



Clinical trial results:

A Phase 3/4, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, 52-Week Study to Evaluate the Efficacy and Safety of Belimumab (HGS1006) in Adult Subjects of Black Race With Systemic Lupus Erythematosus (SLE)

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2011-005672-42 |
| Trial protocol | GB |
| Global end of trial date | 28 January 2019 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v2 (current) |
| This version publication date | 07 February 2020 |
| First version publication date | 03 July 2019 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 115471 |
|-----------------------|--------|

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 05 July 2019 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-----------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 28 January 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the efficacy of belimumab in adult SLE participants of self-identified black race.
- To evaluate the safety and tolerability of belimumab in adult SLE participants of self-identified black race.

Protection of trial subjects:

Participants remained under clinical supervision for 3 hours after completion of the first 2 infusions.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 19 February 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 248 |
| Country: Number of subjects enrolled | Brazil: 178 |
| Country: Number of subjects enrolled | Colombia: 42 |
| Country: Number of subjects enrolled | South Africa: 19 |
| Country: Number of subjects enrolled | United Kingdom: 12 |
| Country: Number of subjects enrolled | France: 4 |
| Worldwide total number of subjects | 503 |
| EEA total number of subjects | 16 |

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) | 495 |

| | |
|---------------------|---|
| From 65 to 84 years | 8 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study evaluated the efficacy and safety of belimumab compared with placebo in adult participants with Systemic Lupus Erythematosus (SLE). This was a multicenter study conducted at United States (88 centers), United Kingdom (6), South Africa (5), France (4), Columbia (6) and Brazil (18).

Pre-assignment

Screening details:

A total of 503 participants were randomized of which 496 received at-least one dose of study medication during double-blinded phase (7 participants were randomized but not treated as they were randomized in error). A total of 359 out of 373 participants who completed double-blinded phase opted to continue optional open-label (OL) extension phase.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Double-blinded (Up to Week 52) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Investigator, Monitor, Subject |

Arms

| | |
|------------------------------|-------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo to Belimumab 10 mg/kg |

Arm description:

In double-blinded (DB) phase, participants received matching placebo to belimumab administered as intravenous (IV) infusion plus standard of care through 52 weeks. In OL phase, participants received belimumab 10 milligram per kilogram (mg/kg) administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Placebo was supplied in a 20 milliliters (mL) vial and prepared as a sterile and lyophilized product. Upon reconstitution with 4.8 mL sterile water for injection (SWFI), each vial contained 0.16 milligrams (mg)/milliliter (mL) citric acid, 2.7 mg/mL sodium citrate, 80 mg/mL sucrose, 0.4 mg/mL polysorbate 80, potential of hydrogen ions (pH) 6.5. Each lyophilized vial was for single use.

| | |
|------------------|--|
| Arm title | Belimumab 10 mg/kg to Belimumab 10 mg/kg |
|------------------|--|

Arm description:

In DB phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care through 52 weeks. In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Belimumab 10 mg/kg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Belimumab was supplied in a 20 mL vial containing 400 mg belimumab as a sterile, lyophilized product. Upon reconstitution with SWFI, each vial contained 80 mg/mL belimumab in 0.16 mg/mL citric acid, 2.7 mg/mL sodium citrate, 80 mg/mL sucrose, 0.4 mg/mL polysorbate 80, pH 6.5. Each lyophilized vial was

for single use.

| Number of subjects in period 1^[1] | Placebo to Belimumab 10 mg/kg | Belimumab 10 mg/kg to Belimumab 10 mg/kg |
|---|-------------------------------|--|
| Started | 165 | 331 |
| Completed | 121 | 252 |
| Not completed | 44 | 79 |
| Adverse event, serious fatal | - | 1 |
| Consent withdrawn by subject | 10 | 14 |
| Physician decision | 9 | 12 |
| Site Closed | 3 | 5 |
| Adverse event, non-fatal | 10 | 18 |
| Lost to follow-up | 1 | 8 |
| Lack of efficacy | 9 | 15 |
| Protocol deviation | 2 | 6 |

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 503 participants were randomized of which 496 received at-least one dose of study medication during double-blinded phase (7 participants were randomized but not treated as they were randomized in error).

Period 2

| | |
|------------------------------|---------------------------------|
| Period 2 title | Open-label (Week 52 to Week 76) |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo to Belimumab 10 mg/kg |

Arm description:

In double-blinded (DB) phase, participants received matching placebo to belimumab administered as intravenous (IV) infusion plus standard of care through 52 weeks. In OL phase, participants received belimumab 10 milligram per kilogram (mg/kg) administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Belimumab 10 mg/kg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Belimumab was supplied in a 20 mL vial containing 400 mg belimumab as a sterile, lyophilized product. Upon reconstitution with SWFI, each vial contained 80 mg/mL belimumab in 0.16 mg/mL citric acid, 2.7 mg/mL sodium citrate, 80 mg/mL sucrose, 0.4 mg/mL polysorbate 80, pH 6.5. Each lyophilized vial was for single use.

| | |
|------------------|--|
| Arm title | Belimumab 10 mg/kg to Belimumab 10 mg/kg |
|------------------|--|

Arm description:

In DB phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care through 52 weeks. In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Belimumab 10 mg/kg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Belimumab was supplied in a 20 mL vial containing 400 mg belimumab as a sterile, lyophilized product. Upon reconstitution with SWFI, each vial contained 80 mg/mL belimumab in 0.16 mg/mL citric acid, 2.7 mg/mL sodium citrate, 80 mg/mL sucrose, 0.4 mg/mL polysorbate 80, pH 6.5. Each lyophilized vial was for single use.

| Number of subjects in period 2^[2] | Placebo to Belimumab 10 mg/kg | Belimumab 10 mg/kg to Belimumab 10 mg/kg |
|---|-------------------------------|--|
| Started | 117 | 242 |
| Completed | 107 | 220 |
| Not completed | 10 | 22 |
| Consent withdrawn by subject | 5 | 2 |
| Physician decision | 1 | 4 |
| Site Closed | 2 | 8 |
| Adverse event, non-fatal | 1 | - |
| Lost to follow-up | 1 | 4 |
| Lack of efficacy | - | 2 |
| Protocol deviation | - | 2 |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: A total of 503 participants were randomized of which 496 received at-least one dose of study medication during double-blinded phase (7 participants were randomized but not treated as they were randomized in error).

Baseline characteristics

Reporting groups

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

Reporting group description:

In double-blinded (DB) phase, participants received matching placebo to belimumab administered as intravenous (IV) infusion plus standard of care through 52 weeks. In OL phase, participants received belimumab 10 milligram per kilogram (mg/kg) administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76.

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

Reporting group description:

In DB phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care through 52 weeks. In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76.

| Reporting group values | Placebo to Belimumab 10 mg/kg | Belimumab 10 mg/kg to Belimumab 10 mg/kg | Total |
|---|-------------------------------|--|-------|
| Number of subjects | 165 | 331 | 496 |
| Age categorical Units: Subjects | | | |
| Total Participants | 165 | 331 | 496 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 39.5 | 38.7 | |
| standard deviation | ± 12.06 | ± 11.00 | - |
| Sex: Female, Male Units: Participants | | | |
| Female | 158 | 322 | 480 |
| Male | 7 | 9 | 16 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Black or African American | 165 | 331 | 496 |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Placebo to Belimumab 10 mg/kg |
| Reporting group description: In double-blinded (DB) phase, participants received matching placebo to belimumab administered as intravenous (IV) infusion plus standard of care through 52 weeks. In OL phase, participants received belimumab 10 milligram per kilogram (mg/kg) administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Reporting group title | Belimumab 10 mg/kg to Belimumab 10 mg/kg |
| Reporting group description: In DB phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care through 52 weeks. In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Reporting group title | Placebo to Belimumab 10 mg/kg |
| Reporting group description: In double-blinded (DB) phase, participants received matching placebo to belimumab administered as intravenous (IV) infusion plus standard of care through 52 weeks. In OL phase, participants received belimumab 10 milligram per kilogram (mg/kg) administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Reporting group title | Belimumab 10 mg/kg to Belimumab 10 mg/kg |
| Reporting group description: In DB phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care through 52 weeks. In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Subject analysis set title | Placebo (DB Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In DB phase, participants received matching placebo to belimumab administered as IV infusion plus standard of care through 52 weeks. | |
| Subject analysis set title | Belimumab 10 mg/kg (DB Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In DB phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care through 52 weeks. | |
| Subject analysis set title | Placebo to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Subject analysis set title | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Subject analysis set title | Placebo to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days through Week 52 to Week 76. | |
| Subject analysis set title | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |

| | |
|---|---|
| Subject analysis set title | Placebo to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Subject analysis set title | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Subject analysis set title | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Subject analysis set title | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Subject analysis set title | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Subject analysis set title | Placebo to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Subject analysis set title | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days through Week 52 to Week 76. | |
| Subject analysis set title | Belimumab 10 mg/kg (DB Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| In DB phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care through 52 weeks. | |
| Subject analysis set title | Placebo to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Subject analysis set title | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Subject analysis set title | Placebo (DB Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| In DB phase, participants received matching placebo to belimumab administered as IV infusion plus standard of care through 52 weeks. | |

| | |
|--|---|
| Subject analysis set title | Belimumab 10 mg/kg (DB Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In DB phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care through 52 weeks. | |
| Subject analysis set title | Placebo to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Subject analysis set title | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76. | |
| Subject analysis set title | Placebo (DB Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In DB phase, participants received matching placebo to belimumab administered as IV infusion plus standard of care through 52 weeks. | |
| Subject analysis set title | Belimumab 10 mg/kg (DB Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In DB phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care through 52 weeks. | |
| Subject analysis set title | Placebo (DB Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In DB phase, participants received matching placebo to belimumab administered as IV infusion plus standard of care through 52 weeks. | |
| Subject analysis set title | Belimumab 10 mg/kg (DB Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In DB phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care through 52 weeks. | |
| Subject analysis set title | Belimumab 10 mg/kg (DB Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In DB phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care through 52 weeks. | |
| Subject analysis set title | Belimumab 10 mg/kg (DB Phase) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: In DB phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care through 52 weeks. | |

Primary: Percentage of participants achieving a Systemic Lupus Erythematosus Responder Index (SRI) response rate with the modified Systemic Lupus Erythematosus disease activity index- 2K (SLEDAI-2K) scoring for proteinuria at Week 52 [DB Phase]

| | |
|-----------------|---|
| End point title | Percentage of participants achieving a Systemic Lupus Erythematosus Responder Index (SRI) response rate with the modified Systemic Lupus Erythematosus disease activity index- 2K (SLEDAI-2K) scoring for proteinuria at Week 52 [DB Phase] |
|-----------------|---|

End point description:

SRI response is defined as ≥ 4 point reduction, from Baseline in safety of estrogen in Lupus National Assessment (SELENA) SLEDAI [SS] score (with modified SLEDAI-2K scoring for proteinuria [PU]), 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 [ODS] or 2 new BILAG B ODS compared with Baseline. Analysis performed for comparison between belimumab and placebo with covariates treatment group, Baseline SS score, Baseline complement levels and region. The Modified Intention-To-Treat (mITT) population comprised of safety population excluding participants who had any assessment at 3 sites (202196, 202513 or 107286). One participant in the mITT

population Belimumab 10 mg/kg arm did not have a screening or Baseline PGA assessment; therefore, this participant did not contribute to the SRI/component analysis.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Week 52 | |

| End point values | Placebo (DB Phase) | Belimumab 10 mg/kg (DB Phase) | | |
|-----------------------------------|----------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 149 ^[1] | 298 ^[2] | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 41.6 | 48.7 | | |

Notes:

[1] - mITT Population

[2] - mITT Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|--|
| Comparison groups | Placebo (DB Phase) v Belimumab 10 mg/kg (DB Phase) |
| Number of subjects included in analysis | 447 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1068 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.93 |
| upper limit | 2.11 |

Primary: Percentage of participants achieving a SRI response rate with the modified SLEDAI-2K scoring for proteinuria at Week 24 of OL Phase

| | |
|-----------------|--|
| End point title | Percentage of participants achieving a SRI response rate with the modified SLEDAI-2K scoring for proteinuria at Week 24 of OL Phase ^[3] |
|-----------------|--|

End point description:

SRI response is defined as ≥ 4 point reduction, from OL Baseline in SS score (with the modified SLEDAI-2K scoring for PU), no worsening (increase of < 0.30 points from OL Baseline) in PGA and no new BILAG A ODS or 2 new BILAG B ODS compared with OL Baseline. mITT OL population comprised of Intent-to-Treat (ITT) OL population (all randomized participants who received at least one dose of OL treatment) excluding participants who had any assessment at 3 sites (202196, 202513 or 107286). For participants switching from placebo to belimumab 10 mg/kg IV in the open-label phase, Baseline was defined as the last assessment at the end of the double-blind phase (i.e. Week 52) pre-OL treatment. For participants that received belimumab 10 mg/kg IV during the double-blind phase and continued to receive belimumab 10 mg/kg IV during the open-label phase, Baseline was defined as Day 1 of the double-blind phase. Only those participants with data available at the specified data points were analyzed.

| | |
|---|---------|
| End point type | Primary |
| End point timeframe: | |
| Week 24 of OL phase (Week 76) | |
| Notes: | |
| [3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. | |
| Justification: There are no statistical data to report. | |

| End point values | Placebo to Belimumab 10 mg/kg (OL Phase) | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) | | |
|-----------------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 69 ^[4] | 208 ^[5] | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 18.8 | 73.6 | | |

Notes:

[4] - mITT OL Population

[5] - mITT OL Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with non-serious adverse events (nSAEs) and serious adverse events (SAEs) [OL Phase]

| | |
|-----------------|--|
| End point title | Number of participants with non-serious adverse events (nSAEs) and serious adverse events (SAEs) [OL Phase] ^[6] |
|-----------------|--|

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAE is defined as any untoward medical occurrence that; results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, other situations judged by physician, is associated with liver injury and impaired liver function. Number of participants who had common nSAEs ($\geq 5\%$) and any SAEs are presented. Intent-to-Treat (ITT) OL Population comprised of all randomized participants who received at least one dose of open label treatment. For Safety, participants that completed DB and OL phase, an additional 8 weeks follow-up was conducted (Week 84).

| | |
|---|---------|
| End point type | Primary |
| End point timeframe: | |
| Week 52 to Week 84 | |
| Notes: | |
| [6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. | |
| Justification: There are no statistical data to report. | |

| End point values | Placebo to Belimumab 10 mg/kg (OL Phase) | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) | | |
|-----------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 117 ^[7] | 242 ^[8] | | |
| Units: Participants | | | | |
| nSAEs | 23 | 49 | | |
| SAEs | 6 | 13 | | |

Notes:

[7] - Intent-to-Treat (ITT) OL Population

[8] - Intent-to-Treat (ITT) OL Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with severe AEs [OL Phase]

| | |
|-----------------|--|
| End point title | Number of participants with severe AEs [OL Phase] ^[9] |
|-----------------|--|

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Number of participants with severe AEs have been presented. For Safety, participants that completed DB and OL phase, an additional 8 weeks follow-up was conducted (Week 84).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 52 to Week 84

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical data to report.

| End point values | Placebo to Belimumab 10 mg/kg (OL Phase) | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) | | |
|-----------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 117 ^[10] | 242 ^[11] | | |
| Units: Participants | 10 | 9 | | |

Notes:

[10] - ITT OL Population

[11] - ITT OL Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with AEs leading to treatment discontinuation [OL Phase]

| | |
|-----------------|---|
| End point title | Number of participants with AEs leading to treatment discontinuation [OL Phase] ^[12] |
|-----------------|---|

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Number of participants with AEs leading to treatment discontinuation have been presented. For Safety, participants that completed DB and OL phase, an additional 8 weeks follow-up was conducted (Week 84).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 52 to Week 84

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical data to report.

| End point values | Placebo to Belimumab 10 mg/kg (OL Phase) | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) | | |
|-----------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 117 ^[13] | 242 ^[14] | | |
| Units: Participants | 1 | 0 | | |

Notes:

[13] - ITT OL Population

[14] - ITT OL Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with worst toxicity Grade 3 or 4 for hematology parameters [OL Phase]

| | |
|-----------------|--|
| End point title | Number of participants with worst toxicity Grade 3 or 4 for hematology parameters [OL Phase] ^[15] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of hematology parameters. The parameters assessed were activated partial thromboplastin time (APTT), hemoglobin, leukocytes, neutrophils, platelets and prothrombin time. Grading was assigned as mild (Grade 1), moderate (grade 2), severe (Grade 3) and potentially life-threatening (Grade 4) according to Division of Microbiology and Infectious Diseases (DMID [Modified from DMID Adult Toxicity Tables, 2001]) AE Severity Grading. Number of participants with worst toxicity Grade 3 or 4 for hematology parameters have been presented. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). For Safety, participants that completed DB and OL phase, an additional 8 weeks follow-up was conducted (Week 84).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 52 to Week 84

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical data to report.

| End point values | Placebo to Belimumab 10 mg/kg (OL Phase) | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) | | |
|---------------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 115 ^[16] | 235 ^[17] | | |
| Units: Participants | | | | |
| APTT, Grade 3, n=93,203 | 0 | 1 | | |
| APTT, Grade 4, n=93,203 | 0 | 0 | | |
| Hemoglobin, Grade 3, n=115,235 | 4 | 6 | | |
| Hemoglobin, Grade 4, n=115,235 | 0 | 0 | | |
| Leukocytes, Grade 3, n=114,235 | 0 | 6 | | |
| Leukocytes, Grade 4, n=114,235 | 0 | 0 | | |
| Neutrophils, Grade 3, n=114,234 | 2 | 6 | | |

| | | | | |
|--------------------------------------|---|---|--|--|
| Neutrophils, Grade 4, n=114,234 | 0 | 1 | | |
| Platelets, Grade 3, n=115,235 | 0 | 0 | | |
| Platelets, Grade 4, n=115,235 | 0 | 0 | | |
| Prothrombin time, Grade 3, n=93, 204 | 3 | 2 | | |
| Prothrombin time, Grade 4, n=93, 204 | 1 | 3 | | |

Notes:

[16] - ITT OL Population

[17] - ITT OL Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with worst toxicity Grade of 3 or 4 for clinical chemistry parameters [OL Phase]

| | |
|-----------------|---|
| End point title | Number of participants with worst toxicity Grade of 3 or 4 for clinical chemistry parameters [OL Phase] ^[18] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of liver function and other chemistry parameters. The parameters assessed were alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transferase (GGT), bilirubin, albumin, creatinine, hyperglycemia, hypoglycemia and urate. Grading was assigned as mild (Grade 1), moderate (grade 2), severe (Grade 3) and potentially life-threatening (Grade 4) according to DMID AE Severity Grading. Number of participants with worst toxicity Grade of 3 or 4 for liver function and other chemistry parameters have been presented. Only those participants with data available at the specified data points were analyzed. For Safety, participants that completed DB and OL phase, an additional 8 weeks follow-up was conducted (Week 84).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 52 to Week 84

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical data to report.

| End point values | Placebo to Belimumab 10 mg/kg (OL Phase) | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) | | |
|-----------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 115 ^[19] | 236 ^[20] | | |
| Units: Participants | | | | |
| ALP, Grade 3 | 0 | 0 | | |
| ALP, Grade 4 | 0 | 0 | | |
| ALT, Grade 3 | 0 | 0 | | |
| ALT, Grade 4 | 0 | 0 | | |
| AST, Grade 3 | 0 | 0 | | |
| AST, Grade 4 | 0 | 0 | | |
| Bilirubin, Grade 3 | 0 | 0 | | |
| Bilirubin, Grade 4 | 0 | 0 | | |
| GGT, Grade 3 | 0 | 1 | | |
| GGT, Grade 4 | 0 | 0 | | |
| Albumin, Grade 3 | 0 | 2 | | |
| Albumin, Grade 4 | 1 | 0 | | |
| Creatinine, Grade 3 | 0 | 0 | | |

| | | | | |
|------------------------|---|---|--|--|
| Creatinine, Grade 4 | 0 | 0 | | |
| Hypoglycemia, Grade 3 | 0 | 0 | | |
| Hypoglycemia, Grade 4 | 0 | 0 | | |
| Hyperglycemia, Grade 3 | 1 | 4 | | |
| Hyperglycemia, Grade 4 | 0 | 0 | | |
| Urate, Grade 3 | 0 | 0 | | |
| Urate, Grade 4 | 0 | 0 | | |

Notes:

[19] - ITT OL Population

[20] - ITT OL Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with worst toxicity Grade of 3 or 4 for urinalysis parameters [OL Phase]

| | |
|-----------------|---|
| End point title | Number of participants with worst toxicity Grade of 3 or 4 for urinalysis parameters [OL Phase] ^[21] |
|-----------------|---|

End point description:

Urinalysis parameters assessed were urine protein and protein/creatinine. Urine samples were collected for the measurement of urinalysis parameters by dipstick method. Grading was assigned as mild (Grade 1), moderate (grade 2), severe (Grade 3) and potentially life-threatening (Grade 4) according to DMID AE Severity Grading. Number of participants with worst toxicity grade of 3 or 4 for urinalysis parameters have been presented. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). For Safety, participants that completed DB and OL phase, an additional 8 weeks follow-up was conducted (Week 84).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 52 to Week 84

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical data to report.

| End point values | Placebo to Belimumab 10 mg/kg (OL Phase) | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) | | |
|--|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 115 ^[22] | 234 ^[23] | | |
| Units: Participants | | | | |
| Protein, Grade 3, n=115, 234 | 0 | 0 | | |
| Protein, Grade 4, n=115,234 | 0 | 0 | | |
| Protein/Creatinine, Grade 3,n=112,227 | 5 | 5 | | |
| Protein/Creatinine, Grade 4, n=112,227 | 3 | 0 | | |

Notes:

[22] - ITT OL Population

[23] - ITT OL Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with worst toxicity Grade of 3 or 4 of

immunoglobulins [OL Phase]

| | |
|-----------------|--|
| End point title | Number of participants with worst toxicity Grade of 3 or 4 of immunoglobulins [OL Phase] ^[24] |
|-----------------|--|

End point description:

Serum samples were obtained for the measurement of immunoglobulin G. Grading was assigned as mild (Grade 1), moderate (grade 2), severe (Grade 3) and potentially life threatening (Grade 4) according to DMID AE Severity Grading. Number of participants with worst toxicity grade of 3 or 4 of immunoglobulin G have been presented. Only those participants with data available at the specified data points were analyzed. For Safety, participants that completed DB and OL phase, an additional 8 weeks follow-up was conducted (Week 84).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 52 to Week 84

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical data to report.

| End point values | Placebo to Belimumab 10 mg/kg (OL Phase) | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) | | |
|-----------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 117 ^[25] | 239 ^[26] | | |
| Units: Participants | | | | |
| Grade 3 | 0 | 1 | | |
| Grade 4 | 0 | 0 | | |

Notes:

[25] - ITT OL Population

[26] - ITT OL Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving SRI-SS Response Rate at Week 52 [DB Phase]

| | |
|-----------------|---|
| End point title | Percentage of participants achieving SRI-SS Response Rate at Week 52 [DB Phase] |
|-----------------|---|

End point description:

SRI is defined as ≥ 4 point reduction, from Baseline in SS score, no worsening (increase of < 0.30 points from Baseline) in PGA and no new BILAG A organ domain score or 2 new BILAG B organ domain scores compared with Baseline. Drop-outs and Treatment failures were set to non-responders. Analysis was performed using a logistic regression model for the comparison between belimumab and placebo with covariates treatment group, Baseline SS score (≤ 9 vs. ≥ 10), Baseline complement levels (low C3 and/or C4 vs. no low C3 or C4) and region (US/Canada vs. Rest of World). One participant in the mITT population Belimumab 10 mg/kg arm did not have a screening or Baseline PGA assessment; therefore, this participant did not contribute to the SRI/component analysis.

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

End point timeframe:

Week 52

| End point values | Placebo (DB Phase) | Belimumab 10 mg/kg (DB Phase) | | |
|-----------------------------------|----------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 149 ^[27] | 298 ^[28] | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 41.6 | 49.0 | | |

Notes:

[27] - mITT Population

[28] - mITT Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|--|
| Comparison groups | Placebo (DB Phase) v Belimumab 10 mg/kg (DB Phase) |
| Number of subjects included in analysis | 447 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[29] |
| P-value | = 0.0937 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.42 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.94 |
| upper limit | 2.15 |

Notes:

[29] - Nominal p-value due to step-down sequential testing procedure.

Secondary: Percentage of participants achieving SRI-SS Response Rate with the SELENA SLEDAI for scoring of proteinuria at Week 24 of OL Phase

| | |
|-----------------|--|
| End point title | Percentage of participants achieving SRI-SS Response Rate with the SELENA SLEDAI for scoring of proteinuria at Week 24 of OL Phase |
|-----------------|--|

End point description:

SRI response is defined as ≥ 4 point reduction, from OL Baseline in SS scoring for PU, no worsening (increase of < 0.30 points from OL Baseline) in PGA and no new BILAG A ODS or 2 new BILAG B ODS compared with OL Baseline. For participants switching from placebo to belimumab 10 mg/kg IV in the open-label phase, Baseline was defined as the last assessment at the end of the double-blind phase (i.e. Week 52) pre-OL treatment. For participants that received belimumab 10 mg/kg IV during the double-blind phase and continued to receive belimumab 10 mg/kg IV during the open-label phase, Baseline was defined as Day 1 of the double-blind phase. Only those participants with data available at the specified data points were analyzed.

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

End point timeframe:

Week 24 of OL phase (Week 76)

| End point values | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) | Placebo to Belimumab 10 mg/kg (OL Phase) | | |
|-----------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 208 ^[30] | 67 ^[31] | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 73.1 | 19.4 | | |

Notes:

[30] - mITT OL Population

[31] - mITT OL Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first severe flare (as measured by the modified SLE Flare Index) up to 52 Weeks [DB Phase]

| | |
|-----------------|--|
| End point title | Time to first severe flare (as measured by the modified SLE Flare Index) up to 52 Weeks [DB Phase] |
|-----------------|--|

End point description:

Time to first severe SLE flare is defined as the number of days from treatment start date until the participant met an event (event date – treatment start date +1). Analyses of severe SLE flare was performed on modified SS SLE flare index that excludes severe flares (SF) that were triggered only by an increase in SS score to >12 (this may only represent a modest increase in disease activity). Treatment failures were imputed as SF. Only post-Baseline SF were considered. Analysis was performed using Cox proportional hazards model for the comparison between belimumab and placebo adjusting for Baseline SS-S2K score (≤ 9 vs. ≥ 10), baseline complement levels (at least 1 C3/C4 low vs. no C3/C4 low), and region (US/Canada vs. Rest of World). Median and inter-Quartile range (1st and 3rd Quartiles) have been presented. 99999 indicated data was not available because the number of events was too low to estimate the value.

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

End point timeframe:

Up to 52 Weeks

| End point values | Placebo (DB Phase) | Belimumab 10 mg/kg (DB Phase) | | |
|---------------------------------------|----------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 149 ^[32] | 299 ^[33] | | |
| Units: Days | | | | |
| median (inter-quartile range (Q1-Q3)) | 99999 (346 to 99999) | 99999 (99999 to 99999) | | |

Notes:

[32] - mITT Population

[33] - mITT Population

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo (DB Phase) v Belimumab 10 mg/kg (DB Phase) |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 448 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[34] |
| P-value | = 0.2264 |
| Method | Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.51 |
| upper limit | 1.17 |

Notes:

[34] - Nominal p-value due to step-down sequential testing procedure.

Secondary: Time to first severe flare (as measured by the modified SLE Flare Index) [OL Phase]

| | |
|-----------------|---|
| End point title | Time to first severe flare (as measured by the modified SLE Flare Index) [OL Phase] |
|-----------------|---|

End point description:

Time to first severe SLE flare is defined as the number of days from OL treatment start date until the participant met an event (event date – OL treatment start date +1). Analyses of severe SLE flare was performed on modified SS SLE flare index that excludes SF that were triggered only by an increase in SS score to >12. For participants who died, data were censored at date of death if no SF occurred before death. Only post first OL treatment SF were considered. Median and inter-Quartile range (25th and 75th percentile) have been presented. 99999 indicated data was not available because the number of events was too low to estimate the value.

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

End point timeframe:

Up to Week 24 of OL Phase (Week 76)

| End point values | Placebo to Belimumab 10 mg/kg (OL Phase) | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) | | |
|---------------------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 109 ^[35] | 225 ^[36] | | |
| Units: Days | | | | |
| median (inter-quartile range (Q1-Q3)) | 99999 (99999 to 99999) | 232 (232 to 99999) | | |

Notes:

[35] - mITT OL Population

[36] - mITT OL Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of participants whose average prednisone dose had been reduced by >=25% from Baseline to <=7.5 mg/Day during Week 40 through 52, in participants receiving greater than 7.5 mg/Day at Baseline [DB Phase]

| | |
|---|--|
| End point title | Percent of participants whose average prednisone dose had been reduced by $\geq 25\%$ from Baseline to ≤ 7.5 mg/Day during Week 40 through 52, in participants receiving greater than 7.5 mg/Day at Baseline [DB Phase] |
| End point description: | |
| Average (avg.) daily prednisone (PRED.) dose was calculated taking into account all steroids taken intravenously, intramuscularly, subcutaneously, intradermally and orally for both Systemic Lupus Erythema (SLE) and non-SLE reasons. A responder was defined as having a PRED. reduction [REDN.] by $\geq 25\%$ from Baseline to ≤ 7.5 mg/day during Weeks 40 through 52. At Baseline, the avg. daily prednisone dose [PD] was the sum of all PDs over 7 consecutive days [excluding Day 0], divided (DIV.) by 7. For analysis, the avg. PD was the total PD during Weeks 40 through 52 DIV. by the number of days during Weeks 40 through 52. Analysis was performed using a logistic regression model with covariates treatment group, Baseline PD, Baseline SS-S2K score, (≤ 9 vs ≥ 10), Baseline complement levels (low C3 and/or C4 vs. no low C3 or C4) and region (US/Canada vs. Rest of World). Only those participants with Baseline prednisone dose > 7.5 mg/day were included. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 40 through Week 52 | |

| End point values | Placebo (DB Phase) | Belimumab 10 mg/kg (DB Phase) | | |
|-----------------------------------|----------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 95 ^[37] | 184 ^[38] | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 12.6 | 14.7 | | |

Notes:

[37] - mITT Population

[38] - mITT Population

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo (DB Phase) v Belimumab 10 mg/kg (DB Phase) |
| Number of subjects included in analysis | 279 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[39] |
| P-value | = 0.4996 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.61 |
| upper limit | 2.8 |

Notes:

[39] - Nominal p-value due to step-down sequential testing procedure.

Secondary: Percent of participants whose average prednisone dose had been reduced to ≤ 7.5 mg/Day in participants receiving greater than 7.5 mg/Day at pre-belimumab Baseline (at Week 28 of OL Phase)

| | |
|-----------------|---|
| End point title | Percent of participants whose average prednisone dose had |
|-----------------|---|

been reduced to ≤ 7.5 mg/Day in participants receiving greater than 7.5 mg/Day at pre-belimumab Baseline (at Week 28 of OL Phase)

End point description:

Average daily prednisone dose was calculated taking into account all steroids taken intravenously, intramuscularly, subcutaneously, intradermally and orally for both SLE and non-SLE reasons. A responder was defined as a participant who decreased their daily prednisone dose to ≤ 7.5 mg/day from an OL Baseline dose > 7.5 mg/day. The OL Baseline was defined as the last available value prior to the initiation of treatment with belimumab. The average daily prednisone dose was the sum of all PDs over 7 consecutive days including OL Week 28 divided by 7. Only those participants with data available at the specified data points were analyzed.

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

End point timeframe:

OL Baseline and Week 28 of OL Phase (Week 80)

| End point values | Placebo to Belimumab 10 mg/kg (OL Phase) | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) | | |
|-----------------------------------|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 54 ^[40] | 138 ^[41] | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 14.8 | 31.9 | | |

Notes:

[40] - mITT OL Population

[41] - mITT OL Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with nSAEs and SAEs [DB Phase]

| | |
|-----------------|---|
| End point title | Number of participants with nSAEs and SAEs [DB Phase] |
|-----------------|---|

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. A SAE is defined as any untoward medical occurrence that; results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, other situations judged by physician, is associated with liver injury and impaired liver function. Safety population was defined as all participants who were randomized and treated with at least one dose of study treatment. Number of participants who had common nSAEs ($\geq 5\%$) and any SAEs are presented.

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

End point timeframe:

Up to 52 Weeks

| End point values | Placebo (DB Phase) | Belimumab 10 mg/kg (DB Phase) | | |
|-----------------------------|----------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 165 ^[42] | 331 ^[43] | | |
| Units: Participants | | | | |
| nSAEs | 77 | 196 | | |
| SAEs | 31 | 36 | | |

Notes:

[42] - Safety Population

[43] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with severe AEs [DB Phase]

| | |
|--|---|
| End point title | Number of participants with severe AEs [DB Phase] |
| End point description: An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Number of participants with severe AEs have been presented. | |
| End point type | Secondary |
| End point timeframe: Up to 52 Weeks | |

| End point values | Placebo (DB Phase) | Belimumab 10 mg/kg (DB Phase) | | |
|-----------------------------|----------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 165 ^[44] | 331 ^[45] | | |
| Units: Participants | 37 | 46 | | |

Notes:

[44] - Safety Population

[45] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with AEs leading to treatment discontinuation [DB Phase]

| | |
|--|---|
| End point title | Number of participants with AEs leading to treatment discontinuation [DB Phase] |
| End point description: An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Number of participants with AEs leading to treatment discontinuation have been presented. | |
| End point type | Secondary |
| End point timeframe: Up to 52 Weeks | |

| End point values | Placebo (DB Phase) | Belimumab 10 mg/kg (DB Phase) | | |
|-----------------------------|----------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 165 ^[46] | 331 ^[47] | | |
| Units: Participants | 12 | 22 | | |

Notes:

[46] - Safety Population

[47] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worst toxicity Grade 3 or 4 for hematology parameters [DB Phase]

| | |
|-----------------|--|
| End point title | Number of participants with worst toxicity Grade 3 or 4 for hematology parameters [DB Phase] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of hematology parameters up to 52 Weeks. The parameters assessed were APTT, hemoglobin, leukocytes, neutrophils, platelets and prothrombin time. Grading was assigned as mild (Grade 1), moderate (grade 2), severe (Grade 3) and potentially life threatening according to DMID AE Severity Grading. Number of participants with worst toxicity Grade of 3 or 4 for hematology parameters have been presented. Only those participants with data available at specified time points were analyzed (represented by n=x in the category titles).

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

End point timeframe:

Up to 52 weeks

| End point values | Placebo (DB Phase) | Belimumab 10 mg/kg (DB Phase) | | |
|---------------------------------------|----------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 161 ^[48] | 327 ^[49] | | |
| Units: Participants | | | | |
| APTT, Grade 3, n=159,318 | 0 | 3 | | |
| APTT, Grade 4, n=159,318 | 0 | 2 | | |
| Hemoglobin, Grade 3, n=161,327 | 5 | 15 | | |
| Hemoglobin, Grade 4, n=161,327 | 1 | 0 | | |
| Leukocytes, Grade 3, n=161,327 | 3 | 17 | | |
| Leukocytes, Grade 4, n=161,327 | 1 | 0 | | |
| Neutrophils, Grade 3, n=161,327 | 9 | 28 | | |
| Neutrophils, Grade 4, n=161,327 | 1 | 5 | | |
| Platelets, Grade 3, n=161,327 | 1 | 1 | | |
| Platelets, Grade 4, n=161,327 | 0 | 1 | | |
| Prothrombin time, Grade 3, n=159, 318 | 8 | 10 | | |
| Prothrombin time, Grade 4, n=159,318 | 2 | 6 | | |

Notes:

[48] - Safety Population

[49] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worst toxicity Grade of 3 or 4 for clinical chemistry parameters [DB Phase]

| | |
|-----------------|---|
| End point title | Number of participants with worst toxicity Grade of 3 or 4 for clinical chemistry parameters [DB Phase] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of liver function and other chemistry parameters up to 52 Weeks. The parameters assessed were ALT, AST, GGT, albumin, hyperglycemia and hypoglycemia. Grading was assigned as mild (Grade 1), moderate (grade 2), severe (Grade 3) and potentially life threatening according to DMID AE Severity Grading. Only those participants with worst toxicity Grade of 3 or 4 for other chemistry parameters have been presented. Only those participants with data available at the specified data points were analyzed.

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

End point timeframe:

Up to 52 weeks

| End point values | Placebo (DB Phase) | Belimumab 10 mg/kg (DB Phase) | | |
|-----------------------------|----------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 161 ^[50] | 327 ^[51] | | |
| Units: Participants | | | | |
| ALT, Grade 3 | 0 | 2 | | |
| AST, Grade 3 | 0 | 2 | | |
| GGT, Grade 3 | 6 | 6 | | |
| GGT, Grade 4 | 0 | 1 | | |
| Albumin, Grade 3 | 5 | 3 | | |
| Albumin, Grade 4 | 1 | 1 | | |
| Hyperglycemia, Grade 3 | 4 | 7 | | |
| Hyperglycemia, Grade 4 | 1 | 1 | | |
| Hypoglycemia, Grade 3 | 0 | 4 | | |
| Hypoglycemia, Grade 4 | 3 | 1 | | |

Notes:

[50] - Safety Population

[51] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worst toxicity Grade of 3 or 4 for urinalysis parameters [DB Phase]

| | |
|--|---|
| End point title | Number of participants with worst toxicity Grade of 3 or 4 for urinalysis parameters [DB Phase] |
| End point description: | |
| Urinalysis parameters assessed were urine protein and protein/creatinine. Urine samples were collected for the measurement of urinalysis parameters by dipstick method up to 52 Weeks. Grading was assigned as mild (Grade 1), moderate (grade 2), severe (Grade 3) and potentially life threatening according to DMID AE Severity Grading. Only those participants with worst toxicity grade of 3 or 4 for urinalysis parameters have been presented. Only those participants with data available at specified time points were analyzed (represented by n=x in the category titles). | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 52 weeks | |

| End point values | Placebo (DB Phase) | Belimumab 10 mg/kg (DB Phase) | | |
|--|----------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 161 ^[52] | 324 ^[53] | | |
| Units: Participants | | | | |
| Protein, Grade 3, n=161, 324 | 0 | 1 | | |
| Protein/creatinine, Grade 3, n=161,322 | 8 | 25 | | |
| Protein/creatinine, Grade 4, n=161,322 | 12 | 11 | | |

Notes:

[52] - Safety Population

[53] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

nSAEs and SAEs were collected from the start of study treatment up to Week 52 for Double Blind phase and from Week 52 to Week 84 for OL phase. Participants that completed DB and OL phase, an additional 8 weeks follow-up was conducted (Week 84).

Adverse event reporting additional description:

nSAEs and SAEs were reported for the Safety Population which comprised of all randomized participants who received at least 1 dose of study treatment for Double Blind phase and ITT OL Population which comprised of all randomized participants who received at least 1 dose of OL treatment for OL phase.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 21.1 |

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Placebo (DB Phase) |
|-----------------------|--------------------|

Reporting group description:

In DB phase, participants received matching placebo to belimumab administered as IV infusion plus standard of care through 52 weeks.

| | |
|-----------------------|-------------------------------|
| Reporting group title | Belimumab 10 mg/kg (DB Phase) |
|-----------------------|-------------------------------|

Reporting group description:

In DB phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care through 52 weeks.

| | |
|-----------------------|--|
| Reporting group title | Placebo to Belimumab 10 mg/kg (OL Phase) |
|-----------------------|--|

Reporting group description:

n OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76

| | |
|-----------------------|---|
| Reporting group title | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) |
|-----------------------|---|

Reporting group description:

n OL phase, participants received belimumab 10 mg/kg administered as IV infusion plus standard of care every 28 days from Week 52 through Week 76

| Serious adverse events | Placebo (DB Phase) | Belimumab 10 mg/kg (DB Phase) | Placebo to Belimumab 10 mg/kg (OL Phase) |
|---|--------------------|-------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 31 / 165 (18.79%) | 36 / 331 (10.88%) | 6 / 117 (5.13%) |
| number of deaths (all causes) | 0 | 2 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma of the cervix | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Haematoma | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lupus vasculitis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant hypertension | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Raynaud's phenomenon | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vasculitis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------|-----------------|-----------------|
| Ectopic pregnancy | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 331 (0.60%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Serositis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Soft tissue inflammation | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 331 (0.60%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lupus pneumonitis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleurisy | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 331 (0.60%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung consolidation | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lupus pleurisy | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression suicidal | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Insomnia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic fracture | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary contusion | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Pericarditis | | | |
| subjects affected / exposed | 3 / 165 (1.82%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 1 / 117 (0.85%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 1 / 117 (0.85%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiomyopathy | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 1 / 117 (0.85%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coma | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dystonia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Idiopathic intracranial hypertension | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radiculopathy | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| syncope | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 331 (0.00%) | 1 / 117 (0.85%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chorea | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 1 / 117 (0.85%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Idiopathic orbital inflammation | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Pancreatitis acute | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal perforation | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Butterfly rash | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic lupus erythematosus rash | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Lupus nephritis | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute kidney injury | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Azotaemia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Glomerulonephritis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrotic syndrome | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 3 / 331 (0.91%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SLE arthritis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 165 (0.61%) | 2 / 331 (0.60%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Costochondritis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 331 (0.60%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 331 (0.60%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fibromyalgia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myositis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tendonitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 331 (0.00%) | 1 / 117 (0.85%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 6 / 165 (3.64%) | 2 / 331 (0.60%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 4 / 6 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Amoebic colitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis gonococcal | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atypical pneumonia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dengue fever | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infection | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Paronychia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral tonsillitis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Soft tissue infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperkalaemia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 331 (0.30%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 331 (0.00%) | 0 / 117 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|---|--|--|
| Serious adverse events | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 242 (5.37%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma of the cervix | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lupus vasculitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malignant hypertension | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Raynaud's phenomenon | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vasculitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ectopic pregnancy | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Pyrexia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Serositis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Soft tissue inflammation | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oedema | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Lupus pneumonitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pleurisy | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung consolidation | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lupus pleurisy | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Depression suicidal | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural | | | |

| | | | | |
|---|-----------------|--|--|--|
| complications | | | | |
| Accidental overdose | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint injury | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pelvic fracture | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary contusion | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Wrist fracture | | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac disorders | | | | |
| Pericarditis | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute myocardial infarction | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrial fibrillation | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | |
|---|-----------------|--|--|
| Cardiomyopathy | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coma | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dystonia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Idiopathic intracranial hypertension | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Radiculopathy | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| syncope | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chorea | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hemiparesis | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |

| | | | |
|---|-----------------------------------|--|--|
| Idiopathic orbital inflammation subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 242 (0.00%) 0 / 0 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 242 (0.00%) 0 / 0 0 / 0 | | |
| Colitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 242 (0.00%) 0 / 0 0 / 0 | | |
| Diarrhoea subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 242 (0.00%) 0 / 0 0 / 0 | | |
| Enteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 242 (0.00%) 0 / 0 0 / 0 | | |
| Intestinal obstruction subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 242 (0.00%) 0 / 0 0 / 0 | | |
| Pancreatitis acute subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 242 (0.00%) 0 / 0 0 / 0 | | |
| Small intestinal perforation subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 242 (0.00%) 0 / 0 0 / 0 | | |
| Hepatobiliary disorders | | | |

| | | | |
|---|-----------------|--|--|
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Butterfly rash | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Systemic lupus erythematosus rash | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Lupus nephritis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Azotaemia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Glomerulonephritis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Nephrotic syndrome | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SLE arthritis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Costochondritis | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|-----------------|--|--|--|
| Arthritis | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fibromyalgia | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Musculoskeletal chest pain | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Musculoskeletal pain | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myositis | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Osteoarthritis | | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rhabdomyolysis | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tendonitis | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infections and infestations | | | | |

| | | | | |
|---|-----------------|--|--|--|
| Pneumonia | | | | |
| subjects affected / exposed | 2 / 242 (0.83%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary tract infection | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Amoebic colitis | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Appendicitis | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arthritis gonococcal | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atypical pneumonia | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium difficile infection | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dengue fever | | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulitis | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung infection | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Meningitis | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Paronychia | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sepsis | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Staphylococcal sepsis | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Upper respiratory tract infection | | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Viral tonsillitis | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Soft tissue infection | | | |
| subjects affected / exposed | 1 / 242 (0.41%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 242 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Placebo (DB Phase) | Belimumab 10 mg/kg (DB Phase) | Placebo to Belimumab 10 mg/kg (OL Phase) |
|---|--------------------|-------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 77 / 165 (46.67%) | 196 / 331 (59.21%) | 23 / 117 (19.66%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 4 / 165 (2.42%) | 18 / 331 (5.44%) | 0 / 117 (0.00%) |
| occurrences (all) | 5 | 21 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 18 / 165 (10.91%) | 39 / 331 (11.78%) | 0 / 117 (0.00%) |
| occurrences (all) | 25 | 47 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 9 / 165 (5.45%) | 31 / 331 (9.37%) | 0 / 117 (0.00%) |
| occurrences (all) | 12 | 34 | 0 |
| Nausea | | | |
| subjects affected / exposed | 15 / 165 (9.09%) | 18 / 331 (5.44%) | 0 / 117 (0.00%) |
| occurrences (all) | 21 | 29 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 7 / 165 (4.24%) | 19 / 331 (5.74%) | 0 / 117 (0.00%) |
| occurrences (all) | 8 | 21 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 7 / 165 (4.24%) | 18 / 331 (5.44%) | 0 / 117 (0.00%) |
| occurrences (all) | 7 | 23 | 0 |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 10 / 165 (6.06%) | 18 / 331 (5.44%) | 0 / 117 (0.00%) |
| occurrences (all) | 10 | 18 | 0 |
| Depression | | | |
| subjects affected / exposed | 9 / 165 (5.45%) | 15 / 331 (4.53%) | 0 / 117 (0.00%) |
| occurrences (all) | 9 | 15 | 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|--|-------------------------|-------------------------|----------------------|
| Back pain subjects affected / exposed occurrences (all) | 10 / 165 (6.06%) 12 | 16 / 331 (4.83%) 17 | 7 / 117 (5.98%) 7 |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) | 14 / 165 (8.48%) 20 | 48 / 331 (14.50%) 58 | 4 / 117 (3.42%) 6 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 19 / 165 (11.52%) 24 | 43 / 331 (12.99%) 57 | 7 / 117 (5.98%) 7 |
| Influenza subjects affected / exposed occurrences (all) | 17 / 165 (10.30%) 23 | 28 / 331 (8.46%) 35 | 7 / 117 (5.98%) 8 |
| Sinusitis subjects affected / exposed occurrences (all) | 9 / 165 (5.45%) 9 | 26 / 331 (7.85%) 33 | 0 / 117 (0.00%) 0 |

| | | | |
|---|---|--|--|
| Non-serious adverse events | Belimumab 10 mg/kg to Belimumab 10 mg/kg (OL Phase) | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 49 / 242 (20.25%) | | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 0 / 242 (0.00%) 0 | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 242 (0.00%) 0 | | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting | 0 / 242 (0.00%) 0 0 / 242 (0.00%) 0 | | |

| | | | |
|---|--|--|--|
| subjects affected / exposed occurrences (all) | 0 / 242 (0.00%) 0 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 242 (0.00%) 0 | | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) | 0 / 242 (0.00%) 0 0 / 242 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 3 / 242 (1.24%) 3 | | |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) | 20 / 242 (8.26%) 21 13 / 242 (5.37%) 15 16 / 242 (6.61%) 18 0 / 242 (0.00%) 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 20 June 2012 | Revisions to inclusion criterion (contraception for female participants), requiring clinical supervision for 3 hours after participants received their first 2 infusions, and removing the provision to withdraw participants from the study if 3 or more consecutive doses of investigational product were missed. Additional changes included clarifying timing of several evaluations and doses and clarifying timing of the evaluations and dosing in the 6-month open-label phase. |
| 09 February 2017 | Revising the primary endpoint to the SRI-S2K, reducing the sample size, adding the provision to withdraw participants from the study if 3 or more consecutive doses of investigational product were missed, and modifying the enrollment criteria. Additional changes include aligning the safety sections with the belimumab program standard text and clarifying conduct sections. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported