



Clinical trial results:

A randomized, double-blind, parallel group, international study to evaluate the safety and efficacy of ocrelizumab in combination with methotrexate (MTX) compared to MTX alone in methotrexate-naïve patients with active rheumatoid arthritis.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2006-005353-30 |
| Trial protocol | ES AT LT IT GB |
| Global end of trial date | 29 August 2013 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 10 March 2016 |
| First version publication date | 10 March 2016 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | WA20497 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00485589 |
| 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 616878333, global.trial_information@roche.com |
| Scientific contact | Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 616878333, 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 | 29 August 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 29 January 2010 |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 August 2013 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of ocrelizumab versus placebo, when used in combination with methotrexate (MTX), to reduce or inhibit progression of joint damage in MTX-naïve patients.

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 patient. The study fully adhered to the principles outlined in "Guideline for Good Clinical Practice" ICH Tripartite Guideline [January 1997] or with local law if it afforded greater protection to the patient. For studies conducted in the EU/EEA countries, the investigator ensured compliance with the EU Clinical Trial Directive [2001/20/EC]. For studies conducted in the US or under US 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 Subjects", and part 56, "Institutional Review Boards", were adhered to. In other countries where "Guideline for Good Clinical Practice" exists the Sponsor and the investigators strictly ensured adherence to the stated provisions.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 31 May 2007 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Safety |
| Long term follow-up duration | 12 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Poland: 60 |
| Country: Number of subjects enrolled | Spain: 10 |
| Country: Number of subjects enrolled | United Kingdom: 19 |
| Country: Number of subjects enrolled | Italy: 7 |
| Country: Number of subjects enrolled | Lithuania: 26 |
| Country: Number of subjects enrolled | Argentina: 23 |
| Country: Number of subjects enrolled | Australia: 7 |
| Country: Number of subjects enrolled | Brazil: 68 |
| Country: Number of subjects enrolled | Israel: 11 |
| Country: Number of subjects enrolled | Korea, Republic of: 20 |
| Country: Number of subjects enrolled | Mexico: 30 |
| Country: Number of subjects enrolled | New Zealand: 11 |

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Panama: 13 |
| Country: Number of subjects enrolled | Peru: 25 |
| Country: Number of subjects enrolled | Philippines: 9 |
| Country: Number of subjects enrolled | Russian Federation: 33 |
| Country: Number of subjects enrolled | South Africa: 6 |
| Country: Number of subjects enrolled | Switzerland: 4 |
| Country: Number of subjects enrolled | Taiwan: 14 |
| Country: Number of subjects enrolled | Thailand: 16 |
| Country: Number of subjects enrolled | United States: 201 |
| Worldwide total number of subjects | 613 |
| EEA total number of subjects | 122 |

Notes:

| Subjects enrolled per age group | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 541 |
| From 65 to 84 years | 71 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study population comprised adult patients with active rheumatoid arthritis (RA) of at least 3 months' but less than 5 years' duration who were naïve to methotrexate. Additionally, patients were required to be naïve to any biologic therapy for RA prior to enrollment.

Period 1

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

Arms

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

Arm description:

Participants received placebo intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54, 76, and 78. Participants also received methotrexate 7.5 mg orally weekly starting on Day 1. The dose of methotrexate was increased to a dose of 20 mg per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone or prednisolone.

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

Placebo was supplied in a single-use liquid formulation.

| | |
|------------------|--------------------|
| Arm title | Ocrelizumab 200 mg |
|------------------|--------------------|

Arm description:

Participants received ocrelizumab 200 mg intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54 and 76. Participants also received methotrexate 7.5 mg orally weekly starting on Day 1. The dose of methotrexate was increased to a dose of 20 mg per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone or prednisolone.

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

Dosage and administration details:

Ocrelizumab was supplied in a single-use liquid formulation.

| | |
|------------------|--------------------|
| Arm title | Ocrelizumab 500 mg |
|------------------|--------------------|

Arm description:

Participants received ocrelizumab 500 mg intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54,

and 76. Participants also received methotrexate 7.5 mg orally weekly starting on Day 1. The dose of methotrexate was increased to a dose of 20 mg per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone or prednisolone.

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

Dosage and administration details:

Ocrelizumab was supplied in a single-use liquid formulation.

| Number of subjects in period 1 | Placebo | Ocrelizumab 200 mg | Ocrelizumab 500 mg |
|--|---------|--------------------|--------------------|
| Started | 210 | 200 | 203 |
| Received treatment | 207 | 196 | 202 |
| Completed | 183 | 180 | 185 |
| Not completed | 27 | 20 | 18 |
| Consent withdrawn by subject | 3 | 2 | 2 |
| Insufficient therapeutic response | 10 | 3 | 1 |
| Failure to return | 6 | 5 | 1 |
| Other protocol violation | 1 | - | - |
| Adverse Event/Intercurrent illness | 3 | 3 | 10 |
| Death | 2 | 2 | - |
| Violation of selection criteria at entry | - | 3 | 1 |
| Administrative/Other | 1 | 2 | 1 |
| Refused treatment/did not cooperate | 1 | - | 2 |

Baseline characteristics

Reporting groups

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

Reporting group description:

Participants received placebo intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54, 76, and 78. Participants also received methotrexate 7.5 mg orally weekly starting on Day 1. The dose of methotrexate was increased to a dose of 20 mg per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone or prednisolone.

| | |
|-----------------------|--------------------|
| Reporting group title | Ocrelizumab 200 mg |
|-----------------------|--------------------|

Reporting group description:

Participants received ocrelizumab 200 mg intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54 and 76. Participants also received methotrexate 7.5 mg orally weekly starting on Day 1. The dose of methotrexate was increased to a dose of 20 mg per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone or prednisolone.

| | |
|-----------------------|--------------------|
| Reporting group title | Ocrelizumab 500 mg |
|-----------------------|--------------------|

Reporting group description:

Participants received ocrelizumab 500 mg intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54, and 76. Participants also received methotrexate 7.5 mg orally weekly starting on Day 1. The dose of methotrexate was increased to a dose of 20 mg per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone or prednisolone.

| Reporting group values | Placebo | Ocrelizumab 200 mg | Ocrelizumab 500 mg |
|------------------------|---------|--------------------|--------------------|
| Number of subjects | 210 | 200 | 203 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------------------|-------------|-------------|-------------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 49.2 | 50.8 | 48.6 |
| standard deviation | ± 12.43 | ± 13.17 | ± 12.29 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 153 | 154 | 161 |
| Male | 54 | 42 | 41 |
| Not recorded | 3 | 4 | 1 |

| Reporting group values | Total | | |
|------------------------|-------|--|--|
| Number of subjects | 613 | | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------------------|---|--|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

| | | | |
|--------------------|-----|--|--|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 468 | | |
| Male | 137 | | |
| Not recorded | 8 | | |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received placebo intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54, 76, and 78. Participants also received methotrexate 7.5 mg orally weekly starting on Day 1. The dose of methotrexate was increased to a dose of 20 mg per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone or prednisolone. | |
| Reporting group title | Ocrelizumab 200 mg |
| Reporting group description: | |
| Participants received ocrelizumab 200 mg intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54 and 76. Participants also received methotrexate 7.5 mg orally weekly starting on Day 1. The dose of methotrexate was increased to a dose of 20 mg per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone or prednisolone. | |
| Reporting group title | Ocrelizumab 500 mg |
| Reporting group description: | |
| Participants received ocrelizumab 500 mg intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54, and 76. Participants also received methotrexate 7.5 mg orally weekly starting on Day 1. The dose of methotrexate was increased to a dose of 20 mg per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone or prednisolone. | |

Primary: Change from Baseline in the modified Total Sharp Score (mTSS) at Week 52

| | |
|---|--|
| End point title | Change from Baseline in the modified Total Sharp Score (mTSS) at Week 52 |
| End point description: | |
| The mTSS is a measure of joint damage and includes measures of joint erosion (JE) and joint space narrowing (JSN). The JE score, using the van der Heijde modification, measures erosion severity in 32 hand joints and 12 foot joints. Each hand joint is scored from 0 to 5 and each foot joint is scored from 0 to 10; the total score ranges from 0 to 280. Each joint is scored according to the surface area involved. A score of 10 indicates extensive loss of bone from more than one-half of the articulating bone; a score of 0 indicates no erosion. The JSN score measures the severity of JSN in 30 hand joints (15 per hand) and 12 foot joints (6 per foot). Each joint is scored from 0 to 4; the total score ranges from 0 to 168. A higher score indicates more joint space narrowing. The mTSS ranges from 0 to 448 (280+168). A higher mTSS score indicates greater damage. A negative change score indicates improvement. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline to Week 52 | |

| End point values | Placebo | Ocrelizumab 200 mg | Ocrelizumab 500 mg | |
|--------------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 193 | 187 | 194 | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | 1.59 (± 4.815) | 0.66 (± 4.509) | 0.27 (± 2.908) | |

Statistical analyses

| | |
|---|-------------------------------|
| Statistical analysis title | Placebo vs ocrelizumab 200 mg |
| Comparison groups | Ocrelizumab 200 mg v Placebo |
| Number of subjects included in analysis | 380 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.001 ^[1] |
| Method | Van Elteren's test |

Notes:

[1] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

| | |
|---|-------------------------------|
| Statistical analysis title | Placebo vs ocrelizumab 500 mg |
| Comparison groups | Placebo v Ocrelizumab 500 mg |
| Number of subjects included in analysis | 387 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.0033 ^[2] |
| Method | Van Elteren's test |

Notes:

[2] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

Secondary: Percentage of participants without radiographic progression (RP) at Week 52

| | |
|-----------------|---|
| End point title | Percentage of participants without radiographic progression (RP) at Week 52 |
|-----------------|---|

End point description:

RP was defined as a change from Baseline in the modified Total Sharp Score (mTSS) ≤ 0 . The mTSS is a measure of joint damage and includes measures of joint erosion (JE) and joint space narrowing (JSN). The JE score, using the van der Heijde modification, measures erosion severity in 32 hand joints and 12 foot joints. Each hand joint is scored from 0 to 5 and each foot joint is scored from 0 to 10; the total score ranges from 0 to 280. Each joint is scored according to the surface area involved. A score of 10 indicates extensive loss of bone from more than one-half of the articulating bone; a score of 0 indicates no erosion. The JSN score measures the severity of JSN in 30 hand joints (15 per hand) and 12 foot joints (6 per foot). Each joint is scored from 0 to 4; the total score ranges from 0 to 168. A higher score indicates more joint space narrowing. The mTSS ranges from 0 to 448 (280+168). A higher mTSS score indicates greater damage. A negative change score indicates improvement.

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

End point timeframe:

Baseline to Week 52

| End point values | Placebo | Ocrelizumab 200 mg | Ocrelizumab 500 mg | |
|-----------------------------------|-----------------|---------------------|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 196 | 187 | 192 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 51 (44 to 58) | 66.3 (59.5 to 73.1) | 68.8 (62.2 to 75.3) | |

Statistical analyses

| Statistical analysis title | Placebo vs ocrelizumab 200 mg |
|---|-------------------------------|
| Comparison groups | Ocrelizumab 200 mg v Placebo |
| Number of subjects included in analysis | 383 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.003 ^[3] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Weighted difference |
| Point estimate | 14.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5 |
| upper limit | 24.4 |

Notes:

[3] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

| Statistical analysis title | Placebo vs ocrelizumab 500 mg |
|---|-------------------------------|
| Comparison groups | Ocrelizumab 500 mg v Placebo |
| Number of subjects included in analysis | 388 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.0006 ^[4] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Weighted difference |
| Point estimate | 16.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7.1 |
| upper limit | 26.1 |

Notes:

[4] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

Secondary: Percentage of participants with an improvement $\geq 20\%$, 50%, or 70% in American College of Rheumatology (ACR) score (ACR20/50/70) from Baseline to Week 52

| | |
|-----------------|---|
| End point title | Percentage of participants with an improvement $\geq 20\%$, 50%, or 70% in American College of Rheumatology (ACR) score (ACR20/50/70) from Baseline to Week 52 |
|-----------------|---|

End point description:

Improvement must be seen in tender (68) and swollen (66) joint counts. Joints were assessed and classified as swollen/not swollen and tender/not tender by pressure and joint manipulation. Improvement must also be seen in at least 3 of the following 5 parameters: Separate patient and physician assessments of patient disease activity in the previous 24 hours on a visual analog scale (VAS, the extreme left end of the line "none" [symptom-free and no arthritis symptoms] and the extreme right end "maximum" [maximum arthritis disease activity]; patient assessment of pain in the previous 24 hours on a VAS (extreme left end of the line "none" and the extreme right end "unbearable"); Health Assessment Questionnaire-Disability Index (20 questions, 8 components: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities, 0=without difficulty to 3=unable to do); and C-reactive protein (CRP), or erythrocyte sedimentation rate if CRP was missing.

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

End point timeframe:

Baseline to Week 52

| End point values | Placebo | Ocrelizumab 200 mg | Ocrelizumab 500 mg | |
|-----------------------------------|---------------------|---------------------|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 207 | 196 | 200 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| ACR20 | 57.5 (50.8 to 64.2) | 73 (66.7 to 79.2) | 71 (64.7 to 77.3) | |
| ACR50 | 39.6 (33 to 46.3) | 60.7 (53.9 to 67.6) | 54.5 (47.6 to 61.4) | |
| ACR70 | 20.3 (14.8 to 25.8) | 38.3 (31.5 to 45.1) | 38 (31.3 to 44.7) | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | ACR20 Response - Placebo vs ocrelizumab 200 mg |
| Comparison groups | Placebo v Ocrelizumab 200 mg |
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.0003 ^[5] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Weighted difference |
| Point estimate | 16.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7.3 |
| upper limit | 25.1 |

Notes:

[5] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

| | |
|-----------------------------------|--|
| Statistical analysis title | ACR20 Response - Placebo vs ocrelizumab 500 mg |
| Comparison groups | Placebo v Ocrelizumab 500 mg |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 407 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.0036 ^[6] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Weighted difference |
| Point estimate | 13.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.4 |
| upper limit | 22.4 |

Notes:

[6] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

| | |
|---|--|
| Statistical analysis title | ACR50 Response - Placebo vs ocrelizumab 200 mg |
| Comparison groups | Placebo v Ocrelizumab 200 mg |
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.0001 ^[7] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Weighted difference |
| Point estimate | 21.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 11.9 |
| upper limit | 30.6 |

Notes:

[7] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

| | |
|---|--|
| Statistical analysis title | ACR50 Response - Placebo vs ocrelizumab 500 mg |
| Comparison groups | Placebo v Ocrelizumab 500 mg |
| Number of subjects included in analysis | 407 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.0028 ^[8] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Weighted difference |
| Point estimate | 14.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5 |
| upper limit | 23.9 |

Notes:

[8] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

| | |
|-----------------------------------|--|
| Statistical analysis title | ACR70 Response - Placebo vs ocrelizumab 200 mg |
|-----------------------------------|--|

| | |
|---|------------------------------|
| Comparison groups | Placebo v Ocrelizumab 200 mg |
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.0001 ^[9] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Weighted difference |
| Point estimate | 17.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 9.1 |
| upper limit | 26.7 |

Notes:

[9] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

| | |
|---|--|
| Statistical analysis title | ACR70 Response - Placebo vs ocrelizumab 500 mg |
| Comparison groups | Placebo v Ocrelizumab 500 mg |
| Number of subjects included in analysis | 407 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.0001 ^[10] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Weighted difference |
| Point estimate | 16.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 8.3 |
| upper limit | 25.5 |

Notes:

[10] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

Secondary: Percentage of participants in Disease Activity Score 28 (DAS28) remission at Weeks 24 and 52

| | |
|-----------------|--|
| End point title | Percentage of participants in Disease Activity Score 28 (DAS28) remission at Weeks 24 and 52 |
|-----------------|--|

End point description:

A participant was in DAS28 remission if their DAS28 score < 2.6). The DAS28 is a combined index for measuring disease activity in rheumatic arthritis (RA) and includes swollen and tender joint counts, erythrocyte sedimentation rate (ESR), and general health (GH) status. The index is calculated with the following formula: $\text{DAS28} = (0.56 \times \sqrt{\text{TJC28}}) + (0.28 \times \sqrt{\text{SJC28}}) + (0.7 \times \log(\text{ESR})) + (0.014 \times \text{GH})$, where TJC28 = tender joint count and SJC28 = swollen joint count, each on 28 joints. GH = a patient's global assessment of disease activity in the previous 24 hours on a 100 mm visual analog scale (left end = no disease activity [symptom-free and no arthritis symptoms], right end = maximum disease activity [maximum arthritis disease activity]). When ESR equaled 0 mm/hr, it was set to 1 mm/hr. The DAS28 scale ranges from 0 to 10, where a higher score indicates more disease activity.

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

End point timeframe:

Week 24 and Week 52

| End point values | Placebo | Ocrelizumab 200 mg | Ocrelizumab 500 mg | |
|-----------------------------------|----------------------|------------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 207 | 196 | 200 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 24 | 9.7 (5.6 to 13.7) | 19.9 (14.3 to 25.5) | 18 (12.7 to 23.3) | |
| Week 52 | 7.2 (3.7 to 10.8) | 27 (20.8 to 33.3) | 28 (21.8 to 34.2) | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Week 24 - Placebo vs ocrelizumab 200 mg |
| Comparison groups | Ocrelizumab 200 mg v Placebo |
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.0076 ^[11] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Weighted difference |
| Point estimate | 9.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.5 |
| upper limit | 16.6 |

Notes:

[11] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

| | |
|---|---|
| Statistical analysis title | Week 24 - Placebo vs ocrelizumab 200 mg |
| Comparison groups | Placebo v Ocrelizumab 500 mg |
| Number of subjects included in analysis | 407 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.0221 ^[12] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Weighted difference |
| Point estimate | 7.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.1 |
| upper limit | 14.7 |

Notes:

[12] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

| | |
|---|---|
| Statistical analysis title | Week 52 - Placebo vs ocrelizumab 200 mg |
| Comparison groups | Placebo v Ocrelizumab 200 mg |
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.0001 ^[13] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Weighted difference |
| Point estimate | 19.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 12.3 |
| upper limit | 26.9 |

Notes:

[13] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

| | |
|---|---|
| Statistical analysis title | Week 52 - Placebo vs ocrelizumab 500 mg |
| Comparison groups | Placebo v Ocrelizumab 500 mg |
| Number of subjects included in analysis | 407 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.0001 ^[14] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Weighted difference |
| Point estimate | 20.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 13 |
| upper limit | 27.2 |

Notes:

[14] - The analysis was stratified by region (US, Rest of World) and screening C-reactive protein status (≤ 3 mg/dL or > 3 mg/dL).

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were monitored and recorded throughout the study.

Adverse event reporting additional description:

Safety population: All randomized participants who received at least 1 dose of study medication.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------------|
| Reporting group title | Placebo - treatment period |
|-----------------------|----------------------------|

Reporting group description:

Participants received placebo intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54, 76 and 78. Participants also received methotrexate 20 mg orally per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received acetaminophen 1 g and an antihistamine (diphenhydramine HCl 50 mg or equivalent dose of an alternative) orally 30-60 minutes prior to each infusion of study treatment and methylprednisolone 100 mg intravenously 30 minutes prior to each infusion of study treatment. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone.

| | |
|-----------------------|---|
| Reporting group title | Placebo/ocrelizumab 500 mg - treatment period |
|-----------------------|---|

Reporting group description:

Participants received placebo intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54, 76, and 78 and ocrelizumab 500 mg intravenously on Weeks 100, 102, 124, and 126. Participants also received methotrexate 20 mg orally per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received acetaminophen 1 g and an antihistamine (diphenhydramine HCl 50 mg or equivalent dose of an alternative) orally 30-60 minutes prior to each infusion of study treatment and methylprednisolone 100 mg intravenously 30 minutes prior to each infusion of study treatment. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone.

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Ocrelizumab 200 mg - treatment period |
|-----------------------|---------------------------------------|

Reporting group description:

Participants received placebo intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54 and 76. Participants also received methotrexate 20 mg orally per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received acetaminophen 1 g and an antihistamine (diphenhydramine HCl 50 mg or equivalent dose of an alternative) orally 30-60 minutes prior to each infusion of study treatment and methylprednisolone 100 mg intravenously 30 minutes prior to each infusion of study treatment. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone.

| | |
|-----------------------|--|
| Reporting group title | Ocrelizumab 200 mg/ocrelizumab 500 mg - treatment period |
|-----------------------|--|

Reporting group description:

Participants received ocrelizumab 200 mg intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54 and 76 and ocrelizumab 500 mg intravenously on Weeks 100, 102, 124, and 126. Participants also received methotrexate 20 mg orally per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received acetaminophen 1 g and an antihistamine (diphenhydramine HCl 50 mg or equivalent dose of an alternative) orally 30-60 minutes prior to each infusion of study treatment and methylprednisolone 100 mg intravenously 30 minutes prior to each infusion of study treatment. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone.

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Ocrelizumab 500 mg - treatment period |
|-----------------------|---------------------------------------|

Reporting group description:

Participants received ocrelizumab 500 mg intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54 and 76. Participants also received methotrexate 20 mg orally per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received

acetaminophen 1 g and an antihistamine (diphenhydramine HCl 50 mg or equivalent dose of an alternative) orally 30-60 minutes prior to each infusion of study treatment and methylprednisolone 100 mg intravenously 30 minutes prior to each infusion of study treatment. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone.

| | |
|-----------------------|--|
| Reporting group title | Ocrelizumab 500 mg/ocrelizumab 500 mg - treatment period |
|-----------------------|--|

Reporting group description:

Participants received ocrelizumab 500 mg intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54, 76, 100, 102, 124, and 126. Participants also received methotrexate 20 mg orally per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received acetaminophen 1 g and an antihistamine (diphenhydramine HCl 50 mg or equivalent dose of an alternative) orally 30-60 minutes prior to each infusion of study treatment and methylprednisolone 100 mg intravenously 30 minutes prior to each infusion of study treatment. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Placebo - safety follow-up period |
|-----------------------|-----------------------------------|

Reporting group description:

Participants had received placebo intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54, 76 and 78. Participants also received methotrexate 20 mg orally per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received acetaminophen 1 g and an antihistamine (diphenhydramine HCl 50 mg or equivalent dose of an alternative) orally 30-60 minutes prior to each infusion of study treatment and methylprednisolone 100 mg intravenously 30 minutes prior to each infusion of study treatment. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone.

| | |
|-----------------------|--|
| Reporting group title | Placebo/ocrelizumab 500 mg - safety follow-up period |
|-----------------------|--|

Reporting group description:

Participants had received placebo intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54, 76, and 78 and ocrelizumab 500 mg intravenously on Weeks 100, 102, 124, and 126. Participants also received methotrexate 20 mg orally per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received acetaminophen 1 g and an antihistamine (diphenhydramine HCl 50 mg or equivalent dose of an alternative) orally 30-60 minutes prior to each infusion of study treatment and methylprednisolone 100 mg intravenously 30 minutes prior to each infusion of study treatment. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone.

| | |
|-----------------------|--|
| Reporting group title | Ocrelizumab 200 mg - safety follow-up period |
|-----------------------|--|

Reporting group description:

Participants had received Ocrelizumab intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54 and 76. Participants received methotrexate 20 mg orally per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received acetaminophen 1 g and an antihistamine (diphenhydramine HCl 50 mg or equivalent dose of an alternative) orally 30-60 minutes prior to each infusion of study treatment and methylprednisolone 100 mg intravenously 30 minutes prior to each infusion of study treatment. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone.

| | |
|-----------------------|---|
| Reporting group title | Ocrelizumab 200 mg/ocrelizumab 500 mg-safety follow-up period |
|-----------------------|---|

Reporting group description:

Participants had received ocrelizumab 200 mg intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54 and 76 and ocrelizumab 500 mg intravenously on Weeks 100, 102, 124, and 126. Participants also received methotrexate 20 mg orally per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received acetaminophen 1 g and an antihistamine (diphenhydramine HCl 50 mg or equivalent dose of an alternative) orally 30-60 minutes prior to each infusion of study treatment and methylprednisolone 100 mg intravenously 30 minutes prior to each infusion of study treatment. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone.

| | |
|-----------------------|--|
| Reporting group title | Ocrelizumab 500 mg - safety follow-up period |
|-----------------------|--|

Reporting group description:

Participants had received ocrelizumab 500 mg intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54, 76 and 78. Participants also received methotrexate 20 mg orally per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received

acetaminophen 1 g and an antihistamine (diphenhydramine HCl 50 mg or equivalent dose of an alternative) orally 30-60 minutes prior to each infusion of study treatment and methylprednisolone 100 mg intravenously 30 minutes prior to each infusion of study treatment. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone.

| | |
|-----------------------|--|
| Reporting group title | Ocrelizumab 500 mg/ocrelizumab 500 mg -safety follow-up period |
|-----------------------|--|

Reporting group description:

Participants had received ocrelizumab 500 mg intravenously on Days 1 and 15 and Weeks 24, 26, 52, 54, 76, 100, 102, 124, and 126. Participants also received methotrexate 20 mg orally per week by Week 8, administered in 1 dose or divided into 3 equal doses administered at 12-hour intervals. Participants also received acetaminophen 1 g and an antihistamine (diphenhydramine HCl 50 mg or equivalent dose of an alternative) orally 30-60 minutes prior to each infusion of study treatment and methylprednisolone 100 mg intravenously 30 minutes prior to each infusion of study treatment. Participants also received folate ≥ 5 mg/week either as a single dose or as a divided weekly dose. Participants were also allowed to continue receiving background corticosteroid therapy, at a dose of ≤ 10 mg/day of prednisolone.

| Serious adverse events | Placebo - treatment period | Placebo/ocrelizumab 500 mg - treatment period | Ocrelizumab 200 mg - treatment period |
|---|----------------------------|---|---------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 22 / 207 (10.63%) | 0 / 10 (0.00%) | 21 / 196 (10.71%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon cancer metastatic | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian fibroma | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |

| | | | |
|--|-----------------|----------------|-----------------|
| Aortic aneurysm | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic stenosis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Interstitial lung disease | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary alveolar haemorrhage | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary eosinophilia | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vocal cord polyp | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Road traffic accident | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |

| | | | |
|---|-----------------|----------------|-----------------|
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dislocation of vertebra | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Forearm fracture | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Limb traumatic amputation | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Bronchogenic cyst | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arteriosclerosis coronary artery | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------|----------------|-----------------|
| Supraventricular tachycardia subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Autonomic neuropathy subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carpal tunnel syndrome subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebellar infarction subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Leukoencephalopathy subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dementia subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic cerebral infarction subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |

| | | | | |
|-------------------------------|---|-----------------|----------------|-----------------|
| Agranulocytosis | subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia haemolytic autoimmune | subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| | 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 | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | Deafness bilateral | | | |
| | subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vestibular disorder | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| | subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| | occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Eye disorders | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| | | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| Cataract | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 2 / 207 (0.97%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Abdominal hernia obstructive | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal inflammation | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Colitis | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Drug reaction with eosinophilia and systemic symptoms | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pustular psoriasis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angioedema | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| 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 failure | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 2 / 207 (0.97%) | 0 / 10 (0.00%) | 2 / 196 (1.02%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 2 / 196 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| 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 | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal wall infection | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Acute tonsillitis | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis viral | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Histoplasmosis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Localised infection | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Pneumonia herpes viral | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic candida | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis bacterial | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural infection | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 207 (1.45%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (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 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|-------------------------------|-----------------|--------------------|-----------------|
| Serious adverse events | Ocrelizumab 200 | Ocrelizumab 500 mg | Ocrelizumab 500 |
|-------------------------------|-----------------|--------------------|-----------------|

| | mg/ocrelizumab 500 mg - treatment period | - treatment period | mg/ocrelizumab 500 mg - treatment period |
|--|--|--------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 31 / 202 (15.35%) | 0 / 6 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Colon cancer metastatic | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian fibroma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Vascular disorders | | | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic stenosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |

| | | | |
|--|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 3 / 202 (1.49%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary alveolar haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Pulmonary eosinophilia | | | |

| | | | |
|---|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Vocal cord polyp | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Asthma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dislocation of vertebra | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |

| | | | |
|---|----------------|-----------------|---------------|
| Forearm fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Limb traumatic amputation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |

| | | | |
|---|----------------|-----------------|---------------|
| Bronchogenic cyst | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Arteriosclerosis coronary artery | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Autonomic neuropathy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|---------------|
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebellar infarction | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukoencephalopathy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dementia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic cerebral infarction | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Agranulocytosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Anaemia haemolytic autoimmune | | | |

| | | | |
|---|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Deafness bilateral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Vestibular disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|---------------|
| Abdominal hernia obstructive subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Constipation subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal inflammation subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper gastrointestinal haemorrhage subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |

| | | | |
|---|----------------|-----------------|---------------|
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 2 / 202 (0.99%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Drug reaction with eosinophilia and systemic symptoms | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pustular psoriasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angioedema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |

| | | | |
|--|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 | | | |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Back pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 2 / 202 (0.99%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal wall infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 202 (0.00%) | 0 / 6 (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 |
| Abscess | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|---------------|
| Acute tonsillitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis viral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Histoplasmosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |

| | | | |
|---|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Localised infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia herpes viral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Systemic candida | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis bacterial | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural infection | | | |

| | | | |
|---|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 2 / 202 (0.99%) | 0 / 6 (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 |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (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 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Placebo - safety follow-up period | Placebo/ocrelizumab 500 mg - safety follow-up period | Ocrelizumab 200 mg - safety follow-up period |
|---|-----------------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 11 / 187 (5.88%) | 2 / 9 (22.22%) | 2 / 177 (1.13%) |
| number of deaths (all causes) | 1 | 0 | 2 |
| number of deaths resulting from adverse events | 1 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma of skin | | | |

| | | | |
|--|-----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon cancer metastatic | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (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 |
| Prostate cancer | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (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 |
| Ovarian fibroma | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic stenosis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |

| | | | |
|---|-----------------|---------------|-----------------|
| Non–cardiac chest pain | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary alveolar haemorrhage | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary eosinophilia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vocal cord polyp | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |

| | | | |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (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 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 1 / 177 (0.56%) |
| 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 | | | |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dislocation of vertebra | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Forearm fracture | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|---------------|-----------------|
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Limb traumatic amputation | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (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 |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Bronchogenic cyst | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|---------------|-----------------|
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arteriosclerosis coronary artery | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (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 |
| Nervous system disorders | | | |
| Autonomic neuropathy | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebellar infarction | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |

| | | | |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukoencephalopathy | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dementia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Ischaemic cerebral infarction | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Agranulocytosis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia haemolytic autoimmune | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | | | |

| | | | |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Deafness bilateral | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vestibular disorder | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal hernia obstructive | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|---------------|-----------------|
| Gastritis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal inflammation | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (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 gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| Drug reaction with eosinophilia and systemic symptoms | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (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 |
| Pustular psoriasis | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (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 |
| Angioedema | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 1 / 9 (11.11%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 2 / 177 (1.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |

| | | | |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal wall infection | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute tonsillitis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |

| | | | |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis viral | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Histoplasmosis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Localised infection | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia herpes viral | | | |

| | | | |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic candida | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis bacterial | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural infection | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (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 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 187 (0.53%) | 1 / 9 (11.11%) | 2 / 177 (1.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (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 |

| Serious adverse events | Ocrelizumab 200 mg/ocrelizumab 500 mg-safety follow-up period | Ocrelizumab 500 mg - safety follow-up period | Ocrelizumab 500 mg/ocrelizumab 500 mg -safety follow-up period |
|--|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 4 / 185 (2.16%) | 0 / 6 (0.00%) |
| number of deaths (all causes) | 0 | 3 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon cancer metastatic | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer | | | |

| | | | |
|--|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian fibroma | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic stenosis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|---------------|
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary alveolar haemorrhage | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary eosinophilia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vocal cord polyp | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression | | | |

| | | | |
|---|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dislocation of vertebra | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Forearm fracture | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Limb traumatic amputation | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |

| | | | |
|---|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Congenital, familial and genetic disorders | | | |
| Bronchogenic cyst | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arteriosclerosis coronary artery | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|---------------|
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Autonomic neuropathy | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebellar infarction | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukoencephalopathy | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dementia | | | |

| | | | |
|---|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic cerebral infarction | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Blood and lymphatic system disorders | | | |
| Agranulocytosis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia haemolytic autoimmune | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Ear and labyrinth disorders | | | |

| | | | |
|---|----------------|-----------------|---------------|
| Deafness bilateral | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vestibular disorder | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal hernia obstructive | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|---------------|
| Gastrointestinal inflammation | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Drug reaction with eosinophilia and systemic symptoms | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pustular psoriasis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|---------------|
| Angioedema | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Back pain | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |

| | | | |
|---|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Abdominal wall infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute tonsillitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |

| | | | |
|---|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Encephalitis viral | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Histoplasmosis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Localised infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia herpes viral | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic candida | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |

| | | | |
|---|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Peritonitis bacterial | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (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 |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |

| | | | |
|---|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Placebo - treatment period | Placebo/ocrelizumab 500 mg - treatment period | Ocrelizumab 200 mg - treatment period |
|---|----------------------------|---|---------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 128 / 207 (61.84%) | 4 / 10 (40.00%) | 135 / 196 (68.88%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Thyroid neoplasm | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 23 / 207 (11.11%) | 0 / 10 (0.00%) | 14 / 196 (7.14%) |
| occurrences (all) | 23 | 0 | 14 |
| Surgical and medical procedures | | | |
| Hip arthroplasty | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bunion operation | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Oedema | | | |
| subjects affected / exposed | 2 / 207 (0.97%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|-------------------------|----------------------|-------------------------|
| Wheezing subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 1 / 10 (10.00%) 1 | 0 / 196 (0.00%) 0 |
| Cough subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Sinusitis noninfective subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Investigations Liver function test abnormal subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all) | 21 / 207 (10.14%) 36 | 4 / 10 (40.00%) 4 | 56 / 196 (28.57%) 79 |
| Meniscus injury subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Limb injury subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Muscle strain subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Foot fracture subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |

| | | | |
|--------------------------------------|-------------------|-----------------|------------------|
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 13 / 207 (6.28%) | 0 / 10 (0.00%) | 12 / 196 (6.12%) |
| occurrences (all) | 13 | 0 | 12 |
| Blood and lymphatic system disorders | | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 1 / 10 (10.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal hernia | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 24 / 207 (11.59%) | 0 / 10 (0.00%) | 16 / 196 (8.16%) |
| occurrences (all) | 24 | 0 | 16 |
| Diarrhoea | | | |
| subjects affected / exposed | 14 / 207 (6.76%) | 0 / 10 (0.00%) | 7 / 196 (3.57%) |
| occurrences (all) | 14 | 0 | 7 |
| Dyspepsia | | | |
| subjects affected / exposed | 14 / 207 (6.76%) | 0 / 10 (0.00%) | 8 / 196 (4.08%) |
| occurrences (all) | 14 | 0 | 8 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastric ulcer | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|------------------------|----------------------|-------------------------|
| Gastritis atrophic subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Hepatobiliary disorders Drug-induced liver injury subjects affected / exposed occurrences (all) | 18 / 207 (8.70%) 18 | 0 / 10 (0.00%) 0 | 28 / 196 (14.29%) 28 |
| Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) | 2 / 207 (0.97%) 3 | 0 / 10 (0.00%) 0 | 1 / 196 (0.51%) 1 |
| Erythema subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 1 / 10 (10.00%) 1 | 0 / 196 (0.00%) 0 |
| Rosacea subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Exfoliative rash subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Dermatitis contact subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Angioedema subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Onychoclasia subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 0 / 207 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 196 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------------|-------------------|-----------------|-------------------|
| Periarthritis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 1 / 196 (0.51%) |
| occurrences (all) | 0 | 0 | 1 |
| Back pain | | | |
| subjects affected / exposed | 9 / 207 (4.35%) | 0 / 10 (0.00%) | 10 / 196 (5.10%) |
| occurrences (all) | 9 | 0 | 10 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tenosynovitis stenosaurs | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 36 / 207 (17.39%) | 0 / 10 (0.00%) | 31 / 196 (15.82%) |
| occurrences (all) | 45 | 0 | 38 |
| Cystitis | | | |
| subjects affected / exposed | 3 / 207 (1.45%) | 0 / 10 (0.00%) | 4 / 196 (2.04%) |
| occurrences (all) | 4 | 0 | 6 |
| Tooth infection | | | |
| subjects affected / exposed | 1 / 207 (0.48%) | 1 / 10 (10.00%) | 1 / 196 (0.51%) |
| occurrences (all) | 1 | 1 | 1 |
| Bronchitis | | | |
| subjects affected / exposed | 21 / 207 (10.14%) | 0 / 10 (0.00%) | 22 / 196 (11.22%) |
| occurrences (all) | 21 | 0 | 22 |
| Urinary tract infection | | | |
| subjects affected / exposed | 12 / 207 (5.80%) | 0 / 10 (0.00%) | 21 / 196 (10.71%) |
| occurrences (all) | 12 | 0 | 21 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 11 / 207 (5.31%) | 0 / 10 (0.00%) | 18 / 196 (9.18%) |
| occurrences (all) | 11 | 0 | 18 |
| Sinusitis | | | |
| subjects affected / exposed | 10 / 207 (4.83%) | 0 / 10 (0.00%) | 7 / 196 (3.57%) |
| occurrences (all) | 10 | 0 | 7 |
| Gastroenteritis | | | |

| | | | |
|------------------------------------|-----------------|----------------|------------------|
| subjects affected / exposed | 9 / 207 (4.35%) | 0 / 10 (0.00%) | 10 / 196 (5.10%) |
| occurrences (all) | 9 | 0 | 10 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinea versicolour | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis bacterial | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Hyperlipidaemia | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyslipidaemia | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 207 (0.00%) | 0 / 10 (0.00%) | 0 / 196 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------------|--|---------------------------------------|--|
| Non-serious adverse events | Ocrelizumab 200 mg/ocrelizumab 500 mg - treatment period | Ocrelizumab 500 mg - treatment period | Ocrelizumab 500 mg/ocrelizumab 500 mg - treatment period |
|-----------------------------------|--|---------------------------------------|--|

| | | | |
|--|---|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 6 / 12 (50.00%) | 144 / 202 (71.29%) | 3 / 6 (50.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Thyroid neoplasm subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 18 / 202 (8.91%) 18 | 0 / 6 (0.00%) 0 |
| Surgical and medical procedures Hip arthroplasty subjects affected / exposed occurrences (all) Bunion operation subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 2 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 |
| General disorders and administration site conditions Oedema subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Respiratory, thoracic and mediastinal disorders Wheezing subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Sinusitis noninfective subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 0 / 202 (0.00%) 0 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Investigations | | | |

| | | | |
|---|---------------------|-------------------------|---------------------|
| Liver function test abnormal subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 64 / 202 (31.68%) 91 | 1 / 6 (16.67%) 1 |
| Meniscus injury subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Limb injury subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Muscle strain subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Foot fracture subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 7 / 202 (3.47%) 7 | 0 / 6 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Lymphadenopathy subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Neutropenia subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Anaemia subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |

| | | | |
|--|----------------|-------------------|---------------|
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 202 (0.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal hernia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 22 / 202 (10.89%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 22 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 14 / 202 (6.93%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 14 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 13 / 202 (6.44%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 13 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastric ulcer | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis atrophic | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 27 / 202 (13.37%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 27 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|----------------|-----------------|---------------|
| Rosacea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Exfoliative rash | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Angioedema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Onychoclasia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Periarthritis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 202 (0.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 7 / 202 (3.47%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 7 | 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tenosynovitis stenosaurs | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 202 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |

| | | | |
|---|---------------------|-------------------------|---------------------|
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 23 / 202 (11.39%) 29 | 1 / 6 (16.67%) 1 |
| Cystitis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 4 / 202 (1.98%) 4 | 1 / 6 (16.67%) 1 |
| Tooth infection subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 202 (0.50%) 1 | 0 / 6 (0.00%) 0 |
| Bronchitis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 15 / 202 (7.43%) 15 | 0 / 6 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 25 / 202 (12.38%) 25 | 0 / 6 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 16 / 202 (7.92%) 16 | 0 / 6 (0.00%) 0 |
| Sinusitis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 15 / 202 (7.43%) 15 | 0 / 6 (0.00%) 0 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 202 (0.50%) 1 | 0 / 6 (0.00%) 0 |
| Cellulitis subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Influenza subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Tinea versicolour subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Fungal skin infection subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |

| | | | |
|---|---------------------|----------------------|--------------------|
| Lower respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Sinusitis bacterial subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Hyperlipidaemia subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Vitamin D deficiency subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Dyslipidaemia subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 202 (0.00%) 0 | 0 / 6 (0.00%) 0 |

| Non-serious adverse events | Placebo - safety follow-up period | Placebo/ocrelizumab 500 mg - safety follow-up period | Ocrelizumab 200 mg - safety follow-up period |
|--|--------------------------------------|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 62 / 187 (33.16%) | 3 / 9 (33.33%) | 63 / 177 (35.59%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Thyroid neoplasm subjects affected / exposed occurrences (all) | 1 / 187 (0.53%) 1 | 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 0 / 187 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 |
| Surgical and medical procedures Hip arthroplasty subjects affected / exposed occurrences (all) Bunion operation | 0 / 187 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 |

| | | | |
|---|--|---|--|
| subjects affected / exposed occurrences (all) | 0 / 187 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 |
| General disorders and administration site conditions Oedema subjects affected / exposed occurrences (all) | 0 / 187 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Wheezing subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Sinusitis noninfective subjects affected / exposed occurrences (all) | 0 / 187 (0.00%) 0 2 / 187 (1.07%) 2 0 / 187 (0.00%) 0 | 0 / 9 (0.00%) 0 1 / 9 (11.11%) 1 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 2 / 177 (1.13%) 2 0 / 177 (0.00%) 0 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 0 / 187 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 177 (0.00%) 0 |
| Investigations Liver function test abnormal subjects affected / exposed occurrences (all) Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) | 0 / 187 (0.00%) 0 0 / 187 (0.00%) 0 | 0 / 9 (0.00%) 0 1 / 9 (11.11%) 1 | 0 / 177 (0.00%) 0 1 / 177 (0.56%) 1 |
| Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all) Meniscus injury subjects affected / exposed occurrences (all) Limb injury | 0 / 187 (0.00%) 0 2 / 187 (1.07%) 2 | 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 1 / 177 (0.56%) 1 |

| | | | |
|---|----------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 187 (0.53%) 1 | 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 |
| Muscle strain subjects affected / exposed occurrences (all) | 0 / 187 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 177 (0.00%) 0 |
| Foot fracture subjects affected / exposed occurrences (all) | 0 / 187 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 187 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 |
| Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all) | 1 / 187 (0.53%) 1 | 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 |
| Neutropenia subjects affected / exposed occurrences (all) | 1 / 187 (0.53%) 1 | 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 |
| Anaemia subjects affected / exposed occurrences (all) | 0 / 187 (0.00%) 0 | 0 / 9 (0.00%) 0 | 3 / 177 (1.69%) 3 |
| Eye disorders Conjunctivitis subjects affected / exposed occurrences (all) | 0 / 187 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 |
| Gastrointestinal disorders Abdominal hernia subjects affected / exposed occurrences (all) | 0 / 187 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 |
| Nausea subjects affected / exposed occurrences (all) | 0 / 187 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 177 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 1 / 187 (0.53%) 1 | 0 / 9 (0.00%) 0 | 3 / 177 (1.69%) 3 |
| Dyspepsia | | | |

| | | | |
|--|-----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastric ulcer | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis atrophic | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Drug–induced liver injury | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rosacea | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Exfoliative rash | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 2 / 177 (1.13%) |
| occurrences (all) | 1 | 0 | 2 |
| Dermatitis contact | | | |
| subjects affected / exposed | 2 / 187 (1.07%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Angioedema | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 187 (0.00%) | 1 / 9 (11.11%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Onychoclasia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 1 / 9 (11.11%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Periarthritis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 4 / 187 (2.14%) | 1 / 9 (11.11%) | 2 / 177 (1.13%) |
| occurrences (all) | 4 | 1 | 2 |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 1 / 177 (0.56%) |
| occurrences (all) | 1 | 0 | 1 |
| Tenosynovitis stenosans | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 1 / 9 (11.11%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 7 / 187 (3.74%) | 1 / 9 (11.11%) | 3 / 177 (1.69%) |
| occurrences (all) | 7 | 1 | 3 |
| Cystitis | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 1 / 177 (0.56%) |
| occurrences (all) | 1 | 0 | 1 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 3 / 187 (1.60%) | 1 / 9 (11.11%) | 5 / 177 (2.82%) |
| occurrences (all) | 3 | 1 | 5 |
| Urinary tract infection | | | |

| | | | |
|------------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 5 / 177 (2.82%) |
| occurrences (all) | 0 | 0 | 5 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 1 / 177 (0.56%) |
| occurrences (all) | 0 | 0 | 1 |
| Influenza | | | |
| subjects affected / exposed | 2 / 187 (1.07%) | 1 / 9 (11.11%) | 1 / 177 (0.56%) |
| occurrences (all) | 2 | 1 | 1 |
| Tinea versicolour | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fungal skin infection | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinusitis bacterial | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 1 / 9 (11.11%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |
| Hyperlipidaemia | | | |
| subjects affected / exposed | 1 / 187 (0.53%) | 0 / 9 (0.00%) | 0 / 177 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 2 / 177 (1.13%) |
| occurrences (all) | 0 | 0 | 2 |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| Dyslipidaemia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 0 / 9 (0.00%) | 1 / 177 (0.56%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 187 (0.00%) | 1 / 9 (11.11%) | 0 / 177 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| Non-serious adverse events | Ocrelizumab 200 mg/ocrelizumab 500 mg-safety follow-up period | Ocrelizumab 500 mg - safety follow-up period | Ocrelizumab 500 mg/ocrelizumab 500 mg -safety follow-up period |
|---|---|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 11 (27.27%) | 74 / 185 (40.00%) | 5 / 6 (83.33%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Thyroid neoplasm | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Surgical and medical procedures | | | |
| Hip arthroplasty | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bunion operation | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Oedema | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Wheezing | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |

| | | | |
|--|---------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 185 (0.54%) 1 | 0 / 6 (0.00%) 0 |
| Sinusitis noninfective subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 185 (0.54%) 1 | 0 / 6 (0.00%) 0 |
| Investigations Liver function test abnormal subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Meniscus injury subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Limb injury subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Muscle strain subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 185 (0.54%) 1 | 0 / 6 (0.00%) 0 |
| Foot fracture subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |

| | | | |
|--------------------------------------|----------------|-----------------|----------------|
| Blood and lymphatic system disorders | | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 2 / 185 (1.08%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 3 | 1 |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal hernia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 3 / 185 (1.62%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastric ulcer | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastritis atrophic | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatobiliary disorders | | | |

| | | | |
|---|---------------------|----------------------|---------------------|
| Drug-induced liver injury subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Erythema subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Rosacea subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Exfoliative rash subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 1 / 185 (0.54%) 1 | 0 / 6 (0.00%) 0 |
| Dermatitis contact subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Angioedema subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Onychoclasia subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Periarthritis subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 185 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Back pain | | | |

| | | | |
|-----------------------------------|-----------------|------------------|----------------|
| subjects affected / exposed | 0 / 11 (0.00%) | 6 / 185 (3.24%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 7 | 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 2 / 185 (1.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Tenosynovitis stenosaurs | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 11 (18.18%) | 7 / 185 (3.78%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 7 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 3 / 185 (1.62%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 12 / 185 (6.49%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 12 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |

| | | | |
|------------------------------------|----------------|-----------------|----------------|
| Influenza | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 3 / 185 (1.62%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 4 | 0 |
| Tinea versicolour | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 2 / 185 (1.08%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis bacterial | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Hyperlipidaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Dyslipidaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 185 (0.54%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 185 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 02 September 2008 | <ul style="list-style-type: none">Added the DSMB to review safety data from patients participating in the study.The `Warnings and Precautions` section was updated following the reporting of a case of PML in a patient receiving rituximab for the treatment of RA in a clinical trial setting.Due to the implementation of new technologies, the number of samples taken during the study was streamlined.Recommended retreatment during the open-label phase every 6 months supported by emerging long-term data from the rituximab programConditions for the administration of further courses of ocrelizumab were clarified in cases of infections, pregnancy and development of malignancies.Allowed patients who received rescue medication during the first 52 weeks of the double-blind period to continue in the study until the open-label period instead of withdrawing them into safety follow up.Added a new exploratory low-ranking endpoint assessing the proportion of patients with a total Sharp score of 0 at baseline whose structural joint damage does not change over the course of the study. |
| 14 May 2009 | <ul style="list-style-type: none">The time point of the primary efficacy endpoint (change in mTSS from baseline) was changed from Week 52 to Week 104, and the change in the mTSS from baseline at Week 52 was analyzed as a secondary efficacy variable.As a result of the change to the primary efficacy variable time point from Week 52 to Week 104, instructions for maintaining stable concomitant medication for RA were amended to apply to the 104-week double blind period instead of only the first 52 week double-blind period.Minor clarifications, corrections, and administrative changes. |
| 15 December 2009 | <ul style="list-style-type: none">Following a Sponsor and FDA review of opportunistic infections reported in studies of ocrelizumab in patients with RA or systemic lupus erythematosus (SLE) dosing was discontinued and all patients were to enter Safety Follow-UpAll appropriate aspects of the study procedures were modified to be consistent with the sponsors' decision to terminate study dosing and to ensure the completeness of assessments and maintenance of the blind for all patients up to Week 52 |
| 12 July 2010 | <ul style="list-style-type: none">Added new safety information regarding the opportunistic and fatal infections reported with ocrelizumab in RA patients as of May 2010 that resulted in the RA program being terminated.Removed the requirement for efficacy assessments in the safety follow-up period due to the sponsor's decision to terminate the RA program. |
| 06 September 2012 | <ul style="list-style-type: none">Termination of Safety Follow up for all patients based on the safety profile of patients during the Safety Follow Up period in all RA studies and considering that continuation of Safety follow up was not to provide a benefit to patients above and beyond the management of the patient's RA through usual standard of care and was not going to add meaningful information to the understanding of the safety of ocrelizumab. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|------|--------------|--------------|
|------|--------------|--------------|

| | | |
|-----------------|--|---|
| 16 October 2009 | The study was terminated prematurely by the sponsors before all patients could reach the time point for primary analysis at Week 104. No patient received any further infusions of study medication. | - |
|-----------------|--|---|

Notes:

Limitations and caveats

None reported