) |                             |                               |  |  |
| Percent Change                | 7.0920 (-90.568 to 570.149) | -2.1277 (-85.073 to 1681.884) |  |  |

Notes:

[13] - Intent-to-Treat Population

[14] - Intent-to-Treat Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with a sustained SRI response

|                 |  |
|-----------------|--|
| End point title | Percentage of participants with a sustained SRI response |
|-----------------|--|

End point description:

Sustained SRI response was defined as having a response on the primary efficacy endpoint at Weeks 44, 48, and 52. Data for percentage of participants with a sustained SRI response was presented. Drop Outs and Treatment Failures were considered Non-Responders. Only those participants with data available at specific time point were analyzed.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 52 weeks

| End point values                  | Placebo            | Belimumab 10 mg/kg |  |  |
|-----------------------------------|--------------------|--------------------|--|--|
| Subject group type                | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed       | 39 <sup>[15]</sup> | 53 <sup>[16]</sup> |  |  |
| Units: Percentage of participants |                    |                    |  |  |
| number (not applicable)           |                    |                    |  |  |
| Percentage of participants        | 41.0               | 43.4               |  |  |

Notes:

[15] - Intent-to-Treat Population

[16] - Intent-to-Treat Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants with a sustained ParentGA response

|                 |   |
|-----------------|---|
| End point title | Percentage of participants with a sustained ParentGA response |
|-----------------|---|

End point description:

Sustained ParentGA response was defined as having >0.7 improvement at Weeks 44, 48, and 52 compared at Baseline. Data for percentage of participants with a sustained ParentGA response was presented. Thirteen participants had a score of ≤0.7 at Baseline and therefore, could not be included in the analysis.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 52 weeks

| End point values                  | Placebo            | Belimumab 10 mg/kg |  |  |
|-----------------------------------|--------------------|--------------------|--|--|
| Subject group type                | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed       | 36 <sup>[17]</sup> | 44 <sup>[18]</sup> |  |  |
| Units: Percentage of Participants |                    |                    |  |  |
| number (not applicable)           |                    |                    |  |  |
| Percentage of Participants        | 33.3               | 59.1               |  |  |

Notes:

[17] - Intent-to-Treat Population

[18] - Intent-to-Treat Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs)

|                 |  |
|-----------------|--|
| End point title | Number of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) |
|-----------------|--|

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporarily associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any

untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment or all events of possible drug-induced liver injury with hyperbilirubinemia were categorized as SAE. Number of participants with AEs and SAEs have been reported.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 60 weeks       |           |

| End point values            | Placebo            | Belimumab 10 mg/kg |  |  |
|-----------------------------|--------------------|--------------------|--|--|
| Subject group type          | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed | 40 <sup>[19]</sup> | 53 <sup>[20]</sup> |  |  |
| Units: Participants         |                    |                    |  |  |
| AEs                         | 33                 | 42                 |  |  |
| SAEs                        | 14                 | 9                  |  |  |

Notes:

[19] - Intent-to-Treat Population

[20] - Intent-to-Treat Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum concentration at steady state (C<sub>max</sub>, ss) and minimum concentration at steady state (C<sub>min</sub>, ss)

|                 |   |
|-----------------|---|
| End point title | Maximum concentration at steady state (C <sub>max</sub> , ss) and minimum concentration at steady state (C <sub>min</sub> , ss) <sup>[21]</sup> |
|-----------------|---|

End point description:

The pharmacokinetic (PK) population comprised all participants included in the As- Treated population for whom at least one post belimumab treatment PK sample was obtained and analyzed. The PK model was fitted to the observed serum concentration-time data. The maximum (C<sub>max</sub>) and minimum (C<sub>min</sub>) concentrations reported in this table are model derived values at ss, assuming a 10 mg/kg dose administered once every 28 days.

|   |           |
|---|-----------|
| End point type                          | Secondary |
| End point timeframe:                    |           |
| 28-days dosing interval at steady state |           |

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

| End point values                                    | Belimumab 10 mg/kg |  |  |  |
|---|--------------------|--|--|--|
| Subject group type                                  | Reporting group    |  |  |  |
| Number of subjects analysed                         | 53 <sup>[22]</sup> |  |  |  |
| Units: Micrograms per milliliter                    |                    |  |  |  |
| geometric mean (geometric coefficient of variation) |                    |  |  |  |
| C <sub>max</sub> , ss                               | 315 (± 31.2)       |  |  |  |
| C <sub>min</sub> , ss                               | 50 (± 68.3)        |  |  |  |

Notes:

[22] - PK Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Area under curve of Belimumab at steady state (AUC, ss)

|                 |   |
|-----------------|---|
| End point title | Area under curve of Belimumab at steady state (AUC, ss) <sup>[23]</sup> |
|-----------------|---|

End point description:

The PK model was fitted to the observed serum concentration-time data. The AUC values reported in this table are model derived values at ss, assuming a 10 mg/kg dose administered once every 28 days.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

28-days dosing interval at steady state

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

|   |                    |  |  |  |
|---|--------------------|--|--|--|
| <b>End point values</b>                             | Belimumab 10 mg/kg |  |  |  |
| Subject group type                                  | Reporting group    |  |  |  |
| Number of subjects analysed                         | 53 <sup>[24]</sup> |  |  |  |
| Units: Micrograms per milliliter                    |                    |  |  |  |
| geometric mean (geometric coefficient of variation) |                    |  |  |  |
| Micrograms per milliliter                           | 3012 (± 43.2)      |  |  |  |

Notes:

[24] - PK Population

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious AEs were collected from start of the study to the follow up visit (Up to 60 weeks).

Adverse event reporting additional description:

Intent-to-Treat Population was used to collect adverse events.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Belimumab 10 mg/kg |
|-----------------------|--------------------|

Reporting group description:

Participants received 10 milligrams per kilograms (mg/kg) reconstituted solution intravenously monthly for 48 weeks on a background of standard of care.

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Participants received saline infusion (placebo) intravenously monthly for 48 weeks on a background of standard of care

| Serious adverse events                               | Belimumab 10 mg/kg | Placebo          |  |
|--|--------------------|------------------|--|
| Total subjects affected by serious adverse events    |                    |                  |  |
| subjects affected / exposed                          | 9 / 53 (16.98%)    | 14 / 40 (35.00%) |  |
| number of deaths (all causes)                        | 0                  | 1                |  |
| number of deaths resulting from adverse events       |                    |                  |  |
| General disorders and administration site conditions |                    |                  |  |
| Chest pain   |                    |                  |  |
| subjects affected / exposed                          | 0 / 53 (0.00%)     | 1 / 40 (2.50%)   |  |
| occurrences causally related to treatment / all      | 0 / 0              | 1 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0              | 0 / 0            |  |
| Pyrexia  |                    |                  |  |
| subjects affected / exposed                          | 0 / 53 (0.00%)     | 1 / 40 (2.50%)   |  |
| occurrences causally related to treatment / all      | 0 / 0              | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0              | 0 / 0            |  |
| Respiratory, thoracic and mediastinal disorders      |                    |                  |  |
| Pleural effusion                                     |                    |                  |  |



|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Psychiatric disorders                           |                |                |  |
| Major depression                                |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Suicidal ideation                               |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Suicide attempt                                 |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Injury, poisoning and procedural complications  |                |                |  |
| Ligament sprain                                 |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac disorders                               |                |                |  |
| Pericardial effusion                            |                |                |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) | 0 / 40 (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                        |                |                |  |
| Headache  |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 2 / 40 (5.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Idiopathic intracranial hypertension            |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 53 (1.89%) | 0 / 40 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Post herpetic neuralgia                         |                |                |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) | 0 / 40 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Blood and lymphatic system disorders            |                |                |  |
| Anaemia   |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Thrombocytopenia                                |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Eye disorders                                   |                |                |  |
| Eye swelling                                    |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Retinal vasculitis                              |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                      |                |                |  |
| Pancreatitis acute                              |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| Vasculitis gastrointestinal                     |                |                |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) | 0 / 40 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Vomiting  |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatobiliary disorders                         |                |                |  |
| Hypertransaminaemia                             |                |                |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) | 0 / 40 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Skin and subcutaneous tissue disorders          |                |                |  |
| Rash  |                |                |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) | 0 / 40 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Skin lesion                                     |                |                |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) | 0 / 40 (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                     |                |                |  |
| Lupus nephritis                                 |                |                |  |
| subjects affected / exposed                     | 2 / 53 (3.77%) | 2 / 40 (5.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Glomerulonephritis                              |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                |                |  |
| Osteochondrosis                                 |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| SLE arthritis                                   |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Systemic lupus erythematosus                    |                |                |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) | 0 / 40 (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                     |                |                |  |
| Herpes zoster                                   |                |                |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Abscess limb                                    |                |                |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) | 0 / 40 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Epiglottitis                                    |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastroenteritis                                 |                |                |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) | 0 / 40 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatitis A                                     |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Influenza                                       |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia                                       |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| <b>Vulval abscess</b>                           |                |                |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) | 0 / 40 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| <b>Metabolism and nutrition disorders</b>       |                |                |  |
| <b>Fluid overload</b>                           |                |                |  |
| subjects affected / exposed                     | 0 / 53 (0.00%) | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                            | Belimumab 10 mg/kg | Placebo          |  |
|--|--------------------|------------------|--|
| <b>Total subjects affected by non-serious adverse events</b> |                    |                  |  |
| subjects affected / exposed                                  | 36 / 53 (67.92%)   | 27 / 40 (67.50%) |  |
| <b>Vascular disorders</b>                                    |                    |                  |  |
| <b>Hypertension</b>  |                    |                  |  |
| subjects affected / exposed                                  | 0 / 53 (0.00%)     | 2 / 40 (5.00%)   |  |
| occurrences (all)  | 0                  | 2                |  |
| <b>General disorders and administration site conditions</b>  |                    |                  |  |
| <b>Chest pain</b>  |                    |                  |  |
| subjects affected / exposed                                  | 4 / 53 (7.55%)     | 4 / 40 (10.00%)  |  |
| occurrences (all)  | 4                  | 5                |  |
| <b>Pyrexia</b>   |                    |                  |  |
| subjects affected / exposed                                  | 2 / 53 (3.77%)     | 3 / 40 (7.50%)   |  |
| occurrences (all)  | 2                  | 10               |  |
| <b>Fatigue</b>   |                    |                  |  |
| subjects affected / exposed                                  | 1 / 53 (1.89%)     | 2 / 40 (5.00%)   |  |
| occurrences (all)  | 2                  | 4                |  |
| <b>Reproductive system and breast disorders</b>              |                    |                  |  |

|  |                     |                     |  |
|--|---------------------|---------------------|--|
| Menorrhagia<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 53 (1.89%)<br>1 | 2 / 40 (5.00%)<br>2 |  |
| Dysmenorrhoea<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 53 (0.00%)<br>0 | 2 / 40 (5.00%)<br>5 |  |
| Respiratory, thoracic and mediastinal disorders                                      |                     |                     |  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)                        | 4 / 53 (7.55%)<br>4 | 3 / 40 (7.50%)<br>3 |  |
| Cough<br>subjects affected / exposed<br>occurrences (all)                            | 3 / 53 (5.66%)<br>4 | 3 / 40 (7.50%)<br>3 |  |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)               | 3 / 53 (5.66%)<br>3 | 2 / 40 (5.00%)<br>2 |  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 53 (0.00%)<br>0 | 2 / 40 (5.00%)<br>2 |  |
| Psychiatric disorders  |                     |                     |  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 53 (0.00%)<br>0 | 3 / 40 (7.50%)<br>3 |  |
| Suicidal ideation<br>subjects affected / exposed<br>occurrences (all)                | 0 / 53 (0.00%)<br>0 | 2 / 40 (5.00%)<br>3 |  |
| Investigations   |                     |                     |  |
| Transaminases increased<br>subjects affected / exposed<br>occurrences (all)          | 3 / 53 (5.66%)<br>3 | 1 / 40 (2.50%)<br>1 |  |
| Blood immunoglobulin G decreased<br>subjects affected / exposed<br>occurrences (all) | 1 / 53 (1.89%)<br>1 | 2 / 40 (5.00%)<br>2 |  |
| Nervous system disorders   |                     |                     |  |
| Headache   |                     |                     |  |

|  |                      |                        |  |
|--|----------------------|------------------------|--|
| subjects affected / exposed<br>occurrences (all) | 7 / 53 (13.21%)<br>9 | 10 / 40 (25.00%)<br>17 |  |
| Blood and lymphatic system disorders             |                      |                        |  |
| Leukopenia                                       |                      |                        |  |
| subjects affected / exposed                      | 2 / 53 (3.77%)       | 3 / 40 (7.50%)         |  |
| occurrences (all)                                | 2                    | 3                      |  |
| Neutropenia                                      |                      |                        |  |
| subjects affected / exposed                      | 3 / 53 (5.66%)       | 1 / 40 (2.50%)         |  |
| occurrences (all)                                | 4                    | 1                      |  |
| Anaemia  |                      |                        |  |
| subjects affected / exposed                      | 0 / 53 (0.00%)       | 3 / 40 (7.50%)         |  |
| occurrences (all)                                | 0                    | 3                      |  |
| Gastrointestinal disorders                       |                      |                        |  |
| Diarrhoea  |                      |                        |  |
| subjects affected / exposed                      | 7 / 53 (13.21%)      | 3 / 40 (7.50%)         |  |
| occurrences (all)                                | 9                    | 5                      |  |
| Nausea   |                      |                        |  |
| subjects affected / exposed                      | 5 / 53 (9.43%)       | 3 / 40 (7.50%)         |  |
| occurrences (all)                                | 6                    | 4                      |  |
| Abdominal pain                                   |                      |                        |  |
| subjects affected / exposed                      | 3 / 53 (5.66%)       | 3 / 40 (7.50%)         |  |
| occurrences (all)                                | 4                    | 3                      |  |
| Vomiting   |                      |                        |  |
| subjects affected / exposed                      | 2 / 53 (3.77%)       | 3 / 40 (7.50%)         |  |
| occurrences (all)                                | 2                    | 4                      |  |
| Dyspepsia  |                      |                        |  |
| subjects affected / exposed                      | 1 / 53 (1.89%)       | 3 / 40 (7.50%)         |  |
| occurrences (all)                                | 1                    | 4                      |  |
| Skin and subcutaneous tissue disorders           |                      |                        |  |
| Rash   |                      |                        |  |
| subjects affected / exposed                      | 3 / 53 (5.66%)       | 1 / 40 (2.50%)         |  |
| occurrences (all)                                | 3                    | 1                      |  |
| Renal and urinary disorders                      |                      |                        |  |
| Lupus nephritis                                  |                      |                        |  |
| subjects affected / exposed                      | 1 / 53 (1.89%)       | 2 / 40 (5.00%)         |  |
| occurrences (all)                                | 1                    | 2                      |  |
| Musculoskeletal and connective tissue            |                      |                        |  |

|                                   |                 |                 |  |
|-----------------------------------|-----------------|-----------------|--|
| disorders                         |                 |                 |  |
| Arthralgia                        |                 |                 |  |
| subjects affected / exposed       | 3 / 53 (5.66%)  | 4 / 40 (10.00%) |  |
| occurrences (all)                 | 4               | 10              |  |
| Back pain                         |                 |                 |  |
| subjects affected / exposed       | 2 / 53 (3.77%)  | 3 / 40 (7.50%)  |  |
| occurrences (all)                 | 3               | 4               |  |
| Pain in extremity                 |                 |                 |  |
| subjects affected / exposed       | 2 / 53 (3.77%)  | 2 / 40 (5.00%)  |  |
| occurrences (all)                 | 3               | 2               |  |
| Joint swelling                    |                 |                 |  |
| subjects affected / exposed       | 0 / 53 (0.00%)  | 2 / 40 (5.00%)  |  |
| occurrences (all)                 | 0               | 2               |  |
| Infections and infestations       |                 |                 |  |
| Nasopharyngitis                   |                 |                 |  |
| subjects affected / exposed       | 9 / 53 (16.98%) | 8 / 40 (20.00%) |  |
| occurrences (all)                 | 14              | 11              |  |
| Upper respiratory tract infection |                 |                 |  |
| subjects affected / exposed       | 6 / 53 (11.32%) | 8 / 40 (20.00%) |  |
| occurrences (all)                 | 8               | 8               |  |
| Herpes zoster                     |                 |                 |  |
| subjects affected / exposed       | 4 / 53 (7.55%)  | 2 / 40 (5.00%)  |  |
| occurrences (all)                 | 6               | 2               |  |
| Pharyngitis                       |                 |                 |  |
| subjects affected / exposed       | 3 / 53 (5.66%)  | 3 / 40 (7.50%)  |  |
| occurrences (all)                 | 4               | 3               |  |
| Gastroenteritis                   |                 |                 |  |
| subjects affected / exposed       | 2 / 53 (3.77%)  | 3 / 40 (7.50%)  |  |
| occurrences (all)                 | 3               | 3               |  |
| Urinary tract infection           |                 |                 |  |
| subjects affected / exposed       | 1 / 53 (1.89%)  | 4 / 40 (10.00%) |  |
| occurrences (all)                 | 2               | 8               |  |
| Bronchitis                        |                 |                 |  |
| subjects affected / exposed       | 1 / 53 (1.89%)  | 2 / 40 (5.00%)  |  |
| occurrences (all)                 | 1               | 2               |  |
| Conjunctivitis                    |                 |                 |  |



|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 53 (0.00%) | 2 / 40 (5.00%) |  |
| occurrences (all)           | 0              | 4              |  |
| Influenza                   |                |                |  |
| subjects affected / exposed | 0 / 53 (0.00%) | 2 / 40 (5.00%) |  |
| occurrences (all)           | 0              | 2              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 21 February 2012 | Amendment No. 1: Updated Medical Monitor information. Additional pharmacokinetic samples were taken for children not in Cohort 1 or 2. Addition of three hours observation post infusion was done. Time and Events Table including immunogenicity, vaccine titer procedure and physical assessments was updated. Other Secondary Endpoints were updated. Study Conclusion criteria was added. Minor typographical errors corrected.  |
| 31 January 2013  | Amendment No. 2: Included the following changes: Exclusion Criterion #1 excludes if B cell targeted therapy is within 1 year of Day 0 and Exclusion #23 omitting HCV confirmation RIBA assay. Extra visits for collection of large blood sample collection were Allowed. Addition of 3 hours observation post infusion for first 3 infusions in Part B. The investigational product may be delivered in either 100 mL or 250mL of saline. Minor typographical errors corrected.  |
| 18 February 2014 | Amendment No. 3: Included the following changes: Updated safety information on PML and Delayed Hypersensitivity Reaction. Changed the exclusion for high dose steroid use from 90 days to 60 days prior to Baseline. Clarification of treatment failure and study withdrawal criteria and Clarification of procedure for destruction of investigational product and used vials was updated. Added a home pregnancy test and follow up phone call at 16 Week post last dose. Extended visit window in Part B and Part C. Minor typographical and formatting errors corrected.   |
| 03 November 2014 | Amendment No. 4: Changed the Screening inclusion criterion SELENA SLEDAI to $\geq 6$ . Changed randomization strata for Cohort 3 to stratification by age and SELENA SLEDAI 6-12 and $\geq 13$ . Added requirement that 50% of participants were recruited with SS score of $\geq 8$ . Changed exclusion #4 intravenous (IV) cyclophosphamide within 60 days of Day 0. Added allowance for stable Grade 3 lymphopenia with exclusion #24. Updated GSK liver chemistry stopping criteria and added of study drug restart criteria. Clarification of laboratory tests needed to complete SS and BILAG assessments. Added immunogenicity testing in Part C. Clarification of NSAIDs use in Part A. Minor typographical errors corrected.  |
| 22 April 2015    | Amendment No. 5: Country Specific Amendment for Russian Federation: Restart of study treatment after liver event is not applicable to Investigator sites in Russia. Updated phone number of back-up Medical Monitor.   |
| 12 December 2016 | Amendment No. 6: Updated Author information, Medical Monitor information and site address. Total study target amended to 'at least 70' from 100 participants. Estimates for sample size re-estimation add to the protocol. Target for participants less than 13 years old amended to at least 14 from 20. Target for Cohort 2 amended from 12 to "at least 10". PedsQL amended in time and events table such that it is instructed to be taken at Day 0. Anti-dsDNA; C3/C4 added to time and events table for 6 month visits in Part B. Deleted immunogenicity sample collection once a subject has left the study. Collect additional PK samples in the participants in Japan at the first 12 week and 6 month visit in Part B. Minor typographical errors corrected. Clarification of reporting of AEs, SAEs, and AESI. Change in Part C from "non-belimumab phase" to "safety follow up phase". |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported