



Clinical trial results:

A Randomised, Double-Blind, Placebo Controlled, Parallel-Group, Multicenter Study To Evaluate The Efficacy and Safety of Two Doses of Ocrelizumab in Patients With WHO or ISN Class III or IV Nephritis Due To Systemic Lupus Erythematosus

Summary

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2006-005357-29 |
| Trial protocol | GB FR DE HU ES NL PT SE PL BG |
| Global end of trial date | 28 October 2013 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 19 May 2016 |
| First version publication date | 07 August 2015 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set2 data eras identified as part of QC that require correction |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | WA20500 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00626197 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | F. Hoffmann-La Roche AG |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070 |
| Public contact | Roche Trial Information Hotline , F. Hoffmann-La Roche AG , 41 61 6878333, global.trial_information@roche.com |
| Scientific contact | Roche Trial Information Hotline , F. Hoffmann-La Roche AG , 41 61 6878333, global.trial_information@roche.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 | 19 November 2013 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 October 2013 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To investigate the ability of the ocrelizumab regimen in combination with Standard Of Care (SOC) treatment to induce a complete or partial renal response, as assessed by renal function, urinary sediment and proteinuria in participants with International Society of Nephrology/Renal Pathology Society (ISN/RPS) or World Health Organization (WHO) class III or IV lupus nephritis.

Protection of trial subjects:

The investigator ensured that this study was conducted in full conformance with the principles of the "Declaration of Helsinki" or with the laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the individual and fully adhered to the principles outlined in "Guideline for Good Clinical Practice" International Conference on Harmonisation (ICH) Tripartite Guideline [January 1997] or with local law if it affords greater protection to the participant. For studies conducted in the European Union/European Economic Area (EU/EEA) countries, the investigator ensured compliance with the EU Clinical Trial Directive [2001/20/EC]. For studies conducted in the United State of America (USA) or under US Investigational new drug (IND), the investigator additionally ensured that the basic principles of "Good Clinical Practice" as outlined in the current version of 21 CFR, subchapter D, part 312, "Responsibilities of Sponsors and Investigators", part 50, "Protection of Human Patients", and part 56, "Institutional Review Boards", were adhered to.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 15 February 2008 |
| 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 | Netherlands: 6 |
| Country: Number of subjects enrolled | Spain: 10 |
| Country: Number of subjects enrolled | Sweden: 1 |
| Country: Number of subjects enrolled | United Kingdom: 4 |
| Country: Number of subjects enrolled | Bulgaria: 10 |
| Country: Number of subjects enrolled | France: 18 |
| Country: Number of subjects enrolled | Germany: 10 |
| Country: Number of subjects enrolled | Hungary: 11 |
| Country: Number of subjects enrolled | Argentina: 56 |
| Country: Number of subjects enrolled | Brazil: 18 |
| Country: Number of subjects enrolled | Canada: 3 |
| Country: Number of subjects enrolled | Chile: 2 |
| Country: Number of subjects enrolled | Colombia: 43 |

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Costa Rica: 4 |
| Country: Number of subjects enrolled | Hong Kong: 5 |
| Country: Number of subjects enrolled | Indonesia: 3 |
| Country: Number of subjects enrolled | Malaysia: 18 |
| Country: Number of subjects enrolled | Mexico: 21 |
| Country: Number of subjects enrolled | Peru: 16 |
| Country: Number of subjects enrolled | Philippines: 15 |
| Country: Number of subjects enrolled | Russian Federation: 10 |
| Country: Number of subjects enrolled | Serbia: 5 |
| Country: Number of subjects enrolled | South Africa: 5 |
| Country: Number of subjects enrolled | Korea, Republic of: 17 |
| Country: Number of subjects enrolled | Taiwan: 8 |
| Country: Number of subjects enrolled | Thailand: 22 |
| Country: Number of subjects enrolled | Turkey: 4 |
| Country: Number of subjects enrolled | United States: 36 |
| Worldwide total number of subjects | 381 |
| EEA total number of subjects | 70 |

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) | 7 |
| Adults (18-64 years) | 372 |
| From 65 to 84 years | 2 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening was done from Day -14 to Day -1.

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 | Placebo |

Arm description:

Participants received placebo matched to ocrelizumab infusion intravenously (IV) on Days 1 and 15, followed by placebo matched to ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or mycophenolate mofetil (MMF) 1 grams per day (g/day) in the first week increased to 3 g/day. Participants also received methylprednisolone 100 milligram (mg) infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of placebo. Participants also received oral prednisone at a starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

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

Dosage and administration details:

Participants received placebo IV on days 1 and 15, followed by placebo IV at Week 16 and then every 16 weeks up to 48 weeks.

| | |
|------------------|--------------------|
| Arm title | Ocrelizumab 400 mg |
|------------------|--------------------|

Arm description:

Participants received 400 mg ocrelizumab IV on Days 1 and 15, followed by 400 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|-----------------------|
| Investigational medicinal product name | Ocrelizumab |
| Investigational medicinal product code | |
| Other name | RO4964913 |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received ocrelizumab on Days 1 and 15, followed by 400 mg IV at Week 16 and then every 16 weeks up to 48 weeks.

| | |
|------------------|---------------------|
| Arm title | Ocrelizumab 1000 mg |
|------------------|---------------------|

Arm description:

Participants received 1000 mg ocrelizumab IV on Days 1 and 15, followed by 1000 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ocrelizumab |
| Investigational medicinal product code | |
| Other name | RO4964913 |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received ocrelizumab on Days 1 and 15, followed by 1000 mg IV at Week 16 and then every 16 weeks up to 48 weeks.

| Number of subjects in period 1 | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg |
|---------------------------------------|---------|--------------------|---------------------|
| Started | 126 | 127 | 128 |
| Completed | 49 | 83 | 74 |
| Not completed | 77 | 44 | 54 |
| Adverse event, serious fatal | 6 | 3 | 6 |
| Consent withdrawn by subject | 7 | 17 | 17 |
| Failure to return | 6 | 6 | 5 |
| Adverse event, non-fatal | 2 | 1 | 1 |
| Administrative reasons | 55 | 15 | 19 |
| Did not cooperate | 1 | 2 | 6 |

Baseline characteristics

Reporting groups

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

Reporting group description:

Participants received placebo matched to ocrelizumab infusion intravenously (IV) on Days 1 and 15, followed by placebo matched to ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or mycophenolate mofetil (MMF) 1 grams per day (g/day) in the first week increased to 3 g/day. Participants also received methylprednisolone 100 milligram (mg) infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of placebo. Participants also received oral prednisone at a starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

| | |
|-----------------------|--------------------|
| Reporting group title | Ocrelizumab 400 mg |
|-----------------------|--------------------|

Reporting group description:

Participants received 400 mg ocrelizumab IV on Days 1 and 15, followed by 400 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

| | |
|-----------------------|---------------------|
| Reporting group title | Ocrelizumab 1000 mg |
|-----------------------|---------------------|

Reporting group description:

Participants received 1000 mg ocrelizumab IV on Days 1 and 15, followed by 1000 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

| Reporting group values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg |
|------------------------|---------|--------------------|---------------------|
| Number of subjects | 126 | 127 | 128 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------------------|-------|--------|-------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 31.3 | 31.9 | 30.6 |
| standard deviation | ± 9.9 | ± 10.2 | ± 8.9 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 107 | 115 | 110 |
| Male | 19 | 12 | 18 |

| Reporting group values | Total | | |
|------------------------|-------|--|--|
| Number of subjects | 381 | | |

| | | | |
|---|-----|--|--|
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | - | | |
| Gender categorical Units: Subjects | | | |
| Female | 332 | | |
| Male | 49 | | |

End points

End points reporting groups

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

Reporting group description:

Participants received placebo matched to ocrelizumab infusion intravenously (IV) on Days 1 and 15, followed by placebo matched to ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or mycophenolate mofetil (MMF) 1 grams per day (g/day) in the first week increased to 3 g/day.

Participants also received methylprednisolone 100 milligram (mg) infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of placebo. Participants also received oral prednisone at a starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

| | |
|-----------------------|--------------------|
| Reporting group title | Ocrelizumab 400 mg |
|-----------------------|--------------------|

Reporting group description:

Participants received 400 mg ocrelizumab IV on Days 1 and 15, followed by 400 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

| | |
|-----------------------|---------------------|
| Reporting group title | Ocrelizumab 1000 mg |
|-----------------------|---------------------|

Reporting group description:

Participants received 1000 mg ocrelizumab IV on Days 1 and 15, followed by 1000 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

| | |
|----------------------------|-----------|
| Subject analysis set title | OCR + SOC |
|----------------------------|-----------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

This analysis set included all participants who were treated with ocrelizumab (OCR).

| | |
|----------------------------|-------------------------------------|
| Subject analysis set title | Placebo-Mycophenolate Mofetil (MMF) |
|----------------------------|-------------------------------------|

| | |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

Subject analysis set description:

Placebo - MMF group included participants whose SOC treatment included MMF as an immunosuppressant treatment.

| | |
|----------------------------|-------------------------|
| Subject analysis set title | Placebo-Euro Lupus (EL) |
|----------------------------|-------------------------|

| | |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

Subject analysis set description:

Placebo-EL group included participants whose SOC treatment included Cyclophosphamide (Euro-lupus) as part of the immunosuppressant treatment.

Primary: Percentage of Participants who Achieved a Complete Renal Response (CRR) or a Partial Renal Response (PRR) at Week 48

| | |
|-----------------|---|
| End point title | Percentage of Participants who Achieved a Complete Renal Response (CRR) or a Partial Renal Response (PRR) at Week 48 ^[1] |
|-----------------|---|

End point description:

CRR was defined as: 1. Normal serum creatinine (and with no more than a 25 percent [%] increase from Baseline); 2. Improvement in urinary protein:urinary creatinine ratio to less than or equal to (\leq) 0.5. PRR was defined as at least 50 percent (%) reduction in proteinuria from Baseline, without more than 25% increase of serum creatinine at Week 48, compared with Baseline. If Baseline urine protein:urine creatinine ratio was greater than ($>$) 3, a urine protein:urine creatinine ratio of less than ($<$) 3 needed to be achieved.

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

End point timeframe:

Week 48

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: The primary endpoint was analyzed via an overall response (CRR+PRR) analysis and the separate complete and partial response rates were only summarized descriptively.

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-----------------------------------|-----------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 75 | 75 | 73 | 148 |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| CRR | 34.7 | 42.7 | 31.5 | 37.2 |
| PRR | 20 | 24 | 35.6 | 29.7 |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Achieved Overall Response

| | |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved Overall Response |
|-----------------|--|

End point description:

Overall response rate (ORR) equals (=) CRR + PRR. CRR was defined as: 1. Normal serum creatinine (and with no more than a 25% increase from baseline) 2. Improvement in urinary protein:urinary creatinine ratio to ≤ 0.5 . PRR was defined as at least 50 % reduction in proteinuria from Baseline, without more than 25% increase of serum creatinine at Week 48, compared with Baseline. If Baseline urine protein:urine creatinine ratio is > 3 , a urine protein:urine creatinine ratio of < 3 needs to be achieved.

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

End point timeframe:

Week 48

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-----------------------------------|------------------------|-----------------------|------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 75 | 75 | 73 | 148 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 54.7 (43.4 to 65.9) | 66.7 (56 to 77.3) | 67.1 (56.3 to 77.9) | 66.9 (59.3 to 74.5) |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Placebo v Ocrelizumab 400 mg |
| Number of subjects included in analysis | 150 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 12.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.3 |
| upper limit | 27.5 |

| | |
|---|--------------------------------|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | Placebo v Ocrelizumab 1000 mg |
| Number of subjects included in analysis | 148 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 13.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.4 |
| upper limit | 29.2 |

| | |
|---|--------------------------------|
| Statistical analysis title | Statistical Analysis 3 |
| Comparison groups | Placebo v OCR + SOC |
| Number of subjects included in analysis | 223 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.065 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 12.7 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.8 |
| upper limit | 26.1 |

Secondary: Percentage of Participants who Achieved a Renal Response (Partial or Complete) by Week 36, and Sustain or Improve This Response Until Week 48

| | |
|---|---|
| End point title | Percentage of Participants who Achieved a Renal Response (Partial or Complete) by Week 36, and Sustain or Improve This Response Until Week 48 |
| End point description: | |
| CRR was defined as: 1. Normal serum creatinine (and with no more than a 25% increase from Baseline) 2. Inactive urinary sediment 3. Improvement in urinary protein:urinary creatinine ratio to ≤ 0.5 . PRR was defined as at least 50 % reduction in proteinuria from Baseline, without more than 25% increase of serum creatinine at Week 48, compared with Baseline. If Baseline urine protein:urine creatinine ratio was >3 , a urine protein:urine creatinine ratio of <3 needed to be achieved. | |
| End point type | Secondary |
| End point timeframe: | |
| Weeks 36, 40, 44, and 48 | |

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-----------------------------------|------------------|--------------------|---------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[2] | 0 ^[3] | 0 ^[4] | 0 ^[5] |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |

Notes:

[2] - Due to early termination of the study, no secondary outcome analyses were performed.

[3] - Due to early termination of the study, no secondary outcome analyses were performed.

[4] - Due to early termination of the study, no secondary outcome analyses were performed.

[5] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Complete Renal Response

| | |
|--|---------------------------------|
| End point title | Time to Complete Renal Response |
| End point description: | |
| Time to complete renal response was proposed to be analyzed using a stratified log rank test with race and SOC as stratification factors. Comparisons of ocrelizumab versus placebo were to be expressed as p-values, estimated hazard ratios, adjusted proportions of participants who achieved a complete renal response and their 95% confidence intervals. Kaplan-Meier curves were to be produced. Due to early termination of the study the analyses were not performed. | |
| End point type | Secondary |
| End point timeframe: | |
| Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48 | |

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-------------------------------|------------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[6] | 0 ^[7] | 0 ^[8] | 0 ^[9] |
| Units: Weeks | | | | |
| median (full range (min-max)) | (to) | (to) | (to) | (to) |

Notes:

[6] - Due to early termination of the study, no secondary outcome analyses were performed.

[7] - Due to early termination of the study, no secondary outcome analyses were performed.

[8] - Due to early termination of the study, no secondary outcome analyses were performed.

[9] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve (AUC) of Calculated Glomerular Filtration Rate (cGFR) Between Baseline and Week 48

| | |
|-----------------|---|
| End point title | Area Under the Curve (AUC) of Calculated Glomerular Filtration Rate (cGFR) Between Baseline and Week 48 |
|-----------------|---|

End point description:

The improvement of AUC of cGFR was to be measured between Baseline and Week 48. This was to be analyzed with Analysis of Covariance (ANCOVA) with race and SOC as covariates.

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

End point timeframe:

Baseline and Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and Week 48

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|--------------------------------------|-------------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[10] | 0 ^[11] | 0 ^[12] | 0 ^[13] |
| Units: mL/min)*weeks | | | | |
| arithmetic mean (standard deviation) | () | () | () | () |

Notes:

[10] - Due to early termination of the study, no secondary outcome analyses were performed.

[11] - Due to early termination of the study, no secondary outcome analyses were performed.

[12] - Due to early termination of the study, no secondary outcome analyses were performed.

[13] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved A Reduction In Systemic Lupus Erythematosis Disease Activity Index (SLEDAI) -2K Score

| | |
|-----------------|---|
| End point title | Percentage of Participants Who Achieved A Reduction In Systemic Lupus Erythematosis Disease Activity Index (SLEDAI) -2K Score |
|-----------------|---|

End point description:

SLEDAI-2K measures disease activity at the visit or within the preceding 10 days. It comprised of 24 descriptors, covering 9 organ systems, and reflects disease activity over the previous 10 days. The total SLEDAI-2K score falls between 0 and 105, with higher scores representing higher disease activity

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

End point timeframe:

Baseline and Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-----------------------------------|-------------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[14] | 0 ^[15] | 0 ^[16] | 0 ^[17] |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |

Notes:

[14] - Due to early termination of the study, no secondary outcome analyses were performed.

[15] - Due to early termination of the study, no secondary outcome analyses were performed.

[16] - Due to early termination of the study, no secondary outcome analyses were performed.

[17] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Renal Flare In Those Participants who Demonstrated at least a Partial Renal Response

| | |
|-----------------|--|
| End point title | Time to First Renal Flare In Those Participants who Demonstrated at least a Partial Renal Response |
|-----------------|--|

End point description:

Renal flares may be either proteinuric or nephritic as defined below: Proteinuric Flares are defined as follows: In participants who achieve a urine protein:urine creatinine (Upr:Ucr) ≤ 0.5 , an increase to Upr:Ucr >1 ; In participants with an Upr:Ucr >0.5 , a doubling of Upr:Ucr (with a minimum increase to Upr:Ucr >2).

Nephritic Flare defined as: Increase in serum creatinine of $\geq 30\%$ from the lowest value achieved in the study accompanied by Increase Upr:Ucr >1 Or New/worsening active urine sediment on two consecutive occasions, in the absence of urinary tract infection or other causes of hematuria.

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

End point timeframe:

Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-------------------------------|-------------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[18] | 0 ^[19] | 0 ^[20] | 0 ^[21] |
| Units: Weeks | | | | |
| median (full range (min-max)) | (to) | (to) | (to) | (to) |

Notes:

[18] - Due to early termination of the study, no secondary outcome analyses were performed.

[19] - Due to early termination of the study, no secondary outcome analyses were performed.

[20] - Due to early termination of the study, no secondary outcome analyses were performed.

[21] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved Clinically Meaningful Improvement in the Physical and Mental Component Scores of the Short Form 36 (SF36) from Baseline to Week 48

| | |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved Clinically Meaningful Improvement in the Physical and Mental Component Scores of the Short Form 36 (SF36) from Baseline to Week 48 |
|-----------------|--|

End point description:

The SF36 Health Survey is a 36-item, patient-reported survey of patient health. The SF-36 consists of eight scaled scores, which are the weighted sums of the questions in their section. Each scale is directly transformed into a 0-100 scale. A score of zero is equivalent to maximum disability and a score of 100 is equivalent to no disability. The eight sections are: vitality, physical functioning, bodily pain, general health perceptions physical role functioning, emotional role functioning, social role functioning, and mental health.

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

End point timeframe:

Baseline and Weeks 1, 12, 24, 36, and 48

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-----------------------------------|-------------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[22] | 0 ^[23] | 0 ^[24] | 0 ^[25] |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |

Notes:

[22] - Due to early termination of the study, no secondary outcome analyses were performed.

[23] - Due to early termination of the study, no secondary outcome analyses were performed.

[24] - Due to early termination of the study, no secondary outcome analyses were performed.

[25] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved Clinically Meaningful Improvement in Fatigue Using the Functional Assessment of Chronic Illness Therapy (Facit) Fatigue Questionnaire from Baseline to Week 48

| | |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved Clinically Meaningful Improvement in Fatigue Using the Functional Assessment of Chronic Illness Therapy (Facit) Fatigue Questionnaire from Baseline to Week 48 |
|-----------------|--|

End point description:

The FACIT Fatigue Scale is a short, 13-item, easy-to-administer tool that measures an individual's level of fatigue during their usual daily activities over the past week. The level of fatigue is measured on a

four point Likert scale (4 = not at all fatigued to 0 = very much fatigued).

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Weeks 1, 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48 | |

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-----------------------------------|-------------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[26] | 0 ^[27] | 0 ^[28] | 0 ^[29] |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |

Notes:

[26] - Due to early termination of the study, no secondary outcome analyses were performed.

[27] - Due to early termination of the study, no secondary outcome analyses were performed.

[28] - Due to early termination of the study, no secondary outcome analyses were performed.

[29] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved Clinically Meaningful Improvement in Pain Using the Modified Brief Pain Inventory Short Form (mBPI-SF) from Baseline to Week 48

| | |
|-----------------|---|
| End point title | Percentage of Participants Who Achieved Clinically Meaningful Improvement in Pain Using the Modified Brief Pain Inventory Short Form (mBPI-SF) from Baseline to Week 48 |
|-----------------|---|

End point description:

m-BPI-sf is a self-administered 11-point Likert rating scale to rate pain in the past 24 hours. A single item pertains to worst pain in the past 24 hours with a range of 0 (no pain) to 10 (worst imaginable pain).

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Weeks 1, 12, 24, 36, and 48 | |

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-----------------------------------|-------------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[30] | 0 ^[31] | 0 ^[32] | 0 ^[33] |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |

Notes:

[30] - Due to early termination of the study, no secondary outcome analyses were performed.

[31] - Due to early termination of the study, no secondary outcome analyses were performed.

[32] - Due to early termination of the study, no secondary outcome analyses were performed.

[33] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Visits Over the 48-Week Treatment Period

| | |
|-----------------|--|
| End point title | Health Care Visits Over the 48-Week Treatment Period |
|-----------------|--|

End point description:

The number of health care visits (including doctor's office visits, Emergency room/ Accident and Emergency [ER/A&E] visits and hospitalizations) over the 48-week treatment period were recorded.

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

End point timeframe:

Weeks 1, 24, and 48

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-----------------------------|-------------------|--------------------|---------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[34] | 0 ^[35] | 0 ^[36] | 0 ^[37] |
| Units: visits | | | | |
| number (not applicable) | | | | |

Notes:

[34] - Due to early termination of the study, no secondary outcome analyses were performed.

[35] - Due to early termination of the study, no secondary outcome analyses were performed.

[36] - Due to early termination of the study, no secondary outcome analyses were performed.

[37] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved a CRR or PRR And who Received A Corticosteroid dose of <10 Milligrams per Day (mg/day) from Week 24 to Week 48

| | |
|-----------------|--|
| End point title | Percentage of Participants who Achieved a CRR or PRR And who Received A Corticosteroid dose of <10 Milligrams per Day (mg/day) from Week 24 to Week 48 |
|-----------------|--|

End point description:

CRR was defined as: 1. Normal serum creatinine (and with no more than a 25% increase from Baseline) 2. Inactive urinary sediment 3. Improvement in urinary protein:urinary creatinine ratio to ≤ 0.5 . PRR was defined as at least 50% reduction in proteinuria from Baseline, without more than 25% increase of serum creatinine at Week 48, compared with Baseline. If Baseline urine protein:urine creatinine ratio was >3 , a urine protein:urine creatinine ratio of <3 needed to be achieved.

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

End point timeframe:

Weeks 24, 28, 32, 36, 40, 44, and 48

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-----------------------------------|-------------------|--------------------|---------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[38] | 0 ^[39] | 0 ^[40] | 0 ^[41] |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |

Notes:

[38] - Due to early termination of the study, no secondary outcome analyses were performed.

[39] - Due to early termination of the study, no secondary outcome analyses were performed.

[40] - Due to early termination of the study, no secondary outcome analyses were performed.

[41] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved a CRR or PRR And who Received a Corticosteroid Dose of <5 mg/day by Week 48

| | |
|-----------------|---|
| End point title | Percentage of Participants who Achieved a CRR or PRR And who Received a Corticosteroid Dose of <5 mg/day by Week 48 |
|-----------------|---|

End point description:

CRR was defined as: 1. Normal serum creatinine (and with no more than a 25% increase from Baseline) 2. Inactive urinary sediment 3. Improvement in urinary protein:urinary creatinine ratio to ≤ 0.5 . PRR was defined as at least 50% reduction in proteinuria from Baseline, without more than 25% increase of serum creatinine at Week 48, compared with Baseline. If Baseline urine protein:urine creatinine ratio was >3 , a urine protein: urine creatinine ratio of <3 needed to be achieved.

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

End point timeframe:

Week 48

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-----------------------------------|-------------------|--------------------|---------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[42] | 0 ^[43] | 0 ^[44] | 0 ^[45] |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |

Notes:

[42] - Due to early termination of the study, no secondary outcome analyses were performed.

[43] - Due to early termination of the study, no secondary outcome analyses were performed.

[44] - Due to early termination of the study, no secondary outcome analyses were performed.

[45] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Average Corticosteroid Burden Measured by AUC of the Cumulative Corticosteroid Dose Between 16 and 48 Weeks

| | |
|-----------------|---|
| End point title | Average Corticosteroid Burden Measured by AUC of the Cumulative Corticosteroid Dose Between 16 and 48 Weeks |
|-----------------|---|

End point description:

AUC is the area under the curve (mathematically known as definite integral) in a plot of concentration of

drug in blood plasma against time. AUC was to be used to determine the average corticosteroid burden.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Weeks 16, 20, 24, 28, 32, 36, 40, 44, and 48 | |

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|--------------------------------------|-------------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[46] | 0 ^[47] | 0 ^[48] | 0 ^[49] |
| Units: (mg/mL)*weeks | | | | |
| arithmetic mean (standard deviation) | () | () | () | () |

Notes:

[46] - Due to early termination of the study, no secondary outcome analyses were performed.

[47] - Due to early termination of the study, no secondary outcome analyses were performed.

[48] - Due to early termination of the study, no secondary outcome analyses were performed.

[49] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Stopped Immunosuppressants After Week 48

| | |
|-----------------|---|
| End point title | Percentage of Participants who Stopped Immunosuppressants After Week 48 |
|-----------------|---|

End point description:

The number of participants who stopped immunosuppressants were to be determined by survey.

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

End point timeframe:

Week 48

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-----------------------------------|-------------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[50] | 0 ^[51] | 0 ^[52] | 0 ^[53] |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |

Notes:

[50] - Due to early termination of the study, no secondary outcome analyses were performed.

[51] - Due to early termination of the study, no secondary outcome analyses were performed.

[52] - Due to early termination of the study, no secondary outcome analyses were performed.

[53] - Due to early termination of the study, no secondary outcome analyses were performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Absolute Counts of Cluster of Differentiation (CD) 19 Positive (+) Cells per Visit

| | |
|---|---|
| End point title | Mean Absolute Counts of Cluster of Differentiation (CD) 19 Positive (+) Cells per Visit |
| End point description: CD19 is a cell surface molecule which assembles with the antigen receptor of B lymphocytes. It is a critical signal transduction molecule that regulates B lymphocyte development, activation, and differentiation. CD19+ cells were measured as cells per microliter (cells/uL). | |
| End point type | Secondary |
| End point timeframe: Baseline, Day 15, Week 4, 16, 32, 48, and by infusion (pre and post infusion) on Day 1, 15, Week 16, 32 | |

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|--|--------------------|--------------------|---------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 70 ^[54] | 73 ^[55] | 70 ^[56] | 141 ^[57] |
| Units: cells/uL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=70,71,66,137,44,26) | 203.5 (± 191.4) | 256.3 (± 300.2) | 224.1 (± 231.7) | 240.8 (± 268.9) |
| Day 15 (n=66,70,68,138,40,26) | 262.7 (± 273.9) | 1.9 (± 1.9) | 2.2 (± 3.4) | 2 (± 2.7) |
| Week 4 (n=68,67,67,134,41,27) | 209.7 (± 221.4) | 1.4 (± 2.5) | 1.3 (± 1.6) | 1.4 (± 2.1) |
| Week 16 (n=70,72,69,141,45,25) | 125.9 (± 186.9) | 2.6 (± 3.6) | 2 (± 3.8) | 2.3 (± 3.7) |
| Week 32 (n=68,73,68,141,45,23) | 116.6 (± 154.3) | 7.8 (± 25.8) | 2.1 (± 2.7) | 5.1 (± 18.8) |
| Week 48 (n=68,71,66,137,45,23) | 110 (± 114.3) | 11.7 (± 43.6) | 2.6 (± 8.9) | 7.3 (± 32.2) |
| Day 1 Pre-infusion (n=70,71,67,138,44,26) | 203.5 (± 191.4) | 256.3 (± 300.2) | 222.8 (± 230.2) | 240 (± 268) |
| Day 1 Post-infusion (n=70,69,68,137,43,27) | 103.1 (± 115.1) | 11.1 (± 28.6) | 5.7 (± 8.5) | 8.4 (± 21.3) |
| Day 15 Pre-infusion (n=68,68,70,138,43,25) | 264.4 (± 276.6) | 1.9 (± 1.9) | 2.1 (± 3.3) | 2 (± 2.7) |
| Day 15 Post-infusion (n=67,65,68,133,42,25) | 91.2 (± 109.2) | 1 (± 1.3) | 0.9 (± 1.4) | 0.9 (± 1.3) |
| Week 16 Pre-infusion (n=67,66,66,132,43,24) | 127.8 (± 190.1) | 2.5 (± 3.3) | 2.1 (± 3.9) | 2.3 (± 3.6) |
| Week 16 Post-infusion (n=61,66,66,132,40,21) | 52.7 (± 72.6) | 1.2 (± 1.6) | 0.8 (± 1) | 1 (± 1.3) |
| Week 32 Pre-infusion (n=60,63,63,126,39,21) | 125 (± 161.1) | 5.1 (± 16.5) | 2 (± 2.7) | 3.6 (± 11.8) |
| Week 32 Post-infusion (n=60,63,59,122,38,22) | 46.2 (± 54.4) | 1 (± 1.5) | 0.7 (± 1.4) | 0.9 (± 1.4) |

Notes:

[54] - number (n) = number of participants analyzed at the specified visit.

[55] - n = number of participants analyzed at the specified visit.

[56] - n = number of participants analyzed at the specified visit.

[57] - n = number of participants analyzed at the specified visit.

| End point values | Placebo-Mycophenolate Mofetil (MMF) | Placebo-Euro Lupus (EL) | | |
|------------------|-------------------------------------|-------------------------|--|--|
|------------------|-------------------------------------|-------------------------|--|--|

| Subject group type | Subject analysis set | Subject analysis set | | |
|--|----------------------|----------------------|--|--|
| Number of subjects analysed | 45 ^[58] | 27 ^[59] | | |
| Units: cells/uL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=70,71,66,137,44,26) | 213.7 (± 201.7) | 186.3 (± 175) | | |
| Day 15 (n=66,70,68,138,40,26) | 327.4 (± 324.9) | 163.3 (± 115.8) | | |
| Week 4 (n=68,67,67,134,41,27) | 253.4 (± 263.9) | 143.3 (± 107.4) | | |
| Week 16 (n=70,72,69,141,45,25) | 154.3 (± 222.2) | 74.7 (± 75.3) | | |
| Week 32 (n=68,73,68,141,45,23) | 141.2 (± 172.5) | 68.5 (± 96.8) | | |
| Week 48 (n=68,71,66,137,45,23) | 134.9 (± 123.3) | 61.3 (± 75) | | |
| Day 1 Pre-infusion (n=70,71,67,138,44,26) | 213.7 (± 201.7) | 186.3 (± 175) | | |
| Day 1 Post-infusion (n=70,69,68,137,43,27) | 102.4 (± 114.3) | 104.3 (± 118.6) | | |
| Day 15 Pre-infusion (n=68,68,70,138,43,25) | 322.5 (± 323.5) | 164.5 (± 118) | | |
| Day 15 Post-infusion (n=67,65,68,133,42,25) | 106.3 (± 130.8) | 65.8 (± 50.4) | | |
| Week 16 Pre-infusion (n=67,66,66,132,43,24) | 156.5 (± 226.3) | 76.3 (± 76.5) | | |
| Week 16 Post-infusion (n=61,66,66,132,40,21) | 64.2 (± 83) | 30.9 (± 40.2) | | |
| Week 32 Pre-infusion (n=60,63,63,126,39,21) | 153.4 (± 180.6) | 72.2 (± 100.4) | | |
| Week 32 Post-infusion (n=60,63,59,122,38,22) | 56.9 (± 62.5) | 27.6 (± 29.5) | | |

Notes:

[58] - n = number of participants analyzed at the specified visit.

[59] - n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with CD19+ Absolute B Cell Counts <10 cells per microliter (cells/uL) by Visit

| | |
|-----------------|---|
| End point title | Percentage of Participants with CD19+ Absolute B Cell Counts <10 cells per microliter (cells/uL) by Visit |
|-----------------|---|

End point description:

CD19 is a cell surface molecule which assembles with the antigen receptor of B lymphocytes. It is a critical signal transduction molecule that regulates B lymphocyte development, activation, and differentiation. n = number of participants analyzed at the specified visit. A value of 999 denotes that no data are available for the specified data point.

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

End point timeframe:

Baseline, Day 15, Week 4, 16, 32, 48, and by infusion (pre and post infusion) on Day 1, 15, Week 16, 32

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|---|--------------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 70 ^[60] | 73 ^[61] | 70 ^[62] | 141 ^[63] |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Baseline (n=70,71,66,137,44,26) | 4.3 | 4.2 | 1.5 | 2.9 |
| Day 15 (n=66,70,68,138,40,26) | 4.5 | 100 | 97.1 | 98.6 |
| Week 4 (n=68,67,67,134,41,27) | 4.4 | 98.5 | 100 | 99.3 |
| Week 16 (n=70,72,69,141,45,25) | 4.3 | 95.8 | 97.1 | 96.5 |
| Week 32 (n=68,73,68,141,45,23) | 7.4 | 91.8 | 95.6 | 93.6 |
| Week 48 (n=68,71,66,137,45,23) | 5.9 | 88.7 | 98.5 | 93.4 |
| Day 1 Pre-infusion (n=70,71,67,138,44,26) | 4.3 | 4.2 | 1.5 | 2.9 |
| Day 1 Post-infusion (n=70,69,68,137,43,27) | 10 | 81.2 | 83.8 | 82.5 |
| Day 15 Pre-infusion (n=68,68,70,138,43,25) | 4.4 | 100 | 97.1 | 98.6 |
| Day 15 Post-infusion (n=67,65,68,133,42,25) | 7.5 | 100 | 100 | 100 |
| Week 16 Pre-infusion (n=67,66,66,132,43,24) | 4.5 | 97 | 97 | 97 |
| Week 16 Post-infusion (n=61,66,66,132,40,21) | 11.5 | 100 | 100 | 100 |
| Week 32 Pre-infusion (n=60,63,63,126,39,21) | 3.3 | 93.7 | 95.2 | 94.4 |
| Week 32 Post-infusion (n=60,63,59,122,38,22) | 15 | 100 | 100 | 100 |

Notes:

[60] - n = number of participants analyzed at the specified visit.

[61] - n = number of participants analyzed at the specified visit.

[62] - n = number of participants analyzed at the specified visit.

[63] - n = number of participants analyzed at the specified visit.

| End point values | Placebo- Mycophenolate Mofetil (MMF) | Placebo-Euro Lupus (EL) | | |
|--|--|----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 45 ^[64] | 27 ^[65] | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Baseline (n=70,71,66,137,44,26) | 6.8 | 999 | | |
| Day 15 (n=66,70,68,138,40,26) | 7.5 | 999 | | |
| Week 4 (n=68,67,67,134,41,27) | 7.3 | 999 | | |
| Week 16 (n=70,72,69,141,45,25) | 6.7 | 999 | | |
| Week 32 (n=68,73,68,141,45,23) | 8.9 | 4.3 | | |
| Week 48 (n=68,71,66,137,45,23) | 4.4 | 8.7 | | |
| Day 1 Pre-infusion (n=70,71,67,138,44,26) | 6.8 | 999 | | |
| Day 1 Post-infusion (n=70,69,68,137,43,27) | 14 | 3.7 | | |
| Day 15 Pre-infusion (n=68,68,70,138,43,25) | 7 | 999 | | |
| Day 15 Post-infusion (n=67,65,68,133,42,25) | 11.9 | 999 | | |
| Week 16 Pre-infusion (n=67,66,66,132,43,24) | 7 | 999 | | |

| | | | | |
|---|------|------|--|--|
| Week 16 Post-infusion (n=61,66,66,132,40,21) | 12.5 | 9.5 | | |
| Week 32 Pre-infusion (n=60,63,63,126,39,21) | 5.1 | 999 | | |
| Week 32 Post-infusion (n=60,63,59,122,38,22) | 10.5 | 22.7 | | |

Notes:

[64] - n = number of participants analyzed at the specified visit.

[65] - n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with CD19+ Absolute B Cell Counts <20 cells/uL by Visit

| | |
|-----------------|--|
| End point title | Percentage of Participants with CD19+ Absolute B Cell Counts <20 cells/uL by Visit |
|-----------------|--|

End point description:

CD19 is a cell surface molecule which assembles with the antigen receptor of B lymphocytes. It is a critical signal transduction molecule that regulates B lymphocyte development, activation, and differentiation. A value of 999 denotes that no data are available for the specified data point. n = number of participants analyzed at the specified visit.

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

End point timeframe:

Baseline, Day 15, Week 4, 16, 32, 48, and by infusion (pre and post infusion) on Day 1, 15, Week 16, 32

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|---|--------------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 70 ^[66] | 73 ^[67] | 70 ^[68] | 141 ^[69] |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Baseline (n=70,71,66,137,44,26) | 7.1 | 11.3 | 3 | 7.3 |
| Day 15 (n=66,70,68,138,40,26) | 7.6 | 100 | 98.5 | 99.3 |
| Week 4 (n=68,67,67,134,41,27) | 10.3 | 100 | 100 | 100 |
| Week 16 (n=70,72,69,141,45,25) | 11.4 | 98.6 | 98.6 | 98.6 |
| Week 32 (n=68,73,68,141,45,23) | 13.2 | 93.2 | 100 | 96.5 |
| Week 48 (n=68,71,66,137,45,23) | 17.6 | 91.5 | 98.5 | 94.9 |
| Day 1 Pre-infusion (n=70,71,67,138,44,26) | 7.1 | 11.3 | 3 | 7.2 |
| Day 1 Post-infusion (n=70,69,68,137,43,27) | 22.9 | 87 | 91.2 | 89.1 |
| Day 15 Pre-infusion (n=68,68,70,138,43,25) | 7.4 | 100 | 98.6 | 99.3 |
| Day 15 Post-infusion (n=67,65,68,133,42,25) | 17.9 | 100 | 100 | 100 |
| Week 16 Pre-infusion (n=67,66,66,132,43,24) | 10.4 | 98.5 | 98.5 | 98.5 |
| Week 16 Post-infusion (n=61,66,66,132,40,21) | 41 | 100 | 100 | 100 |
| Week 32 Pre-infusion (n=60,63,63,126,39,21) | 8.3 | 95.2 | 100 | 97.6 |

| | | | | |
|---|----|-----|-----|-----|
| Week 32 Post-infusion (n=60,63,59,122,38,22) | 35 | 100 | 100 | 100 |
|---|----|-----|-----|-----|

Notes:

[66] - n = number of participants analyzed at the specified visit.

[67] - n = number of participants analyzed at the specified visit.

[68] - n = number of participants analyzed at the specified visit.

[69] - n = number of participants analyzed at the specified visit.

| End point values | Placebo- Mycophenolate Mofetil (MMF) | Placebo-Euro Lupus (EL) | | |
|---|--|----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 45 ^[70] | 27 ^[71] | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Baseline (n=70,71,66,137,44,26) | 11.4 | 999 | | |
| Day 15 (n=66,70,68,138,40,26) | 10 | 3.8 | | |
| Week 4 (n=68,67,67,134,41,27) | 12.2 | 7.4 | | |
| Week 16 (n=70,72,69,141,45,25) | 13.3 | 8 | | |
| Week 32 (n=68,73,68,141,45,23) | 15.6 | 8.7 | | |
| Week 48 (n=68,71,66,137,45,23) | 13.3 | 26.1 | | |
| Day 1 Pre-infusion (n=70,71,67,138,44,26) | 11.4 | 999 | | |
| Day 1 Post-infusion (n=70,69,68,137,43,27) | 20.9 | 25.9 | | |
| Day 15 Pre-infusion (n=68,68,70,138,43,25) | 9.3 | 4 | | |
| Day 15 Post-infusion (n=67,65,68,133,42,25) | 21.4 | 12 | | |
| Week 16 Pre-infusion (n=67,66,66,132,43,24) | 11.6 | 8.3 | | |
| Week 16 Post-infusion (n=61,66,66,132,40,21) | 32.5 | 57.1 | | |
| Week 32 Pre-infusion (n=60,63,63,126,39,21) | 10.3 | 4.8 | | |
| Week 32 Post-infusion (n=60,63,59,122,38,22) | 26.3 | 50 | | |

Notes:

[70] - n = number of participants analyzed at the specified visit.

[71] - n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with CD19+ Absolute B Cell Counts Less than the Lower Limit of Normal (LLN) by Visit

| | |
|-----------------|---|
| End point title | Percentage of Participants with CD19+ Absolute B Cell Counts Less than the Lower Limit of Normal (LLN) by Visit |
|-----------------|---|

End point description:

CD19 is a cell surface molecule which assembles with the antigen receptor of B lymphocytes. It is a critical signal transduction molecule that regulates B lymphocyte development, activation, and differentiation. <LLN = 80 cells/uL.

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

End point timeframe:

Baseline, Day 15, Week 4, 16, 32, 48, and by infusion (pre and post infusion) on Day 1, 15, Week 16, 32

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|---|--------------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 70 ^[72] | 73 ^[73] | 70 ^[74] | 141 ^[75] |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Baseline (n=70,71,66,137,44,26) | 27.1 | 36.6 | 33.3 | 35 |
| Day 15 (n=66,70,68,138,40,26) | 28.8 | 100 | 100 | 100 |
| Week 4 (n=68,67,67,134,41,27) | 39.7 | 100 | 100 | 100 |
| Week 16 (n=70,72,69,141,45,25) | 57.1 | 100 | 100 | 100 |
| Week 32 (n=68,73,68,141,45,23) | 52.9 | 97.3 | 100 | 98.6 |
| Week 48 (n=68,71,66,137,45,23) | 51.5 | 97.2 | 100 | 98.5 |
| Day 1 Pre-infusion (n=70,71,67,138,44,26) | 27.1 | 36.6 | 32.8 | 34.8 |
| Day 1 Post-infusion (n=70,69,68,137,43,27) | 55.7 | 97.1 | 100 | 98.5 |
| Day 15 Pre-infusion (n=68,68,70,138,43,25) | 30.9 | 100 | 100 | 100 |
| Day 15 Post-infusion (n=67,65,68,133,42,25) | 58.2 | 100 | 100 | 100 |
| Week 16 Pre-infusion (n=67,66,66,132,43,24) | 56.7 | 100 | 100 | 100 |
| Week 16 Post-infusion (n=61,66,66,132,40,21) | 80.3 | 100 | 100 | 100 |
| Week 32 Pre-infusion (n=60,63,63,126,39,21) | 50 | 98.4 | 100 | 99.2 |
| Week 32 Post-infusion (n=60,63,59,122,38,22) | 88.3 | 100 | 100 | 100 |

Notes:

[72] - n = number of participants analyzed at the specified visit.

[73] - n = number of participants analyzed at the specified visit.

[74] - n = number of participants analyzed at the specified visit.

[75] - n = number of participants analyzed at the specified visit.

| End point values | Placebo- Mycophenolate Mofetil (MMF) | Placebo-Euro Lupus (EL) | | |
|---|--|----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 45 ^[76] | 27 ^[77] | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Baseline (n=70,71,66,137,44,26) | 29.5 | 23.1 | | |
| Day 15 (n=66,70,68,138,40,26) | 30 | 26.9 | | |
| Week 4 (n=68,67,67,134,41,27) | 39 | 40.7 | | |
| Week 16 (n=70,72,69,141,45,25) | 48.9 | 72 | | |
| Week 32 (n=68,73,68,141,45,23) | 35.6 | 87 | | |
| Week 48 (n=68,71,66,137,45,23) | 37.8 | 78.3 | | |
| Day 1 Pre-infusion (n=70,71,67,138,44,26) | 29.5 | 23.1 | | |
| Day 1 Post-infusion (n=70,69,68,137,43,27) | 53.5 | 59.3 | | |
| Day 15 Pre-infusion (n=68,68,70,138,43,25) | 32.6 | 28 | | |

| | | | | |
|---|------|------|--|--|
| Day 15 Post-infusion (n=67,65,68,133,42,25) | 52.4 | 68 | | |
| Week 16 Pre-infusion (n=67,66,66,132,43,24) | 48.8 | 70.8 | | |
| Week 16 Post-infusion (n=61,66,66,132,40,21) | 72.5 | 95.2 | | |
| Week 32 Pre-infusion (n=60,63,63,126,39,21) | 30.8 | 85.7 | | |
| Week 32 Post-infusion (n=60,63,59,122,38,22) | 84.2 | 95.5 | | |

Notes:

[76] - n = number of participants analyzed at the specified visit.

[77] - n = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving a Major Clinical Response or a Partial Clinical Response

| | |
|-----------------|---|
| End point title | Percentage of Participants Achieving a Major Clinical Response or a Partial Clinical Response |
|-----------------|---|

End point description:

A major clinical response was defined as British Isles Lupus Assessment Group (BILAG) C scores or better at Week 24 without developing any new A or two new B scores up to Week 24 and maintenance of this response without developing a moderate or severe flare between Week 24 and Week 48. A partial clinical response was defined as BILAG C scores or better at Week 24 and maintaining this response without developing a flare for 16 consecutive weeks. The BILAG is an organ-specific 86-question assessment based on the principle of the doctor's intent to treat, which requires an assessment of improved (1), the same (2), worse (3), or new (4) over the last month. Within each organ system, multiple manifestations and laboratory tests are combined into a single score for that organ. The resulting scores for each organ can be A through E, where A is very active disease, B is moderate activity, C is mild stable disease, D is resolved activity, and E indicates the organ was never involved.

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

End point timeframe:

Baseline and Weeks 1, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48

| End point values | Placebo | Ocrelizumab 400 mg | Ocrelizumab 1000 mg | OCR + SOC |
|-----------------------------------|-------------------|-----------------------|------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[78] | 0 ^[79] | 0 ^[80] | 0 ^[81] |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |

Notes:

[78] - Due to early termination of the study, no secondary analyses were performed.

[79] - Due to early termination of the study, no secondary analyses were performed.

[80] - Due to early termination of the study, no secondary analyses were performed.

[81] - Due to early termination of the study, no secondary analyses were performed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from Screening until study termination.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 13.1 |
|--------------------|------|

Reporting groups

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

Reporting group description:

Participants received placebo matched to ocrelizumab infusion intravenously (IV) on Days 1 and 15, followed by placebo matched to ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or mycophenolate mofetil (MMF) 1 grams per day (g/day) in the first week increased to 3 g/day. Participants also received methylprednisolone 100 milligram (mg) infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of placebo. Participants also received oral prednisone at a starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

| | |
|-----------------------|---------------------|
| Reporting group title | Ocrelizumab 1000 mg |
|-----------------------|---------------------|

Reporting group description:

Participants received 1000 mg ocrelizumab IV on Days 1 and 15, followed by 1000 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

| | |
|-----------------------|--------------------|
| Reporting group title | Ocrelizumab 400 mg |
|-----------------------|--------------------|

Reporting group description:

Participants received 400 mg ocrelizumab IV on Days 1 and 15, followed by 400 mg ocrelizumab infusion IV on Week 16 and then every 16 weeks up to 48 weeks along with one of the two standard-of-care (SOC) immunosuppressant regimens at the discretion of the investigator. The SOC regimens were: Euro-Lupus (cyclophosphamide 500 mg every 2 weeks for 6 doses followed by azathioprine maintenance at 1-2 milligrams per kilogram per day [mg/kg/day]), or MMF 1 g/day in the first week increased to 3 g/day. Participants also received methylprednisolone 100 mg infusion IV or according to local guidelines, completed at least 30 minutes prior to each infusion of ocrelizumab. Participants also received oral prednisone at starting dose of 0.75 mg/kg/day with a maximum dose of 60 mg/day from Day 2. Beginning on Day 16 the doses were tapered and continued for 10 weeks to a target dose of 10 mg/day.

| Serious adverse events | Placebo | Ocrelizumab 1000 mg | Ocrelizumab 400 mg |
|---|-------------------|---------------------|--------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 36 / 125 (28.80%) | 38 / 127 (29.92%) | 52 / 126 (41.27%) |
| number of deaths (all causes) | 6 | 6 | 3 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Anogenital warts | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervix carcinoma | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Gastric cancer | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Rectal adenoma | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal cell carcinoma | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Malignant hypertension | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion missed | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Gestational hypertension | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Adverse drug reaction | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Chest pain | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | 0 / 127 (0.00%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 2 / 126 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Polyserositis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | 0 / 127 (0.00%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Reproductive system and breast disorders | | | |
| Amenorrhoea | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Cervical dysplasia | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian mass | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 2 / 126 (1.59%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Pulmonary oedema | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Blood creatine increased | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Thermal burn | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Pleuropericarditis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Stress cardiomyopathy | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 | | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular disorder | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Convulsion | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Headache | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lupus encephalitis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Migraine | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vasculitis cerebral | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Blood and lymphatic system disorders | | | |
| Agranulocytosis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 3 / 127 (2.36%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 3 / 126 (2.38%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia of chronic disease | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Antiphospholipid syndrome | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 2 / 126 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 2 / 126 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 5 / 127 (3.94%) | 2 / 126 (1.59%) |
| occurrences causally related to treatment / all | 0 / 1 | 3 / 5 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 1 / 127 (0.79%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| 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 | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Enteritis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 haemorrhage | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal ulcer | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Hepatobiliary disorders | | | |
| Hepatitis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Lupus nephritis | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephritis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrotic syndrome | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Proteinuria | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal disorder | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 failure | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | 1 / 127 (0.79%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 2 / 126 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Renal failure chronic | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Tubulointerstitial nephritis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Urinary bladder haemorrhage | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Muscle contracture | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 3 / 125 (2.40%) | 2 / 127 (1.57%) | 3 / 126 (2.38%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Abscess limb | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Bacterial sepsis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| 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 | 1 / 125 (0.80%) | 2 / 127 (1.57%) | 5 / 126 (3.97%) |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 3 | 2 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis infectious | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 3 / 125 (2.40%) | 0 / 127 (0.00%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis viral | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| H1N1 influenza | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematoma infection | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Herpes virus infection | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 3 / 127 (2.36%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster disseminated | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impetigo | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| infection | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngitis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Legionella infection | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neurocryptococcosis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenic infection | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 125 (1.60%) | 8 / 127 (6.30%) | 4 / 126 (3.17%) |
| occurrences causally related to treatment / all | 1 / 2 | 4 / 8 | 2 / 5 |
| deaths causally related to treatment / all | 0 / 1 | 2 / 3 | 0 / 0 |
| Pneumonia cytomegaloviral | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomembranous colitis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 2 / 126 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyoderma | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salmonella bacteraemia | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Salmonella sepsis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 125 (0.80%) | 1 / 127 (0.79%) | 2 / 126 (1.59%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 1 / 126 (0.79%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Strongyloidiasis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Tuberculosis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 0 / 127 (0.00%) | 0 / 126 (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 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 2 / 127 (1.57%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 2 / 127 (1.57%) | 0 / 126 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Sinusitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 125 (0.00%) | 1 / 127 (0.79%) | 0 / 126 (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 |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | 2 / 127 (1.57%) | 4 / 126 (3.17%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | 3 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 125 (0.00%) | 0 / 127 (0.00%) | 2 / 126 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| 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 | Placebo | Ocrelizumab 1000 mg | Ocrelizumab 400 mg |
|---|-------------------|---------------------|--------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 96 / 125 (76.80%) | 91 / 127 (71.65%) | 101 / 126 (80.16%) |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 11 / 125 (8.80%) | 17 / 127 (13.39%) | 14 / 126 (11.11%) |
| occurrences (all) | 12 | 19 | 18 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 7 / 125 (5.60%) | 12 / 127 (9.45%) | 12 / 126 (9.52%) |
| occurrences (all) | 8 | 15 | 19 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 9 / 125 (7.20%) | 5 / 127 (3.94%) | 6 / 126 (4.76%) |
| occurrences (all) | 9 | 6 | 6 |
| Headache | | | |
| subjects affected / exposed | 11 / 125 (8.80%) | 11 / 127 (8.66%) | 15 / 126 (11.90%) |
| occurrences (all) | 18 | 12 | 21 |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|-------------------------|-------------------------|-------------------------|
| Anaemia subjects affected / exposed occurrences (all) | 5 / 125 (4.00%) 5 | 7 / 127 (5.51%) 7 | 13 / 126 (10.32%) 17 |
| Leukopenia subjects affected / exposed occurrences (all) | 7 / 125 (5.60%) 11 | 12 / 127 (9.45%) 17 | 18 / 126 (14.29%) 24 |
| Neutropenia subjects affected / exposed occurrences (all) | 6 / 125 (4.80%) 7 | 7 / 127 (5.51%) 10 | 15 / 126 (11.90%) 27 |
| General disorders and administration site conditions | | | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 8 / 125 (6.40%) 9 | 4 / 127 (3.15%) 4 | 2 / 126 (1.59%) 5 |
| Pyrexia subjects affected / exposed occurrences (all) | 1 / 125 (0.80%) 1 | 2 / 127 (1.57%) 3 | 7 / 126 (5.56%) 7 |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 3 / 125 (2.40%) 3 | 7 / 127 (5.51%) 8 | 5 / 126 (3.97%) 5 |
| Diarrhoea subjects affected / exposed occurrences (all) | 22 / 125 (17.60%) 29 | 32 / 127 (25.20%) 36 | 26 / 126 (20.63%) 35 |
| Dyspepsia subjects affected / exposed occurrences (all) | 4 / 125 (3.20%) 5 | 3 / 127 (2.36%) 3 | 9 / 126 (7.14%) 10 |
| Gastritis subjects affected / exposed occurrences (all) | 2 / 125 (1.60%) 2 | 2 / 127 (1.57%) 3 | 11 / 126 (8.73%) 15 |
| Nausea subjects affected / exposed occurrences (all) | 7 / 125 (5.60%) 7 | 4 / 127 (3.15%) 5 | 13 / 126 (10.32%) 16 |
| Vomiting subjects affected / exposed occurrences (all) | 7 / 125 (5.60%) 7 | 4 / 127 (3.15%) 4 | 11 / 126 (8.73%) 11 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|-------------------------|-------------------------|-------------------------|
| Cough subjects affected / exposed occurrences (all) | 7 / 125 (5.60%) 8 | 4 / 127 (3.15%) 5 | 11 / 126 (8.73%) 12 |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) | 8 / 125 (6.40%) 8 | 1 / 127 (0.79%) 1 | 3 / 126 (2.38%) 3 |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 3 / 125 (2.40%) 4 | 7 / 127 (5.51%) 7 | 7 / 126 (5.56%) 7 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 5 / 125 (4.00%) 5 | 6 / 127 (4.72%) 8 | 7 / 126 (5.56%) 9 |
| Back pain subjects affected / exposed occurrences (all) | 6 / 125 (4.80%) 6 | 8 / 127 (6.30%) 8 | 6 / 126 (4.76%) 8 |
| Muscle spasms subjects affected / exposed occurrences (all) | 7 / 125 (5.60%) 7 | 4 / 127 (3.15%) 4 | 8 / 126 (6.35%) 8 |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) | 10 / 125 (8.00%) 16 | 10 / 127 (7.87%) 12 | 14 / 126 (11.11%) 17 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 10 / 125 (8.00%) 11 | 4 / 127 (3.15%) 4 | 7 / 126 (5.56%) 10 |
| Herpes zoster subjects affected / exposed occurrences (all) | 6 / 125 (4.80%) 6 | 9 / 127 (7.09%) 11 | 8 / 126 (6.35%) 9 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 16 / 125 (12.80%) 23 | 13 / 127 (10.24%) 20 | 17 / 126 (13.49%) 24 |
| Oral candidiasis | | | |

| | | | |
|---|-------------------------|-------------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 1 / 125 (0.80%) 1 | 1 / 127 (0.79%) 1 | 7 / 126 (5.56%) 10 |
| Pharyngitis subjects affected / exposed occurrences (all) | 4 / 125 (3.20%) 4 | 7 / 127 (5.51%) 7 | 13 / 126 (10.32%) 13 |
| Sinusitis subjects affected / exposed occurrences (all) | 3 / 125 (2.40%) 4 | 7 / 127 (5.51%) 12 | 3 / 126 (2.38%) 5 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 19 / 125 (15.20%) 28 | 23 / 127 (18.11%) 43 | 22 / 126 (17.46%) 42 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 13 / 125 (10.40%) 13 | 18 / 127 (14.17%) 35 | 24 / 126 (19.05%) 43 |
| Metabolism and nutrition disorders | | | |
| Dyslipidaemia subjects affected / exposed occurrences (all) | 11 / 125 (8.80%) 14 | 2 / 127 (1.57%) 2 | 5 / 126 (3.97%) 5 |
| Hypokalaemia subjects affected / exposed occurrences (all) | 9 / 125 (7.20%) 12 | 4 / 127 (3.15%) 4 | 9 / 126 (7.14%) 16 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 16 October 2008 | This amendment was made to clarify the flexibility of protocol in applying the regional participant management strategies using SOC regimens for treatment of LN and to ensure participant safety during administration of immunosuppressive therapies, to clarify the use of corticosteroids during the trial and to clarify screening procedures and use of medications during screening to help recruitment. |
| 04 January 2010 | On 19th October 2009 this Study (WA20500/ACT4072g) was stopped due to an imbalance of serious and opportunistic infections in the ocrelizumab treated patients versus the placebo arm. This was identified through the ongoing safety review of participant data and following interactions with both the US FDA and the BELONG Data and Safety Monitoring Board (DSMB). There was no further study drug infusions either blinded or open label in the Double Blind Treatment Period, Study Extension Treatment Period or Open Label Period. Patients who received ocrelizumab entered the Safety Follow Up period after completing the withdrawal visit and followed the Safety Follow Up assessments and Schedule. Participants who received placebo were not required to take part in the Safety Follow Up and were discontinued from the study. |
| 28 September 2012 | Safety data from the participants ongoing in the study were evaluated and the sponsor decided to terminate further Safety follow-up in participants treated with ocrelizumab. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated early due to an imbalance in serious infections in ocrelizumab-treated participants versus placebo-treated participants. Only 139 of the 381 participants randomized completed the 48 week treatment period.

Notes: