



Clinical trial results:

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

Summary

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

Results information

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

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 205646 |
|-----------------------|--------|

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 03 September 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 July 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

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

Notes:

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

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

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

Period 1

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

Arms

| | |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Belimumab + Placebo |

Arm description:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

Standard therapy was administered.

| | |
|------------------|-----------------------|
| Arm title | Belimumab + Rituximab |
|------------------|-----------------------|

Arm description:

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

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

Dosage and administration details:

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

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

Dosage and administration details:

Standard therapy was administered.

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

Dosage and administration details:

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

| | |
|------------------|------------------------------|
| Arm title | Belimumab + Standard therapy |
|------------------|------------------------------|

Arm description:

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

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

Dosage and administration details:

Standard therapy was administered.

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

Dosage and administration details:

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

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

Baseline characteristics

Reporting groups

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

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

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

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

End points

End points reporting groups

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

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

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

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

Notes:

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

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

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

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: | |
| Odds ratio was calculated using logistic regression model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, and Baseline prednisone equivalent dose. Belimumab + Placebo arm excluded from model. | |
| Comparison groups | Belimumab + Rituximab v Belimumab + Standard therapy |
| Number of subjects included in analysis | 191 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.32 |
| upper limit | 1.54 |

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| Odds ratio was calculated using logistic regression model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose. Belimumab + Standard therapy arm was excluded from model. | |
| Comparison groups | Belimumab + Rituximab v Belimumab + Placebo |
| Number of subjects included in analysis | 216 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.5342 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.27 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.6 |
| upper limit | 2.71 |

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

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

End point description:

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

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

End point timeframe:

Week 64

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

Notes:

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

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

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

Statistical analyses

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

Statistical analysis description:

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

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

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

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

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

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

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

End point description:

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

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

End point timeframe:

Week 104

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

Notes:

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

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

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

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 2 |
|----------------------------|------------------------|

Statistical analysis description:

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

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

Statistical analysis title

Statistical Analysis 1

Statistical analysis description:

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

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

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

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

End point description:

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

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

End point timeframe:

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

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

Weeks 64, 80 and 104

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 52 to Week 104 | |

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

From Week 80 to Week 104

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

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

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first severe flare

| | |
|---|----------------------------|
| End point title | Time to first severe flare |
| End point description: | |
| Time to first severe SLE flare was the number of days from treatment start date until the participant met an event. Time to first severe flare was defined as event date minus treatment start date plus 1. Time to first severe flare was measured by Modified SLE flare index which identifies whether a participant had experienced a mild/moderate or severe flare. Analysis of first severe flare was performed on the modified SLE Flare index that excludes severe flares that were triggered only by an increase in SLEDAI-2K score to greater than 12. 99999 indicates that data was not available as only <75% of participants experienced the event within the treatment arm. Hence, third-quartile could not be derived | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Week 104 | |

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

Notes:

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

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

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

Statistical analyses

| Statistical analysis title | Statistical Analysis 2 |
|---|--|
| Statistical analysis description: | |
| Hazard ratio was calculated using Cox proportional hazards model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Placebo arm excluded from model. | |
| Comparison groups | Belimumab + Rituximab v Belimumab + Standard therapy |
| Number of subjects included in analysis | 191 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.03 |
| upper limit | 2.63 |

| Statistical analysis title | Statistical Analysis 1 |
|--|---|
| Statistical analysis description: | |
| Hazard ratio was calculated using Cox proportional hazards model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Standard therapy arm was excluded from model. | |
| Comparison groups | Belimumab + Placebo v Belimumab + Rituximab |
| Number of subjects included in analysis | 216 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.215 |
| Method | Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.57 |
| upper limit | 1.13 |

Secondary: Time to first flare

| | |
|-----------------|---------------------|
| End point title | Time to first flare |
|-----------------|---------------------|

End point description:

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

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

End point timeframe:

Up to Week 104

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

Notes:

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

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

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

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 2 |
|----------------------------|------------------------|

Statistical analysis description:

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

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

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

Statistical analysis description:

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

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

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

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

End point description:

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

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

End point timeframe:

Up to Week 104

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

Notes:

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

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

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

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|--|---|
| Statistical analysis description: | |
| Hazard ratio was calculated using Cox proportional hazards model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Standard therapy arm was excluded from model. | |
| Comparison groups | Belimumab + Placebo v Belimumab + Rituximab |
| Number of subjects included in analysis | 216 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.5127 |
| Method | Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.42 |
| upper limit | 5.78 |

| Statistical analysis title | Statistical Analysis 2 |
|---|--|
| Statistical analysis description: | |
| Hazard ratio was calculated using Cox proportional hazards model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Placebo arm excluded from model. | |
| Comparison groups | Belimumab + Rituximab v Belimumab + Standard therapy |
| Number of subjects included in analysis | 191 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.23 |
| upper limit | 2.1 |

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

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

End point description:

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

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

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to Week 104 | |

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

Notes:

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

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

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

Statistical analyses

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

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

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

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

Statistical analysis description:

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

| | |
|-------------------|---|
| Comparison groups | Belimumab + Placebo v Belimumab + Rituximab |
|-------------------|---|

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

Secondary: Duration of disease control

| | |
|---|-----------------------------|
| End point title | Duration of disease control |
| End point description: | |
| Duration of disease control was defined as SLEDAI-2K score ≤ 2 , achieved without immunosuppressants and with corticosteroids at a prednisone equivalent dose of ≤ 5 mg/day. The duration of disease control (PI assessed) was the longest period between 2 visits that the participant was a disease control responder at all visits and calculated as the first visit of disease control minus last visit of disease control plus 1. SLEDAI-2K consisted of 24 individual items within each of 9 organ systems. Each item was given a weighted score (1 to 8, higher score indicates increased activity) and summed if present at the time of visit or in preceding 10 days. SLEDAI-2K score was the sum of all 24 individual items from SLEDAI-2K, ranges from 0 (no symptoms) to 105 (presence of all defined symptoms), higher scores representing increased disease activity. Only those participants with at least one assessment where disease control was met were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Week 104 | |

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of clinical remission

| | |
|-----------------|--------------------------------|
| End point title | Duration of clinical remission |
|-----------------|--------------------------------|

End point description:

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

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

End point timeframe:

Up to Week 104

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

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

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

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

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

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

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

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

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type Secondary

End point timeframe:

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

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

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

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

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

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

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

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

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

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

Baseline (Day 1), Week 52 and Week 104

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

Notes:

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

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

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

Statistical analyses

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

Statistical analysis description:

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

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

Notes:

[58] - Week 52

| Statistical analysis title | Statistical Analysis 2 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

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

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

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 3 |
| Statistical analysis description: | |
| Odds ratio at Week 104 was calculated using Logistic regression model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Standard therapy arm was excluded from the model. | |
| Comparison groups | Belimumab + Placebo v Belimumab + Rituximab |
| Number of subjects included in analysis | 216 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.8641 [59] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.26 |
| upper limit | 3.15 |
| Notes: | |
| [59] - Week 104 | |

| | |
|--|--|
| Statistical analysis title | Statistical Analysis 4 |
| Statistical analysis description: | |
| Odds ratio at Week 104 was calculated using Logistic regression model with covariates: Baseline SLEDAI-2K, Baseline immunosuppressant, Baseline prednisone equivalent dose and treatment group. Belimumab + Placebo arm was excluded from the model. | |
| Comparison groups | Belimumab + Rituximab v Belimumab + Standard therapy |
| Number of subjects included in analysis | 191 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.26 |
| upper limit | 5.64 |

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

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

End point description:

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

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

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Weeks 4, 8, 12, 16, 20, 24, 26, 28, 32, 36, 40, 44, 48, 52, 60, 64, 72, 80, 88, 96 and 104 | |

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

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

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

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

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

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

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

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

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

Notes:

[69] - Intent-to-Treat Population

[70] - Intent-to-Treat Population

[71] - Intent-to-Treat Population

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

Up to Week 104

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

Notes:

[72] - InIntent-to-Treat Population

[73] - Intent-to-Treat Population

[74] - Intent-to-Treat Population

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

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

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

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

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

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

| | |
|--|---|
| End point title | Change from Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score by visit |
| End point description: The FACIT-Fatigue scale was a 13-item questionnaire completed by the participant, which provides a measure of fatigue/quality of life, with a 7-day recall period. The participant scored each item on a 5-point scale: 0 (Not at all) to 4 (Very much). The higher score for the questions, the greater the fatigue. The total score was the sum of the responses from all questions (inverted for reversed items) multiplied by 13, then divided by the number of questions answered, ranging from 0 (worse fatigue) to 52 (no fatigue) where a higher score indicates an improvement in the participant's health status and decrease in the score indicates worse fatigue/quality of life. Baseline value was the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was defined as the post-dose visit value minus Baseline value. Only those participants with data available at specified time points were analyzed (represented by n=X in category titles). | |
| End point type | Secondary |
| End point timeframe: Baseline (Day 1) and Weeks 8, 12, 26, 40, 52, 64, 72 and 104 | |

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

End point timeframe:

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

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

Notes:

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

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

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

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

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------|
| Reporting group title | Belimumab + Placebo |
|-----------------------|---------------------|

Reporting group description:

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

| | |
|-----------------------|------------------------------|
| Reporting group title | Belimumab + Standard therapy |
|-----------------------|------------------------------|

Reporting group description:

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

| | |
|-----------------------|-----------------------|
| Reporting group title | Belimumab + Rituximab |
|-----------------------|-----------------------|

Reporting group description:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported