Clinical trial results:
A Randomized, Double-Blind, Parallel Group, International Study to Evaluate the Safety and Efficacy of Ocrelizumab Compared to Placebo in Patients with Active Rheumatoid Arthritis Who Have an Inadequate Response to at Least One Anti-TNF- Therapy

Summary

EudraCT number	2006-005330-20
Trial protocol	BE DE FR HU ES CZ NL SI SE IT SK
Global end of trial date	14 May 2018

Results information

Result version number	v3 (current)
This version publication date	25 May 2019
First version publication date	15 July 2015
Version creation reason	
Summary attachment (see zip file)	WA20495 Redacted CSR Synopsis (WA20495_Redacted_CSRSynopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	WA20495

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00476996
WHO universal trial number (UTN)	-
Other trial identifiers	ACT3986g: ACT3986g

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, globa.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	17 May 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial to investigate the efficacy and safety of Ocrelizumab in combination with Methotrexate (MTX) or Leflunomide given either alone or in combination with other non-biologic DMARDs in patients with active Rheumatoid arthritis (RA) who had an inadequate response to anti-TNF-α therapy.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy:

Subjects received either leflunomide or methotrexate for ≥ 12 weeks, with a stable dose for the last 4 weeks.

Evidence for comparator: -

Actual start date of recruitment	15 May 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Regulatory reason
Long term follow-up duration	8 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Brazil: 31
Country: Number of subjects enrolled	Canada: 36
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	Czech Republic: 16
Country: Number of subjects enrolled	Germany: 18
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	France: 20
Country: Number of subjects enrolled	Hungary: 18
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Israel: 20
Country: Number of subjects enrolled	Japan: 106
Country: Number of subjects enrolled	Mexico: 30

Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	New Zealand: 4
Country: Number of subjects enrolled	Panama: 1
Country: Number of subjects enrolled	Peru: 17
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Argentina: 14
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Slovakia: 4
Country: Number of subjects enrolled	Slovenia: 10
Country: Number of subjects enrolled	United States: 416
Worldwide total number of subjects	836
EEA total number of subjects	145

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)	681
From 65 to 84 years	155
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited across 25 countries.

Pre-assignment

Screening details:

Study population comprised adult subjects with active RA of ≥ 3 months duration who had an inadequate clinical response due to toxicity or inadequate efficacy, to previous or current treatment with one or more anti-TNF-α therapies.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo × 2 IV + non-biologic DMARD therapy

Arm description:

Subjects received Ocrelizumab matching Placebo Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15) in combination with any non-biologic DMARDs.

Arm type	Placebo
Investigational medicinal product name	Ocrelizumab matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Matching placebo, administered IV, separated by 14 day intervals (day 1 and day 15).

Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	MTX
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

7.5-25 mg/week (oral or parenteral) for at least 12 weeks, with the last 4 weeks prior to baseline at stable dose.

Investigational medicinal product name	Leflunomide
Investigational medicinal product code	
Other name	LFL
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Leflunomide was administered once daily, 10-20 mg for at least 12 weeks, with the last 4 weeks, prior to baseline at a stable dose.

Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion

Routes of administration	Not mentioned

Dosage and administration details:

Methylprednisolone was administered by IV, slow infusion of 100 mg, completed at least 30 minutes prior to each infusion of study treatment.

Investigational medicinal product name	Acetaminophen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 gram of acetaminophen taken by mouth 30 to 60 minutes prior to the start of the placebo infusion.

Investigational medicinal product name	Diphenhydramine HCl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg of Diphenhydramine HCl taken by mouth 30 to 60 minutes prior to the start of the placebo infusion

Arm title	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy

Arm description:

Subjects received 200 mg Ocrelizumab administered Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15) in combination with any non-biologic DMARDs.

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab
Investigational medicinal product code	
Other name	Ocrevus
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 mg x2 administered by IV, separated by 14 day intervals (day 1 and day 15).

Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	MTX
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

7.5-25 mg/week (oral or parenteral) for at least 12 weeks, with the last 4 weeks prior to baseline at stable dose.

Investigational medicinal product name	Leflunomide
Investigational medicinal product code	
Other name	LFL
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Leflunomide was administered once daily, 10-20 mg for at least 12 weeks, with the last 4 weeks, prior to baseline at a stable dose.

Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Parenteral use

Dosage and administration details:

Methylprednisolone was administered by IV, slow infusion of 100 mg, completed at least 30 minutes prior to each infusion of study treatment.

Investigational medicinal product name	Acetaminophen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 gram of acetaminophen taken by mouth 30 to 60 minutes prior to the start of the Ocrelizumab infusion.

Investigational medicinal product name	Diphenhydramine HCl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg taken by mouth 30 to 60 minutes prior to the start of the Ocrelizumab infusion.

Arm title	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy

Arm description:

Subjects received 500 mg Ocrelizumab administered Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15) in combination with any non-biologic DMARDs.

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab
Investigational medicinal product code	
Other name	Ocrevus
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

500mg x2 administered by IV, separated by 14 day intervals (day 1 and day 15).

Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	MTX
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

7.5-25 mg/week (oral or parenteral) for at least 12 weeks, with the last 4 weeks prior to baseline at stable dose.

Investigational medicinal product name	Leflunomide
Investigational medicinal product code	
Other name	LFL
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Leflunomide was administered once daily, 10-20 mg for at least 12 weeks, with the last 4 weeks, prior to baseline at a stable dose.

Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Parenteral use

Dosage and administration details:

Methylprednisolone was administered by IV, slow infusion of 100 mg, completed at least 30 minutes

prior to each infusion of study treatment.

Investigational medicinal product name	Acetaminophen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 gram of acetaminophen taken by mouth 30 to 60 minutes prior to the start of the Ocrelizumab infusion.

Investigational medicinal product name	Diphenhydramine HCl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg taken by mouth 30 to 60 minutes prior to the start of the Ocrelizumab infusion.

Number of subjects in period 1	Placebo × 2 IV + non-biologic DMARD therapy	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy
Started	277	277	282
Completed	205	222	237
Not completed	72	55	45
Consent withdrawn by subject	12	7	7
Adverse event, non-fatal	11	13	7
Death	2	1	1
Non-compliance with study drug	-	2	-
Lost to follow-up	-	4	3
Early termination of study	24	20	21
Protocol deviation	1	3	-
Lack of efficacy	22	5	6

Period 2

Period 2 title	Study extension period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Eligible subjects received open-label
treatment with Ocrelizumab 500 mg x 2, separated by at least 3 months from the last infusion, at the discretion of the investigator

Arms

Arm title	Ocrelizumab 500 mg × 2 IV + Non-biologic DMARD (OLE)

Arm description:

Subjects received 500 mg Ocrelizumab administered Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15)

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab
Investigational medicinal product code	
Other name	Ocrevus
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

500mg x2 administered by IV, separated by 14 day intervals (day 1 and day 15).

Number of subjects in period 2	Ocrelizumab 500 mg × 2 IV + Non-biologic DMARD (OLE)
Started	664
Completed	0
Not completed	664
Consent withdrawn by subject	50
Adverse event, non-fatal	8
Death	7
Non-compliance with study drug	4
Lost to follow-up	4
Early termination of study	578
Lack of efficacy	13

Baseline characteristics

Reporting groups	
Reporting group title	Placebo × 2 IV + non-biologic DMARD therapy
Reporting group description:	
Subjects received Ocrelizumab matching Placebo Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15) in combination with any non-biologic DMARDs.	
Reporting group title	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy
Reporting group description:	
Subjects received 200 mg Ocrelizumab administered Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15) in combination with any non-biologic DMARDs.	
Reporting group title	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy
Reporting group description:	
Subjects received 500 mg Ocrelizumab administered Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15) in combination with any non-biologic DMARDs.	

Reporting group values	Placebo × 2 IV + non-biologic DMARD therapy	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy
Number of subjects	277	277	282
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	222	222	237
From 65-84 years	55	55	45
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	54.2	54.5	53.8
standard deviation	± 11.3	± 11.2	± 11.6
Gender Categorical Units: Subjects			
Female	215	214	236
Male	62	63	46
Ethnicity Units: Subjects			
Race Units: Subjects			

Reporting group values	Total		
Number of subjects	836		

Age Categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	681		
From 65-84 years	155		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical Units: Subjects			
Female	665		
Male	171		
Ethnicity Units: Subjects			

Race Units: Subjects			

End points

End points reporting groups

Reporting group title	Placebo × 2 IV + non-biologic DMARD therapy
Reporting group description:	
Subjects received Ocrelizumab matching Placebo Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15) in combination with any non-biologic DMARDs.	
Reporting group title	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy
Reporting group description:	
Subjects received 200 mg Ocrelizumab administered Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15) in combination with any non-biologic DMARDs.	
Reporting group title	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy
Reporting group description:	
Subjects received 500 mg Ocrelizumab administered Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15) in combination with any non-biologic DMARDs.	
Reporting group title	Ocrelizumab 500 mg × 2 IV + Non-biologic DMARD (OLE)
Reporting group description:	
Subjects received 500 mg Ocrelizumab administered Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15)	
Subject analysis set title	Intent to Treat (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized subjects who received any part of an infusion of study medication were included in the ITT analysis	
Subject analysis set title	Modified Intent-to-Treat (mITT)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The Modified Intent-to-Treat (mITT) population included all subjects who were in the ITT analysis set and had both baseline radiograph and at least one post-baseline radiograph for campaign 1	
Subject analysis set title	Per Protocol (PP) Population
Subject analysis set type	Per protocol
Subject analysis set description:	
The per protocol analysis population included all subject in the ITT population who adhered to the protocol. Subjects could be excluded if they significantly violated the inclusion/exclusion criteria or deviated from the study protocol	
Subject analysis set title	Modified Per Protocol (mPP) Population
Subject analysis set type	Per protocol
Subject analysis set description:	
A modified per protocol (mPP) population was also defined for radiographic analyses based on campaign 1 data. The mPP population included all subjects in the mITT population who adhered to the protocol. Subjects could be excluded if they significantly violated the inclusion/exclusion criteria or deviated from the study protocol	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety population included all subjects who were randomized and received any part of an infusion of study drug and provided at least one assessment of safety	

Primary: Percentage of subjects with ACR20 responses

End point title	Percentage of subjects with ACR20 responses
End point description:	
ACR20 response: greater than or equal to (≥) 20% improvement in tender or swollen joint counts and 20% improvement in 3 of the following 5 criteria: 1) Physician's global assessment of disease activity, 2) participant assessment of disease activity, 3) Patient Assessment of Pain (visual analog scale [VAS]), 4) participant assessment of functional disability via a Health Assessment Questionnaire (HAQ), and 5)	

erythrocyte sedimentation rate (ESR) at each visit.
Intent-to-Treat (ITT) All randomized participants who received any part of an infusion of study medication were included in the ITT analysis. Number of subjects for whom data was collected is indicated in each time point.

End point type	Primary
End point timeframe:	
Weeks 24 and 48	

End point values	Placebo × 2 IV + non-biologic DMARD therapy	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	277	277	282	
Units: Percentage				
arithmetic mean (confidence interval 95%)				
Percentage of Responders at Week 24	22 (17.1 to 26.9)	42.2 (36.4 to 48.1)	47.9 (42.0 to 53.7)	
Percentage of Responders at Week 48	19.5 (14.8 to 24.2)	48.7 (42.9 to 54.6)	50.7 (44.9 to 56.5)	

Statistical analyses

Statistical analysis title	Week 24
Statistical analysis description:	
At Week 24, analysis was stratified by region and baseline DMARD therapy	
Comparison groups	Placebo × 2 IV + non-biologic DMARD therapy v Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Weighted difference
Point estimate	20.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.8
upper limit	27.9

Statistical analysis title	Week 24
Statistical analysis description:	
At Week 24, analysis was stratified by region and baseline DMARD therapy	
Comparison groups	Placebo × 2 IV + non-biologic DMARD therapy v Ocrelizumab

	500 mg × 2 IV + non-biologic DMARD therapy
Number of subjects included in analysis	559
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Weighted Difference
Point estimate	25.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.7
upper limit	32.7

Statistical analysis title	Week 48
Statistical analysis description:	
At Week 48, analysis was stratified by region and baseline DMARD therapy	
Comparison groups	Placebo × 2 IV + non-biologic DMARD therapy v Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Weighted Difference
Point estimate	29.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.6
upper limit	36.6

Statistical analysis title	Week 48
Statistical analysis description:	
At Week 48, analysis was stratified by region and baseline DMARD therapy	
Comparison groups	Placebo × 2 IV + non-biologic DMARD therapy v Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy
Number of subjects included in analysis	559
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Weighted Difference
Point estimate	30.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	22.8
upper limit	37.7

Secondary: Percentage of subjects with a major clinical response

End point title	Percentage of subjects with a major clinical response

End point description:

Major clinical response was defined as achieving an ACR70 response and maintaining this response for a consecutive period of at least 6 months.
Intent-to-Treat (ITT) All randomized participants who received any part of an infusion of study medication were included in the ITT analysis. Number of subjects for whom data was collected is indicated in each time point.

End point type	Secondary

End point timeframe:

Week 48

End point values	Placebo × 2 IV + non-biologic DMARD therapy	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	277	277	282	
Units: percentage				
number (confidence interval 95%)				
Week 48	1.8 (0.2 to 3.4)	4.0 (1.7 to 6.3)	5.7 (3.0 to 8.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects achieving Disease Activity Score (DAS28) remission

End point title	Percentage of subjects achieving Disease Activity Score (DAS28) remission

End point description:

The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10. Scores below 2.6 indicate best disease control and scores above 5.1 indicate worse disease control. DAS28 Remission is defined as a DAS28 score < 2.6.
Intent-to-Treat (ITT) All randomized participants who received any part of an infusion of study medication were included in the ITT analysis. Number of subjects for whom data was collected is indicated in each time point.

End point type	Secondary

End point timeframe:
Weeks 24 and 48

End point values	Placebo × 2 IV + non-biologic DMARD therapy	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	277	277	282	
Units: Percentage				
number (confidence interval 95%)				
Percentage of Participants at Week 24	1.8 (0.2 to 3.4)	5.8 (3.0 to 8.5)	6.0 (3.3 to 8.8)	
Percentage of Participants at Week 48	1.4 (0.0 to 2.8)	11.9 (8.1 to 15.7)	12.1 (8.3 to 15.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in DAS28 from baseline

End point title	Change in DAS28 from baseline

End point description:

The DAS28 score is a measure of the patient's disease activity calculated using the tender joint count (TJC) [28 joints], swollen joint count (SJC) [28 joints], patient's global assessment of disease activity [visual analog scale: 0=no disease activity to 100=maximum disease activity] and the erythrocyte sedimentation rate (ESR) for a total possible score of 0 to approximately 10.
Intent-to-Treat (ITT) All randomized participants who received any part of an infusion of study medication were included in the ITT analysis. Number of subjects for whom data was collected is indicated in each time point.

End point type	Secondary

End point timeframe:
Weeks 24 and 48

End point values	Placebo × 2 IV + non-biologic DMARD therapy	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	277	277	282	
Units: Number				
arithmetic mean (standard deviation)				
Baseline	6.50 (± 1.014)	6.47 (± 1.217)	6.44 (± 1.039)	
24 weeks	-0.99 (± 1.16)	-1.60 (± 1.30)	-1.91 (± 1.34)	
48 weeks	-1.13 (± 1.40)	-2.11 (± 1.34)	-2.38 (± 1.49)	

Statistical analyses

No statistical analyses for this end point

Secondary: EULAR response rates

End point title	EULAR response rates

End point description:

The EULAR response rate was based on the assessment of disease activity using the DAS28. The EULAR response criteria included not only change in disease activity but current disease activity. To be classified as responders, participants had to have a significant change in DAS28 and a low current disease activity. There were 4 categories of EULAR response rates: good, moderate, good/moderate, and none.
Intent-to-Treat (ITT) All randomized participants who received any part of an infusion of study medication were included in the ITT analysis. Number of subjects for whom data were collected is indicated for each time point.

End point type	Secondary

End point timeframe:

Weeks 24 and 48

End point values	Placebo × 2 IV + non-biologic DMARD therapy	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	277	277	282	
Units: Percentage				
number (not applicable)				
Week 24	31.4	54.2	61.0	
Week 48	24.9	58.8	60.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects achieving an ACR50 response

End point title	Percentage of subjects achieving an ACR50 response

End point description:

ACR50 response is defined as a ≥ 50% improvement (reduction) compared with baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: physician's global assessment of disease activity (MDG), patient's global assessment of disease activity (PGA), patient's assessment of pain, Health Assessment Questionnaire with Disability Index (HAQ-DI), and C-Reactive Protein (CRP).
Intent-to-Treat (ITT) All randomized participants who received any part of an infusion of study

medication were included in the ITT analysis. Number of subjects for whom data were collected is indicated for each time point.

End point type	Secondary

End point timeframe:

Weeks 24 and 48

End point values	Placebo × 2 IV + non-biologic DMARD therapy	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	277	277	282	
Units: Percentage				
number (confidence interval 95%)				
Percentage of Participants at Week 24	7.9 (4.8 to 11.1)	21.3 (16.5 to 26.1)	24.8 (19.8 to 29.9)	
Percentage of Participants at Week 48	9.0 (5.7 to 12.4)	28.5 (23.2 to 33.8)	30.9 (25.5 to 36.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects achieving an ACR70 response

End point title	Percentage of subjects achieving an ACR70 response

End point description:

ACR70 response is defined as a ≥ 70% improvement (reduction) compared with Baseline for both total joint count-68 joints (TJC68) and swollen joint count-66 joints (SJC66), as well as for three of the additional five ACR core set variables: physician's global assessment of disease activity (MDG), patient's global
assessment of disease activity (PGA), patient's assessment of pain, HAQ-DI and CRP.
Intent-to-Treat (ITT) All randomized participants who received any part of an infusion of study medication were included in the ITT analysis. Number of subjects for whom data were collected is indicated for each time point.

End point type	Secondary

End point timeframe:

Weeks 24 and 48

End point values	Placebo × 2 IV + non-biologic DMARD therapy	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	277	277	282	
Units: Percentage				
number (confidence interval 95%)				

Percentage of Participants at Week 24	2.9 (0.9 to 4.9)	7.6 (4.5 to 10.7)	9.9 (6.4 to 13.4)	
Percentage of Participants at Week 48	4.3 (1.9 to 6.7)	11.2 (7.5 to 14.9)	18.1 (13.6 to 22.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with a reduction in the HAQ-DI score

End point title	Percentage of subjects with a reduction in the HAQ-DI score

End point description:

Health Assessment Questionnaire – Disability Index (HAQ-DI): The Stanford Health Assessment Questionnaire disability index is a patient reported questionnaire specific for RA. It consists of 20 questions referring to eight component. Reduction in the HAQ-DI score of 0.25 units from baseline to weeks 24 and 48 represented a minimal clinically relevant improvement.
Intent-to-Treat (ITT) All randomized participants who received any part of an infusion of study medication were included in the ITT analysis. Number of subjects for whom data were collected is indicated for each time point.

End point type	Secondary

End point timeframe:

Weeks 24 and 48

End point values	Placebo × 2 IV + non-biologic DMARD therapy	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	277	277	282	
Units: Percentage				
number (confidence interval 95%)				
Percentage of Participants at Week 24	32.9 (27.3 to 38.4)	52.3 (46.5 to 58.2)	58.5 (52.8 to 64.3)	
Percentage of Participants at Week 48	23.1 (18.1 to 28.1)	50.5 (44.7 to 56.4)	51.8 (45.9 to 57.6)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 to week 48 and week 96	
Adverse event reporting additional description:	
The safety population included all subjects who received at least one treatment with study medication	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	Placebo × 2 IV + non-biologic DMARD therapy
Reporting group description:	
Subjects received Ocrelizumab matching Placebo Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15) in combination with any non-biologic DMARDs.	
Reporting group title	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy
Reporting group description:	
Subjects received 200 mg Ocrelizumab administered Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15) in combination with any non-biologic DMARDs.	
Reporting group title	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy
Reporting group description:	
Subjects received 500 mg Ocrelizumab administered Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15) in combination with any non-biologic DMARDs.	
Reporting group title	Ocrelizumab 500 mg × 2 IV (Open Label Extension)
Reporting group description:	
Subjects received 500 mg Ocrelizumab administered Intravenously (IV) in two infusions, separated by 14 days (day 1 and day 15)	

Serious adverse events	Placebo × 2 IV + non-biologic DMARD therapy	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy
Total subjects affected by serious adverse events			
subjects affected / exposed	41 / 276 (14.86%)	46 / 276 (16.67%)	40 / 284 (14.08%)
number of deaths (all causes)	2	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			

subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Diffuse large B-cell lymphoma			
subjects affected / exposed	1 / 276 (0.36%)	1 / 276 (0.36%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Gastric cancer			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Rectal cancer			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Benign ovarian tumour			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			

subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma metastatic			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoma			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningioma			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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			
Deep vein thrombosis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	2 / 284 (0.70%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			
subjects affected / exposed	1 / 276 (0.36%)	1 / 276 (0.36%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			

subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Arteritis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery stenosis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral venous disease			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Hernia repair			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip arthroplasty			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			

Abortion spontaneous			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Pregnancy			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Death			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Surgical failure			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device dislocation			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lead dislodgement			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 inflammatory response syndrome			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Physical assault			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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			
Ovarian cyst			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Female genital tract fistula			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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	1 / 276 (0.36%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			

subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Organising pneumonia			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Pleurisy			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			

subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 embolism			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 hypertension			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 failure			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus polyp			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 respiratory tract inflammation			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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	1 / 276 (0.36%)	1 / 276 (0.36%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bipolar I disorder			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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			
Ankle fracture			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Dislocation of vertebra			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Hip fracture			
subjects affected / exposed	1 / 276 (0.36%)	1 / 276 (0.36%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Spinal compression fracture			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Tendon rupture			
subjects affected / exposed	2 / 276 (0.72%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			

subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Limb crushing injury			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Foreign body			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acetabulum fracture			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Comminuted fracture			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 restenosis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			

subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple fractures			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative fever			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 graft occlusion			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			

subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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			
Hydrocele			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	1 / 276 (0.36%)	2 / 276 (0.72%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve incompetence			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Atrial fibrillation			
subjects affected / exposed	1 / 276 (0.36%)	1 / 276 (0.36%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 276 (0.36%)	2 / 276 (0.72%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Ventricular extrasystoles			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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

Acute coronary syndrome			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
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 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 failure congestive			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 occlusion			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			

subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 extrasystoles			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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			
Radiculitis lumbosacral			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Dementia			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIIth nerve paralysis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical myelopathy			

subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 disorder			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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			
Anaemia			

subjects affected / exposed	2 / 276 (0.72%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Granulocytopenia			
subjects affected / exposed	1 / 276 (0.36%)	1 / 276 (0.36%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Glaucoma			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Uveitis			

subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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			
Gastric ulcer perforation			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Mesenteric vein thrombosis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Hiatus hernia			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Large intestine perforation			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Nausea			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Peptic ulcer haemorrhage			

subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Sinus bradycardia			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 ischaemic			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			

subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovesical fistula			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroduodenal ulcer			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 perforation			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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			
Cholecystitis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis toxic			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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			
Hyperkeratosis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 ulcer			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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			
Focal segmental glomerulosclerosis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cystitis haemorrhagic			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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			
Basedow's disease			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 276 (0.36%)	1 / 276 (0.36%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Arthropathy			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint range of motion decreased			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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

Osteoarthritis			
subjects affected / exposed	2 / 276 (0.72%)	2 / 276 (0.72%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 276 (0.36%)	1 / 276 (0.36%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	7 / 276 (2.54%)	4 / 276 (1.45%)	4 / 284 (1.41%)
occurrences causally related to treatment / all	0 / 7	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint destruction			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Spinal column stenosis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteochondritis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporotic fracture			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			

subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist deformity			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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			
Appendicitis			

subjects affected / exposed	1 / 276 (0.36%)	1 / 276 (0.36%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	2 / 276 (0.72%)	0 / 276 (0.00%)	0 / 284 (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
Cellulitis			
subjects affected / exposed	3 / 276 (1.09%)	0 / 276 (0.00%)	0 / 284 (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
Enteritis infectious			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Implant site infection			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Paronychia			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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			
subjects affected / exposed	5 / 276 (1.81%)	5 / 276 (1.81%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	3 / 5	3 / 5	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			

subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Serratia infection			
subjects affected / exposed	1 / 276 (0.36%)	0 / 276 (0.00%)	0 / 284 (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
Bacterial infection			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Conjunctivitis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Enterocolitis viral			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis B			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Herpes zoster			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Kidney infection			

subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomembranous colitis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Pulmonary tuberculosis			
subjects affected / exposed	0 / 276 (0.00%)	2 / 276 (0.72%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Sinusitis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Atypical pneumonia			

subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis pneumococcal			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
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 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis infective			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis salmonella			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious colitis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal cyst			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			

subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	2 / 284 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal infection			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sycosis barbae			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida infection			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia pyelonephritis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extradural abscess			

subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Genitourinary tract infection			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incision site cellulitis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 respiratory tract infection			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parotitis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 streptococcal			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 sepsis			

subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethritis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Hypoglycaemia			

subjects affected / exposed	0 / 276 (0.00%)	1 / 276 (0.36%)	0 / 284 (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
Dehydration			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 276 (0.00%)	0 / 276 (0.00%)	0 / 284 (0.00%)
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 500 mg × 2 IV (Open Label Extension)		
Total subjects affected by serious adverse events			
subjects affected / exposed	138 / 664 (20.78%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diffuse large B-cell lymphoma			

subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung neoplasm malignant				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Gastric cancer				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal cancer				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterine leiomyoma				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Benign ovarian tumour				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of lung				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colon cancer				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Lung adenocarcinoma metastatic				

subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Lymphoma				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meningioma				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep vein thrombosis				
subjects affected / exposed	3 / 664 (0.45%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Peripheral vascular disorder				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Arteritis				

subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral artery stenosis			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral venous disease			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vasculitis			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Venous thrombosis			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Hernia repair			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip arthroplasty			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pregnancy				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Non-cardiac chest pain				
subjects affected / exposed	4 / 664 (0.60%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Surgical failure				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device dislocation				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lead dislodgement				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multi-organ failure				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pyrexia				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			

Sudden death				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Systemic inflammatory response syndrome				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Social circumstances				
Physical assault				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Ovarian cyst				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Female genital tract fistula				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Interstitial lung disease				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				

subjects affected / exposed	3 / 664 (0.45%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Organising pneumonia				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleurisy				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Acute respiratory distress syndrome				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Epistaxis				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				

subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary haemorrhage				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pulmonary hypertension				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Sinus polyp				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sleep apnoea syndrome				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract inflammation				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Depression				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bipolar I disorder				

subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dislocation of vertebra			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tendon rupture			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Contusion			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Limb crushing injury			

subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thermal burn				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foreign body				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acetabulum fracture				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Comminuted fracture				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery restenosis				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Femur fracture				

subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple fractures				
subjects affected / exposed	3 / 664 (0.45%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Postoperative fever				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular graft occlusion				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wound dehiscence				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Hydrocele				

subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aortic valve incompetence			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	2 / 664 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	6 / 664 (0.90%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	2 / 664 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ventricular extrasystoles			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute coronary syndrome			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block complete			

subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Arteriosclerosis coronary artery				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cardiomyopathy				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery occlusion				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Supraventricular extrasystoles				

subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Radiculitis lumbosacral			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dementia			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Somnolence			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
VIIth nerve paralysis			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Carotid artery stenosis			
subjects affected / exposed	2 / 664 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	3 / 664 (0.45%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Cervical myelopathy			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			

subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hydrocephalus				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxic-ischaemic encephalopathy				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorder				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Iron deficiency anaemia				

subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Granulocytopenia				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disseminated intravascular coagulation				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Leukopenia				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Cataract				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Glaucoma				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uveitis				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				

Gastric ulcer perforation			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mesenteric vein thrombosis			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 664 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hiatus hernia			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peptic ulcer haemorrhage			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sinus bradycardia			

subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	2 / 664 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis ischaemic			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticular perforation			
subjects affected / exposed	2 / 664 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Duodenal ulcer			

subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer haemorrhage				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterovesical fistula				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroduodenal ulcer				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal perforation				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestinal obstruction				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				

subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatitis toxic				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Hyperkeratosis				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin ulcer				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Focal segmental glomerulosclerosis				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Cystitis haemorrhagic				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				

subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary incontinence				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Basedow's disease				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthritis				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthropathy				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Joint range of motion decreased				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Osteonecrosis			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rheumatoid arthritis			
subjects affected / exposed	7 / 664 (1.05%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Joint destruction			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal column stenosis			
subjects affected / exposed	2 / 664 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	2 / 664 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Osteochondritis			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoporotic fracture			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spondylolisthesis			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wrist deformity			

subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Foot deformity				
subjects affected / exposed	3 / 664 (0.45%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc degeneration				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rotator cuff syndrome				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tenosynovitis				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Appendicitis				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthritis bacterial				

subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Enteritis infectious				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Implant site infection				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Paronychia				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	11 / 664 (1.66%)			
occurrences causally related to treatment / all	5 / 11			
deaths causally related to treatment / all	0 / 1			
Pneumonia pneumococcal				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Serratia infection				

subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Conjunctivitis				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterocolitis viral				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatitis B				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Kidney infection				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonitis				

subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pseudomembranous colitis				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Sinusitis				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis pneumococcal				

subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchopneumonia				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bursitis infective				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis salmonella				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infectious colitis				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pilonidal cyst				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				

subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Streptococcal infection			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sycosis barbae			
subjects affected / exposed	0 / 664 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Candida infection			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile infection			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	2 / 664 (0.30%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Escherichia pyelonephritis			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Extradural abscess			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Genitourinary tract infection			

subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Incision site cellulitis			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Parotitis			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pharyngitis			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia streptococcal			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary sepsis			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			

subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Subcutaneous abscess				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urethritis				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	1 / 664 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femoral neck fracture				
subjects affected / exposed	2 / 664 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Diabetic ketoacidosis				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				
subjects affected / exposed	0 / 664 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				

subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 664 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo × 2 IV + non-biologic DMARD therapy	Ocrelizumab 200 mg × 2 IV + non-biologic DMARD therapy	Ocrelizumab 500 mg × 2 IV + non-biologic DMARD therapy
Total subjects affected by non-serious adverse events			
subjects affected / exposed	152 / 276 (55.07%)	153 / 276 (55.43%)	158 / 284 (55.63%)
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	25 / 276 (9.06%)	41 / 276 (14.86%)	41 / 284 (14.44%)
occurrences (all)	34	62	47
Vascular disorders			
Hypertension			
subjects affected / exposed	21 / 276 (7.61%)	18 / 276 (6.52%)	20 / 284 (7.04%)
occurrences (all)	21	19	20
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 276 (5.43%)	12 / 276 (4.35%)	15 / 284 (5.28%)
occurrences (all)	16	13	20
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 276 (3.62%)	15 / 276 (5.43%)	15 / 284 (5.28%)
occurrences (all)	11	15	18
Nausea			

subjects affected / exposed	15 / 276 (5.43%)	11 / 276 (3.99%)	10 / 284 (3.52%)
occurrences (all)	16	11	10
Psychiatric disorders			
Insomnia			
subjects affected / exposed	12 / 276 (4.35%)	9 / 276 (3.26%)	16 / 284 (5.63%)
occurrences (all)	13	9	16
Infections and infestations			
Bronchitis			
subjects affected / exposed	19 / 276 (6.88%)	28 / 276 (10.14%)	22 / 284 (7.75%)
occurrences (all)	22	35	29
Nasopharyngitis			
subjects affected / exposed	31 / 276 (11.23%)	28 / 276 (10.14%)	22 / 284 (7.75%)
occurrences (all)	45	36	42
Sinusitis			
subjects affected / exposed	14 / 276 (5.07%)	13 / 276 (4.71%)	13 / 284 (4.58%)
occurrences (all)	14	17	16
Upper respiratory tract infection			
subjects affected / exposed	36 / 276 (13.04%)	37 / 276 (13.41%)	45 / 284 (15.85%)
occurrences (all)	40	43	67
Urinary tract infection			
subjects affected / exposed	23 / 276 (8.33%)	19 / 276 (6.88%)	24 / 284 (8.45%)
occurrences (all)	30	22	32
Influenza			
subjects affected / exposed	9 / 276 (3.26%)	7 / 276 (2.54%)	15 / 284 (5.28%)
occurrences (all)	9	7	17

Non-serious adverse events	Ocrelizumab 500 mg × 2 IV (Open Label Extension)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	361 / 664 (54.37%)		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	128 / 664 (19.28%)		
occurrences (all)	203		
Vascular disorders			
Hypertension			

subjects affected / exposed occurrences (all)	44 / 664 (6.63%) 48		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 0 / 664 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 0 / 664 (0.00%) 0 0 / 664 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 0 / 664 (0.00%) 0		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all)	 64 / 664 (9.64%) 75 69 / 664 (10.39%) 96 53 / 664 (7.98%) 74 96 / 664 (14.46%) 132 78 / 664 (11.75%) 101 0 / 664 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 August 2008	The sample size for this study was based on the need to obtain sufficient safety data across the RA phase III program. The recent introduction of the phase III study WA29496 (FEATURE) has resulted in an additional 300 patients being included in the development program. At least 240 of the subjects randomized into WA20496 will receive exposure to ocrelizumab. As such it was decided to reduce the sample size inWA20495 (SCRIPT) by 200 patients, to a total sample size of 800.
26 April 2010	All patients have finished the 48 Week double blind period of the study. Those who are in the open label extension should continue with their study visits as usual, but will not receive ocrelizumab treatment. Patients in safety follow-up (SFU) should continue with scheduled visits as normal.
15 July 2010	Open label treatment with ocrelizumab is discontinued and the RA program has been terminated by the Sponsor. Patients will not receive any further treatments with ocrelizumab. Patients who were on placebo and did not receive any ocrelizumab in open label study extension period should return for their next scheduled visit, which will be their final study visit. These patients will not be required to enter safety follow-up. Patients who have received at least one dose of ocrelizumab in the study should complete the withdrawal visit on their next scheduled visit and enter the Safety Follow Up (SFU) period. Patients should remain in SFU for at least 48 weeks from the first infusion of their last course; if at this time the peripheral blood B cell count is still low, patients should continue visits every 12 weeks until the B cell count has returned to the baseline value or into the lower limit of the normal range. Patients who are subsequently treated with an alternative B cell depleting therapy such as commercial rituximab will only be followed for 48 weeks from the date of the first infusion of their last course of ocrelizumab, regardless of peripheral blood. B cell count. During SFU, patients should be clinically managed according to the local standard of care and clinical judgement of the investigator. Study extension period (treatment with ocrelizumab is discontinued, patients remaining on the study extension period should enter Safety Follow Up (SFU) on their next scheduled visit)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported