



Clinical trial results:

A randomized, double blind (sponsor open), comparative, multicenter study to evaluate the safety and efficacy of subcutaneous belimumab (GSK1550188) and intravenous rituximab coadministration in subjects with primary Sjögren's syndrome

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2015-000400-26 |
| Trial protocol | SE NO DE ES NL GB FR IT |
| Global end of trial date | 23 June 2020 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 29 May 2021 |
| First version publication date | 29 May 2021 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 201842 |
|-----------------------|--------|

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 | 14 October 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 June 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Safety and tolerability of anti- B lymphocyte stimulator (anti-BLyS)/ anti-cluster of differentiation 20 (anti-CD 20) co-administration therapy and anti-BLyS and anti-CD 20 monotherapies.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 17 February 2016 |
| 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 | Argentina: 2 |
| Country: Number of subjects enrolled | Canada: 8 |
| Country: Number of subjects enrolled | France: 24 |
| Country: Number of subjects enrolled | Germany: 12 |
| Country: Number of subjects enrolled | Italy: 11 |
| Country: Number of subjects enrolled | Netherlands: 4 |
| Country: Number of subjects enrolled | Norway: 5 |
| Country: Number of subjects enrolled | Spain: 6 |
| Country: Number of subjects enrolled | Sweden: 4 |
| Country: Number of subjects enrolled | United Kingdom: 10 |
| Worldwide total number of subjects | 86 |
| EEA total number of subjects | 66 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 | 0 |

| | |
|---------------------------|----|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 71 |
| From 65 to 84 years | 15 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 10 countries across 31 centers. Participants were randomized to receive one of the four treatments; Placebo, Belimumab + Rituximab Co-administration therapy, Belimumab Monotherapy or Rituximab Monotherapy.

Pre-assignment

Screening details:

A total of 162 participants were screened of which 76 were screen failures. A total of 86 participants were enrolled in this study.

Period 1

| | |
|------------------------------|----------------------------------|
| Period 1 title | Treatment Period (Up to Week 52) |
| 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 | Placebo |

Arm description:

Participants received belimumab matching placebo weekly subcutaneous injections up to Week 52 and rituximab matching placebo infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment General Follow-Up (GFU) period.

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

Dosage and administration details:

Participants received rituximab placebo infusions at Weeks 8 and 10.

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

Dosage and administration details:

Participants received belimumab placebo weekly subcutaneous injections up to Week 52.

| | |
|------------------|---|
| Arm title | Belimumab + Rituximab Co-administration therapy |
|------------------|---|

Arm description:

Participants received belimumab 200 milligrams (mg) weekly subcutaneous injections for 24 weeks followed by belimumab matching placebo injections weekly up to Week 52; along with rituximab 1000 mg intravenous infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment GFU period.

| | |
|--|------------------|
| 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: | |
| Participants received belimumab 200 milligrams (mg) weekly subcutaneous injections up to Week 52. | |
| Investigational medicinal product name | Belimumab placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Participants received belimumab placebo weekly subcutaneous injections up to Week 52. | |
| Investigational medicinal product name | Rituximab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Participants received rituximab 1000 mg intravenous (IV) infusions at Weeks 8 and 10. | |
| Arm title | Belimumab Monotherapy |
| Arm description: | |
| Participants received 200 mg weekly subcutaneous injections of belimumab up to Week 52 and rituximab matching placebo infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment GFU period. | |
| 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: | |
| Participants received belimumab 200 milligrams (mg) weekly subcutaneous injections up to Week 52. | |
| Investigational medicinal product name | Rituximab placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Participants received rituximab placebo infusions at Weeks 8 and 10. | |
| Arm title | Rituximab Monotherapy |
| Arm description: | |
| Participants received 1000 mg intravenous rituximab infusions at Weeks 8 and 10 and weekly subcutaneous injections of belimumab matching placebo up to Week 52 in the treatment period. Participants then entered in a 16-week no-treatment GFU period. | |
| Arm type | Active comparator |
| Investigational medicinal product name | Rituximab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Participants received rituximab 1000 mg intravenous (IV) infusions at Weeks 8 and 10. | |
| Investigational medicinal product name | Belimumab placebo |
| Investigational medicinal product code | |
| Other name | |

| | |
|--------------------------|------------------|
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received belimumab placebo weekly subcutaneous injections up to Week 52.

| Number of subjects in period 1 | Placebo | Belimumab + Rituximab Co- administration therapy | Belimumab Monotherapy |
|--------------------------------|---------|---|--------------------------|
| | | | |
| Started | 13 | 24 | 24 |
| Completed | 9 | 17 | 19 |
| Not completed | 4 | 7 | 5 |
| Adverse event, serious fatal | - | 1 | - |
| Consent withdrawn by subject | 1 | 1 | 2 |
| Physician decision | 1 | - | - |
| Adverse event, non-fatal | 1 | 4 | 2 |
| Reached stopping criteria | - | - | 1 |
| Lack of efficacy | 1 | 1 | - |

| Number of subjects in period 1 | Rituximab Monotherapy |
|--------------------------------|--------------------------|
| Started | 25 |
| Completed | 17 |
| Not completed | 8 |
| Adverse event, serious fatal | - |
| Consent withdrawn by subject | 5 |
| Physician decision | 1 |
| Adverse event, non-fatal | 2 |
| Reached stopping criteria | - |
| Lack of efficacy | - |

Period 2

| | |
|------------------------------|---|
| Period 2 title | General follow-up (GFU) (Up to Week 68) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|---|---|
| Arm title | Placebo |
| Arm description: | |
| Participants received belimumab matching placebo weekly subcutaneous injections up to Week 52 and rituximab matching placebo infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment General Follow-Up (GFU) period. | |
| Arm type | Placebo |
| Investigational medicinal product name | Rituximab placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Participants received rituximab placebo infusions at Weeks 8 and 10. | |
| Investigational medicinal product name | Belimumab placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Participants received belimumab placebo weekly subcutaneous injections up to Week 52. | |
| Arm title | Belimumab + Rituximab Co-administration therapy |
| Arm description: | |
| Participants received belimumab 200 milligrams (mg) weekly subcutaneous injections for 24 weeks followed by belimumab matching placebo injections weekly up to Week 52; along with rituximab 1000 mg intravenous infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment GFU period. | |
| 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: | |
| Participants received belimumab 200 milligrams (mg) weekly subcutaneous injections up to Week 52. | |
| Investigational medicinal product name | Belimumab placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Participants received belimumab placebo weekly subcutaneous injections up to Week 52. | |
| Investigational medicinal product name | Rituximab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Participants received rituximab 1000 mg intravenous (IV) infusions at Weeks 8 and 10. | |
| Arm title | Belimumab Monotherapy |
| Arm description: | |
| Participants received 200 mg weekly subcutaneous injections of belimumab up to Week 52 and rituximab matching placebo infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment GFU period. | |

| | |
|--|------------------|
| 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:

Participants received belimumab 200 milligrams (mg) weekly subcutaneous injections up to Week 52.

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

Dosage and administration details:

Participants received rituximab placebo infusions at Weeks 8 and 10.

| | |
|------------------|-----------------------|
| Arm title | Rituximab Monotherapy |
|------------------|-----------------------|

Arm description:

Participants received 1000 mg intravenous rituximab infusions at Weeks 8 and 10 and weekly subcutaneous injections of belimumab matching placebo up to Week 52 in the treatment period. Participants then entered in a 16-week no-treatment GFU period.

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

Dosage and administration details:

Participants received rituximab 1000 mg intravenous (IV) infusions at Weeks 8 and 10.

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

Dosage and administration details:

Participants received belimumab placebo weekly subcutaneous injections up to Week 52.

| Number of subjects in period 2 | Placebo | Belimumab + Rituximab Co- administration therapy | Belimumab Monotherapy |
|--------------------------------|---------|---|--------------------------|
| | | | |
| Started | 9 | 17 | 19 |
| Completed | 8 | 17 | 19 |
| Not completed | 1 | 0 | 0 |
| Lost to follow-up | 1 | - | - |

| Number of subjects in period 2 | Rituximab Monotherapy |
|--------------------------------|--------------------------|
| Started | 17 |
| Completed | 16 |
| Not completed | 1 |

| | |
|-------------------|---|
| Lost to follow-up | 1 |
|-------------------|---|

Baseline characteristics

Reporting groups

| | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: Participants received belimumab matching placebo weekly subcutaneous injections up to Week 52 and rituximab matching placebo infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment General Follow-Up (GFU) period. | |
| Reporting group title | Belimumab + Rituximab Co-administration therapy |
| Reporting group description: Participants received belimumab 200 milligrams (mg) weekly subcutaneous injections for 24 weeks followed by belimumab matching placebo injections weekly up to Week 52; along with rituximab 1000 mg intravenous infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment GFU period. | |
| Reporting group title | Belimumab Monotherapy |
| Reporting group description: Participants received 200 mg weekly subcutaneous injections of belimumab up to Week 52 and rituximab matching placebo infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment GFU period. | |
| Reporting group title | Rituximab Monotherapy |
| Reporting group description: Participants received 1000 mg intravenous rituximab infusions at Weeks 8 and 10 and weekly subcutaneous injections of belimumab matching placebo up to Week 52 in the treatment period. Participants then entered in a 16-week no-treatment GFU period. | |

| Reporting group values | Placebo | Belimumab + Rituximab Co- administration therapy | Belimumab Monotherapy |
|--|---------|---|--------------------------|
| Number of subjects | 13 | 24 | 24 |
| Age categorical Units: Subjects | | | |
| All participants | 13 | 24 | 24 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 52.7 | 45.1 | 52.0 |
| standard deviation | ± 12.67 | ± 10.93 | ± 11.49 |
| Sex: Female, Male Units: Participants | | | |
| Female | 13 | 22 | 22 |
| Male | 0 | 2 | 2 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| African American/African Heritage | 1 | 2 | 2 |
| American Indian or Alaskan Native | 0 | 0 | 0 |
| Asian - East Asian Heritage | 0 | 1 | 1 |
| White - Arabic/North African Heritage | 0 | 2 | 3 |
| White-White/Caucasian/European Heritage | 12 | 18 | 18 |
| African American/African and Asian Heritage | 0 | 1 | 0 |

| Reporting group values | Rituximab Monotherapy | Total | |
|---|----------------------------------|--------------|--|
| Number of subjects | 25 | 86 | |
| Age categorical Units: Subjects | | | |
| All participants | 25 | 86 | |
| Age Continuous Units: Years arithmetic mean standard deviation | 55.2 ± 15.07 | - | |
| Sex: Female, Male Units: Participants | | | |
| Female | 23 | 80 | |
| Male | 2 | 6 | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| African American/African Heritage | 1 | 6 | |
| American Indian or Alaskan Native | 1 | 1 | |
| Asian - East Asian Heritage | 2 | 4 | |
| White - Arabic/North African Heritage | 0 | 5 | |
| White-White/Caucasian/European Heritage | 21 | 69 | |
| African American/African and Asian Heritage | 0 | 1 | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: Participants received belimumab matching placebo weekly subcutaneous injections up to Week 52 and rituximab matching placebo infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment General Follow-Up (GFU) period. | |
| Reporting group title | Belimumab + Rituximab Co-administration therapy |
| Reporting group description: Participants received belimumab 200 milligrams (mg) weekly subcutaneous injections for 24 weeks followed by belimumab matching placebo injections weekly up to Week 52; along with rituximab 1000 mg intravenous infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment GFU period. | |
| Reporting group title | Belimumab Monotherapy |
| Reporting group description: Participants received 200 mg weekly subcutaneous injections of belimumab up to Week 52 and rituximab matching placebo infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment GFU period. | |
| Reporting group title | Rituximab Monotherapy |
| Reporting group description: Participants received 1000 mg intravenous rituximab infusions at Weeks 8 and 10 and weekly subcutaneous injections of belimumab matching placebo up to Week 52 in the treatment period. Participants then entered in a 16-week no-treatment GFU period. | |
| Reporting group title | Placebo |
| Reporting group description: Participants received belimumab matching placebo weekly subcutaneous injections up to Week 52 and rituximab matching placebo infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment General Follow-Up (GFU) period. | |
| Reporting group title | Belimumab + Rituximab Co-administration therapy |
| Reporting group description: Participants received belimumab 200 milligrams (mg) weekly subcutaneous injections for 24 weeks followed by belimumab matching placebo injections weekly up to Week 52; along with rituximab 1000 mg intravenous infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment GFU period. | |
| Reporting group title | Belimumab Monotherapy |
| Reporting group description: Participants received 200 mg weekly subcutaneous injections of belimumab up to Week 52 and rituximab matching placebo infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment GFU period. | |
| Reporting group title | Rituximab Monotherapy |
| Reporting group description: Participants received 1000 mg intravenous rituximab infusions at Weeks 8 and 10 and weekly subcutaneous injections of belimumab matching placebo up to Week 52 in the treatment period. Participants then entered in a 16-week no-treatment GFU period. | |

Primary: Number of participants with serious adverse events (SAE) and non-serious AEs (non-SAE)

| | |
|-----------------|---|
| End point title | Number of participants with serious adverse events (SAE) and non-serious AEs (non-SAE) ^[1] |
|-----------------|---|

End point description:

An AE is any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An SAE is any untoward medical occurrence that at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in

disability/incapacity, is a congenital anomaly/birth defect, other situations based on medical or scientific judgment and is associated with liver injury and impaired liver function. Data for number of participants with SAE and non-SAE has been summarized. Safety Population comprised of all participants who received at least one dose of study treatment.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Up to Week 68 | |

Notes:

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

Justification: There are no statistical data to report.

| End point values | Placebo | Belimumab + Rituximab Co-administration therapy | Belimumab Monotherapy | Rituximab Monotherapy |
|-----------------------------|-------------------|---|-----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 ^[2] | 24 ^[3] | 24 ^[4] | 25 ^[5] |
| Units: Participants | | | | |
| Any SAE | 0 | 3 | 2 | 4 |
| Any non-SAE | 12 | 24 | 23 | 17 |

Notes:

[2] - Safety Population

[3] - Safety Population

[4] - Safety Population

[5] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with adverse event of special interests (AESIs)

| | |
|-----------------|---|
| End point title | Number of participants with adverse event of special interests (AESIs) ^[6] |
|-----------------|---|

End point description:

An AE is any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. AESIs were Malignant Neoplasms, Post-Administration Systemic Reactions (PASR), All Infections of Special Interest (opportunistic infections, herpes zoster, tuberculosis and sepsis), Depression/suicide/self-injury, Deaths and study specific AESI which includes: severe skin reaction per GlaxoSmithKline (GSK) Adjudication, cardiac disorders, Posterior Reversible Encephalopathy Syndrome (PRES) and Progressive multifocal leukoencephalopathy (PML). Data for number of participants with AESI has been summarized.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Up to Week 68 | |

Notes:

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

Justification: There are no statistical data to report.

| End point values | Placebo | Belimumab + Rituximab Co- administration therapy | Belimumab Monotherapy | Rituximab Monotherapy |
|------------------------------------|-------------------|---|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 ^[7] | 24 ^[8] | 24 ^[9] | 25 ^[10] |
| Units: Participants | | | | |
| Malignant Neoplasms | 0 | 0 | 0 | 1 |
| PASR | 4 | 2 | 3 | 5 |
| All Infections of Special Interest | 2 | 1 | 3 | 2 |
| Depression/Suicide/Self-injury | 0 | 3 | 5 | 1 |
| Deaths | 0 | 1 | 0 | 0 |
| Severe Skin Reactions | 0 | 0 | 0 | 0 |
| Cardiac Disorders | 0 | 1 | 0 | 1 |
| PRES | 0 | 0 | 0 | 0 |
| PML | 0 | 0 | 0 | 0 |

Notes:

[7] - Safety Population

[8] - Safety Population

[9] - Safety Population

[10] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in European League Against Rheumatism (EULAR) Sjogren's Syndrome Disease Activity Index (ESSDAI) Total scores over time

| | |
|-----------------|--|
| End point title | Change from Baseline in European League Against Rheumatism (EULAR) Sjogren's Syndrome Disease Activity Index (ESSDAI) Total scores over time |
|-----------------|--|

End point description:

ESSDAI is a disease activity index developed by EULAR consortium consisting of twelve clinically relevant organ specific domains. Each domain has 3 or 4 possible activity levels (i.e., no, low, moderate, high [if available]) using a 4-point scale, ranging from 0 (No activity) to 3 (High activity). Higher score indicates high disease activity. Each domain is assigned a weight between 1 and 6. Total ESSDAI Scores are obtained by multiplying level of activity (domain score) by domain weights, ranges between 0 (no activity) and 123 (highest activity). Higher score indicates more disease activity. Baseline value is screening visit value. Change from Baseline was defined as post-dose visit value minus Baseline value. Completer Population comprised of participants who completed 52 Week treatment visits and general follow up phase of study including visit at Week 68. Only those participants with data available at specified data points were analyzed (represented by n=X in category titles).

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

End point timeframe:

Baseline (Screening [within 35 days prior to Day 0]), Week 12, Week 24, Week 36, Week 52 and Week 68

| End point values | Placebo | Belimumab + Rituximab Co- administration therapy | Belimumab Monotherapy | Rituximab Monotherapy |
|-----------------------------|-------------------|---|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 ^[11] | 17 ^[12] | 19 ^[13] | 16 ^[14] |
| Units: Scores on a scale | | | | |

| least squares mean (standard error) | | | | |
|-------------------------------------|--------------------|--------------------|--------------------|--------------------|
| Week 12; n=8, 17, 19 ,15 | -2.00 (± 1.449) | -4.85 (± 0.996) | -3.87 (± 0.949) | -4.22 (± 1.048) |
| Week 24; n=8, 17, 19 ,16 | -2.87 (± 1.324) | -5.32 (± 0.911) | -3.87 (± 0.869) | -5.25 (± 0.940) |
| Week 36; n=8, 17, 19 ,16 | -3.12 (± 1.520) | -4.09 (± 1.045) | -4.23 (± 0.995) | -4.94 (± 1.079) |
| Week 52;n=8, 17, 19 ,16 | -2.87 (± 1.294) | -5.67 (± 0.890) | -4.76 (± 0.850) | -4.32 (± 0.919) |
| Week 68;n=8, 17, 19 ,16 | -1.75 (± 1.400) | -5.73 (± 0.962) | -3.87 (± 0.918) | -4.38 (± 0.994) |

Notes:

[11] - Completer Population

[12] - Completer Population

[13] - Completer Population

[14] - Completer Population

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|--|---|
| Statistical analysis description: | |
| Week 12. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect. | |
| Comparison groups | Placebo v Belimumab + Rituximab Co-administration therapy |
| Number of subjects included in analysis | 25 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Least square (LS) mean difference |
| Point estimate | -2.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.38 |
| upper limit | 0.67 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.758 |

| Statistical analysis title | Statistical Analysis 2 |
|--|---|
| Statistical analysis description: | |
| Week 12. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect. | |
| Comparison groups | Belimumab + Rituximab Co-administration therapy v Belimumab Monotherapy |
| Number of subjects included in analysis | 36 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.99 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.75 |
| upper limit | 1.78 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.382 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Week 12. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---|
| Comparison groups | Belimumab + Rituximab Co-administration therapy v Rituximab Monotherapy |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.63 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.52 |
| upper limit | 2.26 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.442 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Week 12. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---------------------------------|
| Comparison groups | Placebo v Belimumab Monotherapy |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.34 |
| upper limit | 1.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.732 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 5 |
| Statistical analysis description: | |
| Week 12. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect. | |
| Comparison groups | Belimumab Monotherapy v Rituximab Monotherapy |
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.35 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.5 |
| upper limit | 3.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.422 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 6 |
| Statistical analysis description: | |
| Week 24. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect. | |
| Comparison groups | Placebo v Belimumab + Rituximab Co-administration therapy |
| Number of subjects included in analysis | 25 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -2.45 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.67 |
| upper limit | 0.77 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.607 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 7 |
| Statistical analysis description: | |
| Week 24. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect. | |
| Comparison groups | Belimumab + Rituximab Co-administration therapy v Belimumab Monotherapy |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 36 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.46 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.99 |
| upper limit | 1.08 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.265 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 8 |
|-----------------------------------|------------------------|

Statistical analysis description:

Week 24. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---|
| Comparison groups | Belimumab + Rituximab Co-administration therapy v Rituximab Monotherapy |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.68 |
| upper limit | 2.55 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.305 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 9 |
|-----------------------------------|------------------------|

Statistical analysis description:

Week 24. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---------------------------------|
| Comparison groups | Placebo v Belimumab Monotherapy |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.17 |
| upper limit | 2.18 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.584 |

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Statistical Analysis 10 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Week 24. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---|
| Comparison groups | Belimumab Monotherapy v Rituximab Monotherapy |
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 1.39 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.2 |
| upper limit | 3.97 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.29 |

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Statistical Analysis 11 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Week 36. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---|
| Comparison groups | Placebo v Belimumab + Rituximab Co-administration therapy |
| Number of subjects included in analysis | 25 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.66 |
| upper limit | 2.73 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.845 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 12 |
| Statistical analysis description: | |
| Week 36. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect. | |
| Comparison groups | Belimumab + Rituximab Co-administration therapy v Belimumab Monotherapy |
| Number of subjects included in analysis | 36 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.76 |
| upper limit | 3.05 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.449 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 13 |
| Statistical analysis description: | |
| Week 36. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect. | |
| Comparison groups | Belimumab + Rituximab Co-administration therapy v Rituximab Monotherapy |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.15 |
| upper limit | 3.86 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.498 |

| | |
|--|-------------------------|
| Statistical analysis title | Statistical Analysis 14 |
| Statistical analysis description: | |
| Week 36. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect. | |

| | |
|---|---------------------------------|
| Comparison groups | Placebo v Belimumab Monotherapy |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.76 |
| upper limit | 2.53 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.817 |

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Statistical Analysis 15 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Week 36. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---|
| Comparison groups | Belimumab Monotherapy v Rituximab Monotherapy |
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.25 |
| upper limit | 3.66 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.476 |

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Statistical Analysis 16 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Week 52. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---|
| Comparison groups | Placebo v Belimumab + Rituximab Co-administration therapy |
| Number of subjects included in analysis | 25 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -2.8 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.95 |
| upper limit | 0.34 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.57 |

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Statistical Analysis 17 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Week 52. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---|
| Comparison groups | Belimumab + Rituximab Co-administration therapy v Belimumab Monotherapy |
| Number of subjects included in analysis | 36 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.91 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.39 |
| upper limit | 1.56 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.237 |

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Statistical Analysis 18 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Week 52. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---|
| Comparison groups | Belimumab + Rituximab Co-administration therapy v Rituximab Monotherapy |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.36 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.91 |
| upper limit | 1.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.275 |

| | |
|--|---------------------------------|
| Statistical analysis title | Statistical Analysis 19 |
| Statistical analysis description: | |
| Week 52. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect. | |
| Comparison groups | Placebo v Belimumab Monotherapy |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.99 |
| upper limit | 1.21 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.548 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 20 |
| Statistical analysis description: | |
| Week 52. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect. | |
| Comparison groups | Belimumab Monotherapy v Rituximab Monotherapy |
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -0.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.97 |
| upper limit | 2.08 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.261 |

| | |
|--|---|
| Statistical analysis title | Statistical Analysis 21 |
| Statistical analysis description: | |
| Week 68. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect. | |
| Comparison groups | Placebo v Belimumab + Rituximab Co-administration therapy |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 25 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -3.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.39 |
| upper limit | -0.58 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.699 |

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Statistical Analysis 22 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Week 68. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---|
| Comparison groups | Belimumab + Rituximab Co-administration therapy v Belimumab Monotherapy |
| Number of subjects included in analysis | 36 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.54 |
| upper limit | 0.81 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.336 |

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Statistical Analysis 23 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Week 68. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---|
| Comparison groups | Belimumab + Rituximab Co-administration therapy v Rituximab Monotherapy |
| Number of subjects included in analysis | 33 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | -1.35 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.12 |
| upper limit | 1.41 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.379 |

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Statistical Analysis 24 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Week 68. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---------------------------------|
| Comparison groups | Placebo v Belimumab Monotherapy |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | LS mean difference |
| Point estimate | -2.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.47 |
| upper limit | 1.23 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.674 |

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Statistical Analysis 25 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Week 68. Analysis was performed using mixed effects repeated measures model, with Baseline, treatment, visit and interactions of visit with treatment as fixed effects and participant as a random effect.

| | |
|---|---|
| Comparison groups | Belimumab Monotherapy v Rituximab Monotherapy |
| Number of subjects included in analysis | 35 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | LS mean difference |
| Point estimate | 0.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.21 |
| upper limit | 3.24 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.362 |

Secondary: Stimulated salivary flow rate over time

| | |
|-----------------|---|
| End point title | Stimulated salivary flow rate over time |
|-----------------|---|

End point description:

Participants were instructed to chew a piece of paraffin wax for a period of 5 minutes and saliva was collected. The volume of saliva (milliliter) was divided by the duration of the test (minutes) to calculate the stimulated salivary flow rate (milliliter per minute). Baseline value is the screening visit value (within 35 days prior to Day 0). Only those participants with data available at the specified data points were analyzed (represented by n=X in category titles).

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

End point timeframe:

Baseline (Screening [within 35 days prior to Day 0]), Week 12, Week 24, Week 36, Week 52 and Week 68

| End point values | Placebo | Belimumab + Rituximab Co- administration therapy | Belimumab Monotherapy | Rituximab Monotherapy |
|---------------------------------------|---------------------|---|--------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 ^[15] | 17 ^[16] | 19 ^[17] | 16 ^[18] |
| Units: Milliliter per minute | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (Screening); n=8, 17, 19 ,16 | 0.470 (± 0.2470) | 0.714 (± 0.6294) | 0.425 (± 0.3292) | 0.618 (± 0.6211) |
| Week 12; n=8, 17, 19 ,16 | 0.486 (± 0.2045) | 0.754 (± 0.8342) | 0.493 (± 0.3733) | 0.581 (± 0.5265) |
| Week 24; n=8, 17, 19 ,16 | 0.554 (± 0.3054) | 0.784 (± 0.7900) | 0.454 (± 0.4105) | 0.724 (± 0.8901) |
| Week 36; n=8, 17, 19 ,15 | 0.404 (± 0.2497) | 1.039 (± 1.1027) | 0.506 (± 0.4261) | 0.689 (± 0.5907) |
| Week 52; n=8, 17, 19 ,16 | 0.531 (± 0.3782) | 0.999 (± 1.1457) | 0.582 (± 0.6084) | 0.693 (± 0.7813) |
| Week 68; n=8, 17, 19 ,15 | 0.361 (± 0.1628) | 0.879 (± 0.8167) | 0.517 (± 0.4499) | 0.733 (± 0.7850) |

Notes:

[15] - Completer Population

[16] - Completer Population

[17] - Completer Population

[18] - Completer Population

Statistical analyses

No statistical analyses for this end point

Secondary: Oral dryness numeric response scale (NRS) over time

| | |
|-----------------|---|
| End point title | Oral dryness numeric response scale (NRS) over time |
|-----------------|---|

End point description:

Oral dryness was reported by participants on a numeric response scale, ranging from 0 (no dryness) to 10 (maximal dryness), higher score indicates worst imaginable dryness. Baseline value is the screening visit value (within 35 days prior to Day 0). Only those participants with data available at the specified data points were analyzed (represented by n=X in category titles).

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Screening [within 35 days prior to Day 0]), Week 12, Week 24, Week 36, Week 52 and Week 68 | |

| End point values | Placebo | Belimumab + Rituximab Co-administration therapy | Belimumab Monotherapy | Rituximab Monotherapy |
|--|-------------------|---|-----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 ^[19] | 17 ^[20] | 19 ^[21] | 16 ^[22] |
| Units: Scores on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (Screening); n= 8, 17, 19, 16 | 7.6 (± 1.51) | 7.4 (± 1.46) | 7.2 (± 2.14) | 7.3 (± 1.91) |
| Week 12; n=8, 17, 19, 16 | 6.1 (± 2.59) | 5.7 (± 1.96) | 6.9 (± 2.32) | 5.1 (± 2.77) |
| Week 24; n=8, 17, 19, 15 | 5.8 (± 2.38) | 5.3 (± 1.83) | 6.8 (± 2.51) | 5.6 (± 2.72) |
| Week 36; n=8, 17, 19, 16 | 5.8 (± 2.76) | 5.9 (± 2.26) | 6.6 (± 2.19) | 6.2 (± 2.51) |
| Week 52; n=8, 17, 19, 16 | 5.6 (± 2.13) | 5.7 (± 1.92) | 7.0 (± 2.40) | 6.3 (± 2.32) |
| Week 68; n=8, 17, 19, 16 | 6.6 (± 2.26) | 6.1 (± 2.63) | 6.9 (± 2.34) | 6.1 (± 2.62) |

Notes:

[19] - Completer Population

[20] - Completer Population

[21] - Completer Population

[22] - Completer Population

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values for B-cells (cluster of differentiation 20 [CD20]) within salivary gland biopsy at Week 24

| | |
|--|--|
| End point title | Absolute values for B-cells (cluster of differentiation 20 [CD20]) within salivary gland biopsy at Week 24 |
| End point description: | |
| Minor salivary gland biopsies were taken for histological analysis to quantify CD20 B Cells. Only those participants with data available at the specified data points were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| At Week 24 | |

| End point values | Placebo | Belimumab + Rituximab Co-administration therapy | Belimumab Monotherapy | Rituximab Monotherapy |
|--------------------------------------|--------------------------|---|--------------------------|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 ^[23] | 10 ^[24] | 15 ^[25] | 12 ^[26] |
| Units: Cells per millimeter square | | | | |
| arithmetic mean (standard deviation) | 380.21719 (± 569.908102) | 8.65550 (± 20.199794) | 396.86058 (± 781.245844) | 650.76069 (± 1311.360352) |

Notes:

[23] - Completer Population

[24] - Completer Population

[25] - Completer Population

[26] - Completer Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-SAEs were collected up to Week 68.

Adverse event reporting additional description:

Safety Population was used to assess SAEs and non-SAEs which comprised of all participants who received at least one dose of study treatment.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

Reporting groups

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

Reporting group description:

Participants received belimumab matching placebo weekly subcutaneous injections up to Week 52 and rituximab matching placebo infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment General Follow-Up (GFU) period.

| | |
|-----------------------|---|
| Reporting group title | Belimumab + Rituximab Co-administration therapy |
|-----------------------|---|

Reporting group description:

Participants received belimumab 200 milligrams (mg) weekly subcutaneous injections for 24 weeks followed by belimumab matching placebo injections weekly up to Week 52; along with rituximab 1000 mg intravenous infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment GFU period.

| | |
|-----------------------|-----------------------|
| Reporting group title | Belimumab Monotherapy |
|-----------------------|-----------------------|

Reporting group description:

Participants received 200 mg weekly subcutaneous injections of belimumab up to Week 52 and rituximab matching placebo infusions at Weeks 8 and 10 in the treatment period. Participants then entered in a 16-week no-treatment GFU period.

| | |
|-----------------------|-----------------------|
| Reporting group title | Rituximab Monotherapy |
|-----------------------|-----------------------|

Reporting group description:

Participants received 1000 mg intravenous rituximab infusions at Weeks 8 and 10 and weekly subcutaneous injections of belimumab matching placebo up to Week 52 in the treatment period. Participants then entered in a 16-week no-treatment GFU period.

| Serious adverse events | Placebo | Belimumab + Rituximab Co- administration therapy | Belimumab Monotherapy |
|---|----------------|---|--------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 3 / 24 (12.50%) | 2 / 24 (8.33%) |
| number of deaths (all causes) | 0 | 1 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Tendon rupture | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 24 (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 acute | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Aspiration | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Sjogren's syndrome | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 24 (4.17%) |
| 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 | | | |

| | | | |
|---|----------------|----------------|----------------|
| Bronchitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 24 (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 |
| Ophthalmic herpes zoster | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 24 (4.17%) |
| 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 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 24 (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 |

| | | | |
|---|--------------------------|--|--|
| Serious adverse events | Rituximab Monotherapy | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 25 (16.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Tendon rupture | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Hypotension | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Aspiration | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Sjogren's syndrome | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Bronchitis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ophthalmic herpes zoster | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Placebo | Belimumab + Rituximab Co- administration therapy | Belimumab Monotherapy |
|---|------------------|---|--------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 13 (92.31%) | 24 / 24 (100.00%) | 23 / 24 (95.83%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 2 / 24 (8.33%) |
| occurrences (all) | 0 | 1 | 2 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 5 / 24 (20.83%) | 4 / 24 (16.67%) |
| occurrences (all) | 3 | 7 | 5 |
| Dizziness | | | |

| | | | |
|---|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 2 / 24 (8.33%) 2 | 6 / 24 (25.00%) 9 |
| Migraine subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 1 / 24 (4.17%) 2 | 2 / 24 (8.33%) 2 |
| General disorders and administration site conditions | | | |
| Fatigue subjects affected / exposed occurrences (all) | 3 / 13 (23.08%) 5 | 6 / 24 (25.00%) 6 | 2 / 24 (8.33%) 2 |
| Pyrexia subjects affected / exposed occurrences (all) | 4 / 13 (30.77%) 4 | 3 / 24 (12.50%) 3 | 2 / 24 (8.33%) 2 |
| Asthenia subjects affected / exposed occurrences (all) | 2 / 13 (15.38%) 4 | 2 / 24 (8.33%) 2 | 1 / 24 (4.17%) 1 |
| Influenza like illness subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | 2 / 24 (8.33%) 2 | 2 / 24 (8.33%) 2 |
| Injection site pain subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | 2 / 24 (8.33%) 2 | 2 / 24 (8.33%) 2 |
| Gastrointestinal disorders | | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 3 / 13 (23.08%) 3 | 3 / 24 (12.50%) 5 | 3 / 24 (12.50%) 3 |
| Nausea subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 2 | 1 / 24 (4.17%) 1 | 3 / 24 (12.50%) 3 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | 1 / 24 (4.17%) 1 | 3 / 24 (12.50%) 4 |
| Parotid gland enlargement subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 2 | 2 / 24 (8.33%) 2 | 1 / 24 (4.17%) 2 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|-----------------------|-----------------------|-----------------------|
| Cough subjects affected / exposed occurrences (all) | 2 / 13 (15.38%) 2 | 1 / 24 (4.17%) 1 | 2 / 24 (8.33%) 2 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 0 / 24 (0.00%) 0 | 4 / 24 (16.67%) 4 |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 3 / 13 (23.08%) 4 | 3 / 24 (12.50%) 3 | 1 / 24 (4.17%) 1 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 2 / 13 (15.38%) 2 | 7 / 24 (29.17%) 10 | 7 / 24 (29.17%) 12 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 3 | 2 / 24 (8.33%) 2 | 5 / 24 (20.83%) 5 |
| Pain in extremity subjects affected / exposed occurrences (all) | 2 / 13 (15.38%) 2 | 3 / 24 (12.50%) 3 | 1 / 24 (4.17%) 1 |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 0 / 13 (0.00%) 0 | 2 / 24 (8.33%) 2 | 2 / 24 (8.33%) 3 |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 4 / 13 (30.77%) 10 | 8 / 24 (33.33%) 11 | 6 / 24 (25.00%) 9 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 3 / 13 (23.08%) 4 | 5 / 24 (20.83%) 7 | 3 / 24 (12.50%) 9 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 3 | 3 / 24 (12.50%) 4 | 2 / 24 (8.33%) 3 |
| Bronchitis subjects affected / exposed occurrences (all) | 1 / 13 (7.69%) 1 | 2 / 24 (8.33%) 2 | 3 / 24 (12.50%) 3 |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| Influenza | | | |
| subjects affected / exposed | 3 / 13 (23.08%) | 0 / 24 (0.00%) | 4 / 24 (16.67%) |
| occurrences (all) | 4 | 0 | 4 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 2 / 24 (8.33%) | 2 / 24 (8.33%) |
| occurrences (all) | 1 | 2 | 2 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 2 / 24 (8.33%) | 1 / 24 (4.17%) |
| occurrences (all) | 2 | 3 | 1 |

| Non-serious adverse events | Rituximab Monotherapy | | |
|---|--------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 17 / 25 (68.00%) | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 6 / 25 (24.00%) | | |
| occurrences (all) | 7 | | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |
| Migraine | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |
| Asthenia | | | |

| | | | |
|---|----------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | | |
| Influenza like illness subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | | |
| Injection site pain subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | | |
| Nausea subjects affected / exposed occurrences (all) | 3 / 25 (12.00%) 3 | | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | | |
| Parotid gland enlargement subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | | |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 3 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 5 / 25 (20.00%) 5 | | |

| | | | |
|-----------------------------------|-----------------|--|--|
| Back pain | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 3 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences (all) | 2 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | | |
| occurrences (all) | 4 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 6 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 5 / 25 (20.00%) | | |
| occurrences (all) | 6 | | |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |
| Influenza | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences (all) | 2 | | |
| Oral herpes | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | | |
| occurrences (all) | 4 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 15 October 2015 | Amendment 1: Protocol amended in response to comments received from Swedish regulatory authority. This was country-specific and applied to sites in Sweden. Information about the interim analysis was updated to provide clarity on the timing and number of the analysis. A modification to the withdrawal/stopping criteria language was made to specify that participants will be withdrawn from investigational product (IP) in the event of a life-threatening infection. A statement was also added to clarify that regulatory agency approval is required for the protocol and for substantial amendments to the protocol. |
| 20 November 2015 | Amendment 2: Protocol amended in response to comments received from Norwegian regulatory authority. This was country-specific and applied to all sites in Norway. The protocol was amended to clarify the number of participants required for the interim analysis and the basis for the sample size recalculation following that analysis. Language was also added to provide guidance regarding tuberculosis assessment during screening. |
| 04 January 2016 | Amendment 3: Protocol amended in response to comments received from Italian regulatory authority. This was country-specific and applied to sites in Italy. The protocol was amended to update the list of highly effective methods of contraception and to correct a typographical error regarding the permitted dose of hydroxychloroquine. |
| 13 June 2016 | Amendment 4: The primary reason for this amendment was to modify the participant selection criteria (specifically exclusion criterion number 30 pertaining to exclusionary laboratory thresholds) to better align with the intended population characteristics. Other amendments included the following: Greater clarity was provided regarding the committees involved in monitoring participant safety and review of study data as well as the governance of the study. It has been made clear that a single formal interim analysis is planned. The participant withdrawal and study stopping criteria have been modified. Greater detail was provided regarding prohibited and permitted medications. Additional guidance was provided regarding vaccination. Guidance has been provided for tuberculosis assessment during the screening period. The pregnancy section has been modified to clarify the duration of follow up required. |
| 11 May 2018 | Amendment 5: The primary reason for this amendment was to clarify the definition of "sponsor open" in Section 6.3, with respect to study blinding. Additional minor clarifications have been made throughout the protocol. |
| 25 June 2019 | Amendment 6: The primary reason for this amendment was to clarify the timing of unblinding for GlaxoSmithKline (GSK) staff and site staff. Additional minor updates have been made in several sections of the protocol. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported