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 methodrexate 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 methodrexate 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 methodrexate 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 methodrexate 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 methodrexate 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 methodrexate 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 standard deviation	 49.2 ± 12.43	 50.8 ± 13.17	 48.6 ± 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 methodrexate 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 methodrexate 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 methodrexate 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 ≥ 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 ≥ 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: DAS28 = (0.56 × √(TJC28)) + (0.28 × √(SJC28)) + (0.7 × log(ESR)) + (0.014 × 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 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
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular disorder			
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
Eye disorders			

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	0 / 207 (0.00%)	1 / 10 (10.00%)	0 / 196 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Sinusitis noninfective			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	21 / 207 (10.14%)	4 / 10 (40.00%)	56 / 196 (28.57%)
occurrences (all)	36	4	79
Meniscus injury			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	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	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Drug−induced liver injury			
subjects affected / exposed	18 / 207 (8.70%)	0 / 10 (0.00%)	28 / 196 (14.29%)
occurrences (all)	18	0	28
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	2 / 207 (0.97%)	0 / 10 (0.00%)	1 / 196 (0.51%)
occurrences (all)	3	0	1
Erythema			
subjects affected / exposed	0 / 207 (0.00%)	1 / 10 (10.00%)	0 / 196 (0.00%)
occurrences (all)	0	1	0
Rosacea			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Exfoliative rash			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Angioedema			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Onychoclasis			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 207 (0.00%)	0 / 10 (0.00%)	0 / 196 (0.00%)
occurrences (all)	0	0	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 stenosans			
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	1 / 12 (8.33%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 12 (0.00%)	64 / 202 (31.68%)	1 / 6 (16.67%)
occurrences (all)	0	91	1
Meniscus injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 12 (0.00%)	7 / 202 (3.47%)	0 / 6 (0.00%)
occurrences (all)	0	7	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	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
Onychoclasis			
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 stenosans			
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	0 / 12 (0.00%)	23 / 202 (11.39%)	1 / 6 (16.67%)
occurrences (all)	0	29	1
Cystitis			
subjects affected / exposed	0 / 12 (0.00%)	4 / 202 (1.98%)	1 / 6 (16.67%)
occurrences (all)	0	4	1
Tooth infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 202 (0.50%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	15 / 202 (7.43%)	0 / 6 (0.00%)
occurrences (all)	0	15	0
Urinary tract infection			
subjects affected / exposed	0 / 12 (0.00%)	25 / 202 (12.38%)	0 / 6 (0.00%)
occurrences (all)	0	25	0
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	16 / 202 (7.92%)	0 / 6 (0.00%)
occurrences (all)	0	16	0
Sinusitis			
subjects affected / exposed	0 / 12 (0.00%)	15 / 202 (7.43%)	0 / 6 (0.00%)
occurrences (all)	0	15	0
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 202 (0.50%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tinea versicolour			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Lower respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinusitis bacterial			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 202 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	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	1 / 187 (0.53%)	0 / 9 (0.00%)	0 / 177 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 187 (0.00%)	0 / 9 (0.00%)	0 / 177 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Hip arthroplasty			
subjects affected / exposed	0 / 187 (0.00%)	0 / 9 (0.00%)	0 / 177 (0.00%)
occurrences (all)	0	0	0
Bunion operation			

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

subjects affected / exposed	1 / 187 (0.53%)	0 / 9 (0.00%)	0 / 177 (0.00%)
occurrences (all)	1	0	0
Muscle strain			
subjects affected / exposed	0 / 187 (0.00%)	1 / 9 (11.11%)	0 / 177 (0.00%)
occurrences (all)	0	1	0
Foot fracture			
subjects affected / exposed	0 / 187 (0.00%)	0 / 9 (0.00%)	0 / 177 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 187 (0.00%)	0 / 9 (0.00%)	0 / 177 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 187 (0.53%)	0 / 9 (0.00%)	0 / 177 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	1 / 187 (0.53%)	0 / 9 (0.00%)	0 / 177 (0.00%)
occurrences (all)	1	0	0
Anaemia			
subjects affected / exposed	0 / 187 (0.00%)	0 / 9 (0.00%)	3 / 177 (1.69%)
occurrences (all)	0	0	3
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 187 (0.00%)	0 / 9 (0.00%)	0 / 177 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 187 (0.00%)	0 / 9 (0.00%)	0 / 177 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 187 (0.00%)	0 / 9 (0.00%)	0 / 177 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 187 (0.53%)	0 / 9 (0.00%)	3 / 177 (1.69%)
occurrences (all)	1	0	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
Onychoclasis			
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	0 / 11 (0.00%)	1 / 185 (0.54%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sinusitis noninfective			
subjects affected / exposed	0 / 11 (0.00%)	0 / 185 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)	1 / 185 (0.54%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 11 (0.00%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Meniscus injury			
subjects affected / exposed	1 / 11 (9.09%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	1 / 11 (9.09%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Muscle strain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 185 (0.54%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Foot fracture			
subjects affected / exposed	1 / 11 (9.09%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	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	0 / 11 (0.00%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 11 (0.00%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rosacea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Exfoliative rash			
subjects affected / exposed	0 / 11 (0.00%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 11 (9.09%)	1 / 185 (0.54%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Dermatitis contact			
subjects affected / exposed	0 / 11 (0.00%)	0 / 185 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Angioedema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Onychoclasis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Periarthritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 185 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	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 stenosans			
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	• 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 program • Conditions 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	• 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	• 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-Up • All 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	• 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	• 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