Clinical trial results:
A Multicenter, Parallel-group Study of Long-term Safety and Efficacy of CNTO 136 (sirukumab) for Rheumatoid Arthritis in Subjects Completing Treatment in Studies CNTO136ARA3002 (SIRROUND-D) and CNTO136ARA3003 (SIRROUND-T)

Summary

EudraCT number	2012-001176-10
Trial protocol	LT ES IT DE PT AT GB BE NL PL HR BG
Global end of trial date	01 May 2018

Results information

Result version number	v1 (current)
This version publication date	10 May 2019
First version publication date	10 May 2019

Trial information

Trial identification

Sponsor protocol code	CNTO136ARA3004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01856309
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 Route 202, Raritan, United States, NJ 08869
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.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	01 May 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the study was to evaluate the long-term safety of sirukumab in subjects with rheumatoid arthritis, who were refractory to treatment with modifying antirheumatic drugs or anti-tumor necrosis factor alpha agents.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety evaluations were based upon the type, incidence, and severity of treatment-emergent adverse events (TEAEs) and adverse events (AEs) of special interest reported throughout the study, and on changes in vital sign measurements, clinical laboratory test results, physical examinations, 12-lead electrocardiograms (ECGs), and Columbia-Suicide Severity Rating Scale (C-SSRS).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 August 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 15
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Bulgaria: 9
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Chile: 50
Country: Number of subjects enrolled	Colombia: 29
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Croatia: 8
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Japan: 224
Country: Number of subjects enrolled	Korea, Republic of: 48
Country: Number of subjects enrolled	Lithuania: 81

Country: Number of subjects enrolled	Mexico: 112
Country: Number of subjects enrolled	Malaysia: 5
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Poland: 196
Country: Number of subjects enrolled	Puerto Rico: 4
Country: Number of subjects enrolled	Portugal: 10
Country: Number of subjects enrolled	Romania: 8
Country: Number of subjects enrolled	Russian Federation: 198
Country: Number of subjects enrolled	Serbia: 118
Country: Number of subjects enrolled	Taiwan: 27
Country: Number of subjects enrolled	Ukraine: 101
Country: Number of subjects enrolled	United States: 449
Country: Number of subjects enrolled	South Africa: 71
Worldwide total number of subjects	1820
EEA total number of subjects	360

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)	1539
From 65 to 84 years	281
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects who completed participation in studies CNTO136ARA3002 (NCT01604343) and CNTO136ARA3003 (NCT01606761) and consented to participate in extension study were enrolled in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo to 50 mg q4w Due to EE/LE/CO

Arm description:

Subjects initially randomized to placebo, then at early escape (EE), late escape (LE), or cross over (CO) randomized to sirukumab 50 milligram (mg) every 4 weeks (q4w) during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen (sirukumab 50 mg q4w) upon entering this long-term extension (LTE) study.

Arm type	Experimental
Investigational medicinal product name	Sirukumab 50 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received sirukumab 50 milligram (mg) every 4 weeks (q4w) during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen (sirukumab 50 mg q4w) upon entering this long-term extension (LTE) study.

Arm title	Placebo to 100 mg q2w Due to EE/LE/CO

Arm description:

Subjects initially randomized to placebo, then at EE, LE, or CO randomized to sirukumab 100 mg every two weeks (q2w) during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen upon entering this LTE study.

Arm type	Experimental
Investigational medicinal product name	Sirukumab 100 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects randomized to receive sirukumab 100 mg every two weeks (q2w) during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive sirukumab 100 mg q2w in this LTE study.

Arm title	Sirukumab 50 mg q4w

Arm description:

Subjects initially randomized to sirukumab 50 mg q4w during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen upon entering this LTE study.

Arm type	Experimental
Investigational medicinal product name	Sirukumab 50 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects initially randomized to sirukumab 50 mg q4w during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive sirukumab 100 mg q2w in this LTE study.

Arm title	Sirukumab 100 mg q2w

Arm description:

Subjects initially randomized to sirukumab 100 mg q2w during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen upon entering this LTE study.

Arm type	Experimental
Investigational medicinal product name	Sirukumab 100 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects initially randomized to sirukumab 100 mg q2w during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive sirukumab 100 mg q2w in this LTE study.

Number of subjects in period 1	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w
Started	305	291	606
Subject fromStudyARA3002	197	187	405
Subject fromStudyARA3003	108	104	201
Treated Subjects	305	290	605
Completed	6	3	11
Not completed	299	288	595
Consent withdrawn by subject	11	13	28
Physician decision	6	1	6
Adverse event, non-fatal	31	31	55
Death	4	6	11
Pregnancy	-	-	-
Unspecified	227	225	447
Lost to follow-up	6	2	4
Noncompliance With Study Drug	-	1	4
Lack of efficacy	14	9	40

Number of subjects in period 1	Sirukumab 100 mg q2w
Started	618
Subject fromStudyARA3002	412

Subject fromStudyARA3003	206
Treated Subjects	618
Completed	9
Not completed	609
Consent withdrawn by subject	26
Physician decision	8
Adverse event, non-fatal	65
Death	6
Pregnancy	1
Unspecified	469
Lost to follow-up	8
Noncompliance With Study Drug	1
Lack of efficacy	25

Baseline characteristics

Reporting groups	
Reporting group title	Placebo to 50 mg q4w Due to EE/LE/CO
Reporting group description:	
Subjects initially randomized to placebo, then at early escape (EE), late escape (LE), or cross over (CO) randomized to sirukumab 50 milligram (mg) every 4 weeks (q4w) during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen (sirukumab 50 mg q4w) upon entering this long-term extension (LTE) study.	
Reporting group title	Placebo to 100 mg q2w Due to EE/LE/CO
Reporting group description:	
Subjects initially randomized to placebo, then at EE, LE, or CO randomized to sirukumab 100 mg every two weeks (q2w) during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen upon entering this LTE study.	
Reporting group title	Sirukumab 50 mg q4w
Reporting group description:	
Subjects initially randomized to sirukumab 50 mg q4w during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen upon entering this LTE study.	
Reporting group title	Sirukumab 100 mg q2w
Reporting group description:	
Subjects initially randomized to sirukumab 100 mg q2w during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen upon entering this LTE study.	

Reporting group values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w
Number of subjects	305	291	606
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	246	243	524
From 65 to 84 years	59	48	82
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	54	53.1	53.1
standard deviation	± 11.92	± 11.75	± 11.43
Title for Gender Units: subjects			
Female	241	231	479
Male	64	60	127
Region of Enrollment Units: Subjects			
Argentina	4	5	4
Australia	0	1	1
Austria	1	1	0
Belgium	0	1	0
Bulgaria	0	3	3
Canada	2	0	2
Chile	11	7	14
Colombia	2	6	10

Croatia	1	2	3
France	0	0	1
Germany	2	3	10
Italy	1	0	0
Japan	36	36	74
Lithuania	13	10	26
Malaysia	3	0	1
Mexico	17	16	39
Netherlands	1	2	1
Poland	36	31	67
Portugal	3	0	3
Puerto Rico	1	0	3
Romania	2	0	2
Russia	34	29	63
Serbia	21	23	38
South Africa	13	16	22
Korea, Republic Of	6	5	14
Spain	3	2	5
Taiwan, Province Of China	5	6	12
Ukraine	16	13	31
United Kingdom	0	0	1
United States	71	73	156
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	2	1	3
Asian	50	47	102
Black or African American	10	15	21
White	231	211	433
Other	11	15	40
Multiple	0	0	0
Not reported	1	2	5
Unknown	0	0	2

Reporting group values	Sirukumab 100 mg q2w	Total	
Number of subjects	618	1820	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	526	1539	
From 65 to 84 years	92	281	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	53.4		
standard deviation	± 11.29	-	
Title for Gender Units: subjects			
Female	503	1454	
Male	115	366	

Region of Enrollment Units: Subjects			
Argentina	2	15	
Australia	0	2	
Austria	0	2	
Belgium	0	1	
Bulgaria	3	9	
Canada	3	7	
Chile	18	50	
Colombia	11	29	
Croatia	2	8	
France	0	1	
Germany	5	20	
Italy	1	2	
Japan	78	224	
Lithuania	32	81	
Malaysia	1	5	
Mexico	40	112	
Netherlands	1	5	
Poland	62	196	
Portugal	4	10	
Puerto Rico	0	4	
Romania	4	8	
Russia	72	198	
Serbia	36	118	
South Africa	20	71	
Korea, Republic Of	23	48	
Spain	4	14	
Taiwan, Province Of China	4	27	
Ukraine	41	101	
United Kingdom	2	3	
United States	149	449	
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	5	11	
Asian	110	309	
Black or African American	23	69	
White	443	1318	
Other	31	97	
Multiple	1	1	
Not reported	4	12	
Unknown	1	3	

End points

End points reporting groups

Reporting group title	Placebo to 50 mg q4w Due to EE/LE/CO

Reporting group description:

Subjects initially randomized to placebo, then at early escape (EE), late escape (LE), or cross over (CO) randomized to sirukumab 50 milligram (mg) every 4 weeks (q4w) during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen (sirukumab 50 mg q4w) upon entering this long-term extension (LTE) study.

Reporting group title	Placebo to 100 mg q2w Due to EE/LE/CO

Reporting group description:

Subjects initially randomized to placebo, then at EE, LE, or CO randomized to sirukumab 100 mg every two weeks (q2w) during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen upon entering this LTE study.

Reporting group title	Sirukumab 50 mg q4w

Reporting group description:

Subjects initially randomized to sirukumab 50 mg q4w during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen upon entering this LTE study.

Reporting group title	Sirukumab 100 mg q2w

Reporting group description:

Subjects initially randomized to sirukumab 100 mg q2w during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen upon entering this LTE study.

Subject analysis set title	Sirukumab 100 mg q2w
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects initially randomized to sirukumab 100 mg q2w during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen upon entering this LTE study. One subject who mistakenly took sirukumab 100mg, when was originally assigned to sirukumab 50mg, was analyzed under the sirukumab 100mg group for all safety analyses.

Primary: Percentage of Subjects with Serious Adverse Events (SAEs)

End point title	Percentage of Subjects with Serious Adverse Events (SAEs)[1][2]

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Population included all subjects who were enrolled in this study. One subject who mistakenly took sirukumab 100mg, when was originally assigned to sirukumab 50mg, was analyzed under the sirukumab 100mg group for all safety analyses.

End point type	Primary

End point timeframe:

From baseline of this LTE study up to 4.3 years

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	305	291	605	619
Units: Percentage of subjects				
number (not applicable)	21.3	27.8	26.4	23.1

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Major Adverse Cardiovascular Events (MACE)

End point title	Percentage of Subjects with Major Adverse Cardiovascular Events (MACE)[3][4]

End point description:

MACE was defined as a composite of Myocardial Infarction (MI), stroke, death, hospitalization for unstable angina, and hospitalization for Transient Ischemic Attack (TIA). Adjudication of these events by the Endpoint Adjudication Committee (EAC) was performed in a blinded fashion. Population included all subjects who were enrolled in this study. One subject who mistakenly took sirukumab 100mg, when was originally assigned to sirukumab 50mg, was analyzed under the sirukumab 100mg group for all safety analyses.

End point type	Primary

End point timeframe:

From baseline of this LTE study up to 4.3 years

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	305	291	605	619
Units: Percentage of subjects				
number (not applicable)	2.0	0.7	2.3	1.1

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Malignancies

End point title	Percentage of Subjects with Malignancies[5][6]

End point description:

Percentage of subjects with one or more malignancy was reported. Population included all subjects who were enrolled in this study. One subject who mistakenly took sirukumab 100mg, when was originally assigned to sirukumab 50mg, was analyzed under the sirukumab 100mg group for all safety analyses.

End point type	Primary

End point timeframe:

From baseline of this LTE study up to 4.3 years

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	305	291	605	619
Units: Percentage of subjects				
number (not applicable)	1.0	3.4	1.5	1.8

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Serious Infections

End point title	Percentage of Subjects with Serious Infections[7][8]

End point description:

Percentage of subjects with one or more serious infections was reported. Population included all subjects who were enrolled in this study. One subject who mistakenly took sirukumab 100mg, when was originally assigned to sirukumab 50mg, was analyzed under the sirukumab 100mg group for all safety analyses.

End point type	Primary

End point timeframe:

From baseline of this LTE study up to 4.3 years

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	305	291	605	619
Units: Percentage of subjects				
number (not applicable)	7.9	12.0	10.4	10.7

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Gastrointestinal (GI) Perforations

End point title	Percentage of Subjects with Gastrointestinal (GI)

End point description:

Percentage of subjects with one or more GI perforations was reported. GI perforation is a hole that develops through the entire wall of the stomach, small intestine, large bowel, or gallbladder. Population included all subjects who were enrolled in this study. One subject who mistakenly took sirukumab 100mg, when was originally assigned to sirukumab 50mg, was analyzed under the sirukumab 100mg group for all safety analyses.

End point type	Primary

End point timeframe:

From baseline of this LTE study up to 4.3 years

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	305	291	605	619
Units: Percentage of subjects				
number (not applicable)	0.7	1.4	0.7	0.5

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Hepatobiliary Abnormalities

End point title	Percentage of Subjects with Hepatobiliary Abnormalities[11][12]

End point description:

Percentage of subjects with hepatobiliary abnormalities was reported. Population included all subjects who were enrolled in this study. One subject who mistakenly took sirukumab 100mg, when was originally assigned to sirukumab 50mg, was analyzed under the sirukumab 100mg group for all safety analyses

End point type	Primary

End point timeframe:

From baseline of this LTE study up to 4.3 years

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	305	291	605	619
Units: Percentage of subjects				
number (not applicable)	0	0.3	0.2	0.2

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Serious or Moderate/Severe Systemic Hypersensitivity Reactions, or Serum Sickness Adverse Events

End point title	Percentage of Subjects with Serious or Moderate/Severe Systemic Hypersensitivity Reactions, or Serum Sickness Adverse Events[13][14]

End point description:

Percentage of subject with serious or moderate/severe systemic hypersensitivity reactions, or serum sickness adverse events (AEs) was reported. Population included all subjects who were enrolled in this study. One subject who mistakenly took sirukumab 100mg, when was originally assigned to sirukumab 50mg, was analyzed under the sirukumab 100mg group for all safety analyses.

End point type	Primary

End point timeframe:

From baseline of this LTE study up to 4.3 years

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	305	291	605	619
Units: Percentage of subjects				
number (not applicable)	0.3	0.7	0.2	0.3

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Toxicity Grade 4 Decrease in Neutrophils

End point title	Percentage of Subjects with Toxicity Grade 4 Decrease in Neutrophils[15]

End point description:

Percentage of subjects with toxicity grade 4 decrease in neutrophils was reported. As per National

Cancer Institute's Common Terminology Criteria for Adverse Events, toxicity grade 4 was defined as decrease in neutrophils less than (<) 500 per Cubic Millimeter (mm^3) or < 0.5 * 10^9 per liter. Population included all subjects who were enrolled in this study. One subject who mistakenly took sirukumab 100mg, when was originally assigned to sirukumab 50mg, was analyzed under the sirukumab 100mg group for all safety analyses.

End point type	Secondary

End point timeframe:

From baseline of primary studies through end of this LTE study (Approximately 5.3 years)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	305	291	605	619
Units: Percentage of subjects				
number (not applicable)	1.3	0	0.5	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Toxicity Grade 4 Decrease in Platelets

End point title	Percentage of Subjects with Toxicity Grade 4 Decrease in Platelets[16]

End point description:

Percentage of subjects with toxicity grade 4 decrease in platelets was reported. As per National Cancer Institute's Common Terminology Criteria for Adverse Events, toxicity grade 4 was defined as decreased in platelets <25000/mm^3 or < 25.0 * 10^9 per liter. Population included all subjects who were enrolled in this study. One subject who mistakenly took sirukumab 100mg, when was originally assigned to sirukumab 50mg, was analyzed under the sirukumab 100mg group for all safety analyses.

End point type	Secondary

End point timeframe:

From baseline of primary studies through end of this LTE study (Approximately 5.3 years)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	305	291	605	619
Units: Percentage of subjects				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with ALT >= 3*ULN, ALT >= 5*ULN, ALT >= 8*ULN

End point title	Percentage of Subjects with ALT >= 3*ULN, ALT >= 5*ULN, ALT >= 8*ULN[17]

End point description:

Percentage of subjects with Alanine Aminotranserase (ALT) >= 3*Upper Limit of Normal (ULN), ALT >= 5*ULN or ALT >= 8*ULN was reported. Population included all subjects who were enrolled in this study. 1 subject who mistakenly took sirukumab 100mg, when was originally assigned to sirukumab 50mg, was analyzed under the sirukumab 100mg group for all safety analyses.

End point type	Secondary

End point timeframe:

From baseline of primary studies through end of this LTE study (Approximately 5.3 years)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	305	291	605	619
Units: Percentage of subjects				
number (not applicable)				
ALT >= 3 * ULN	14.1	14.4	15.9	17.1
ALT >= 5 * ULN	2.0	2.4	2.5	3.9
ALT >= 8 * ULN	0	0.7	0.2	0.2

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with AST >= 3 * ULN, AST >= 5 * ULN, AST >= 8 * ULN

End point title	Percentage of Subjects with AST >= 3 * ULN, AST >= 5 * ULN, AST >= 8 * ULN[18]

End point description:

Percentage of subjects with Aspartate Aminotransferase (AST) >= 3*ULN, AST >= 5*ULN and AST >= 8*ULN was reported. Population included all subjects who were enrolled in this study. 1 subject who mistakenly took sirukumab 100mg, when was originally assigned to sirukumab 50mg, was analyzed under the sirukumab 100mg group for all safety analyses.

End point type	Secondary

End point timeframe:

From baseline of primary studies through end of this LTE study (Approximately 5.3 years)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	305	291	605	619
Units: Percentage of subjects				
number (not applicable)				
AST >= 3 * ULN	3.9	6.2	4.5	7.8
AST >= 5 * ULN	0.3	1.7	0.5	1.1
AST >= 8 * ULN	0	0	0.2	0.3

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with either ALT >= 3 * ULN, AST >= 3 * ULN, and Total Bilirubin >= 2 * ULN

End point title	Percentage of Subjects with either ALT >= 3 * ULN, AST >= 3 * ULN, and Total Bilirubin >= 2 * ULN[19]

End point description:

Percentage of subjects with either ALT >= 3*ULN or AST >= 3*ULN and total bilirubin >= 2*ULN was reported. Population included all subjects who were enrolled in this study. 1 subject who mistakenly took sirukumab 100mg, when was originally assigned to sirukumab 50mg, was analyzed under the sirukumab 100mg group for all safety analyses.

End point type	Secondary

End point timeframe:

From baseline of primary studies through end of this LTE study (Approximately 5.3 years)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	305	291	605	619
Units: Percentage of subjects				
number (not applicable)	0	0	0	0.2

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Normal Total Cholesterol Value at Baseline and at Least 1 Abnormal Value Post-Baseline

End point title	Percentage of Subjects with Normal Total Cholesterol Value at Baseline and at Least 1 Abnormal Value Post-Baseline[20]

End point description:

Percentage of subjects with normal total cholesterol value at baseline and at least 1 abnormal value post-baseline was reported. Abnormal total cholesterol value was defined as total cholesterol value more than (>) 200 milligrams per deciliter (mg/dL). Population included all subjects who were enrolled in this study and had total cholesterol baseline value within normal range.

End point type	Secondary

End point timeframe:

From baseline of primary studies through end of this LTE study (Approximately 5.3 years)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	177	163	354	345
Units: Percentage of subjects				
number (not applicable)	86.4	81.6	82.5	87.2

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Normal LDL Value at Baseline and at Least 1 Abnormal Value Post- Baseline

End point title	Percentage of Subjects with Normal LDL Value at Baseline and at Least 1 Abnormal Value Post- Baseline[21]

End point description:

Percentage of subjects with normal LDL value at baseline and at least 1 abnormal value post-baseline was reported. Abnormal LDL value was defined as LDL value > 130 mg/dL. Population included all subjects who were enrolled in this study and had LDL baseline value within normal range.

End point type	Secondary

End point timeframe:

From baseline of primary studies through end of this LTE study (Approximately 5.3 years)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	225	209	459	449
Units: Percentage of Subjects				
number (not applicable)	70.2	67.9	69.7	70.8

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Normal HDL Value at Baseline and at Least 1 Abnormal Value Post-Baseline

End point title	Percentage of Subjects with Normal HDL Value at Baseline and at Least 1 Abnormal Value Post-Baseline[22]

End point description:

Percentage of subjects with normal HDL value at baseline and at least 1 abnormal value post-baseline was reported. Abnormal HDL value was defined as HDL value < 40 mg/dL. Population included all subjects who were enrolled in this study and had HDL baseline value within normal range.

End point type	Secondary

End point timeframe:

From baseline of primary studies through end of this LTE study (Approximately 5.3 years)

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	277	273	533	569
Units: Percentage of Subjects				
number (not applicable)	16.2	14.7	16.1	16.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Normal Triglyceride Value at Baseline and at Least 1 Abnormal Value Post-Baseline

End point title	Percentage of Subjects with Normal Triglyceride Value at Baseline and at Least 1 Abnormal Value Post-Baseline[23]

End point description:

Percentage of subjects with normal triglyceride value at baseline and at least 1 abnormal value post-baseline was reported. Abnormal triglyceride value was defined as triglyceride value > 250 mg/dL. Population included all subjects who were enrolled in this study and had triglyceride baseline value within normal range.

End point type	Secondary

End point timeframe:

From baseline of primary studies through end of this LTE study (Approximately 5.3 years)

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was planned to be analyzed for specified arm only.

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	279	268	554	564
Units: Percentage of subjects				
number (not applicable)	32.6	35.1	36.1	34.4

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Achieved American College of Rheumatology (ACR) 50 Response Through Week 260

End point title	Percentage of Subjects who Achieved American College of Rheumatology (ACR) 50 Response Through Week 260

End point description:

ACR 50 response is >= 50 % improvement in both tender joint count (68) and swollen joint count (66) and >= 50% improvement in 3 of 5 assessments:Participant’s assessment of pain using VAS (0-10 scale, 0=no pain and 10=worst pain),PGA of disease activity by using VAS (0 to 10, [0 =very well to 10=very poor]), Physician’s global assessment of disease activity using VAS(0 to 10,[0=no arthritis activity,10=extremely active arthritis]), Participant’s assessment of physical function measured by HAQ-DI (scale 0=no difficulty,3=inability to perform task in that area), serum C-reactive protein (CRP). Subjects analyzed for efficacy per assigned treatment groups from primary studies, regardless of treatments received. Population included all subjects enrolled in study. For "Placebo to 50mg", "Placebo to 100mg" groups, only efficacy data collected after escape to sirukumab was planned to be reported, with exception of baseline data. 'n':number of subjects analyzed at specified time point.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48, 52, 76, 80, 104, 128, 132, 156, 180, 208, 232 and 260

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	305	291	605	615
Units: Percentage of subjects				
number (not applicable)				
At week 2 (n = 0, 0 ,604, 615)	99999	99999	2.5	2.4
At week 4 (n = 0, 0, 603, 614)	99999	99999	9.1	9.7
At week 6 (n = 0, 0, 511, 527)	99999	99999	16.2	14.6
At week 8 (n = 0, 0, 603, 611)	99999	99999	21.4	20.0
At week 12 (n = 0, 0, 600, 614)	99999	99999	27.7	29.6
At week 16 (n = 0, 0, 603, 614)	99999	99999	31.8	29.2
At week 18 (n = 0, 0, 602, 612)	99999	99999	33.7	32.0
At week 20 (n = 111, 106, 602, 611)	4.5	3.8	36.9	38.1
At week 24 (n = 112, 106, 606, 615)	17.9	10.4	35.1	37.9
At week 28 (n = 180, 173, 600, 612)	24.4	23.1	40.0	39.2
At week 32 (n = 180, 169, 602, 614)	29.2	33.9	42.3	42.2
At week 36 (n = 178, 174, 601, 612)	29.2	33.9	42.3	43.0

At week 40 (n = 175, 173, 595, 612)	38.3	34.7	42.0	42.2
At week 44 (n = 187, 179, 598, 609)	40.1	33.5	43.3	44.3
At week 48 (n = 187, 179, 601, 608)	43.3	27.9	44.6	44.1
At week 52 (n = 191, 182, 605, 617)	41.9	34.1	43.0	44.9
At week 76 (n = 196, 185, 401, 410)	56.6	49.7	52.4	56.1
At week 80 (n = 90, 87, 178, 187)	38.9	26.4	38.2	44.9
At week 104 (n = 283, 267, 571, 575)	48.8	46.1	50.3	53.0
At week 128 (n = 76, 73, 157, 157)	35.5	43.8	42.7	46.5
At week 132 (n = 174, 165, 356, 369)	51.1	46.7	50.0	53.4
At week 156 (n = 242, 227, 499, 506)	48.3	56.4	50.3	52.6
At week 180 (n= 184, 175, 381, 390)	52.3	54.9	54.6	56.4
At week 208 (n = 110, 93, 199, 213)	50.9	50.5	50.8	59.6
At week 232 (n = 33, 28, 66, 70)	48.5	57.1	51.5	57.1
At week 260 (n = 3, 2, 10, 4)	66.7	50.0	60.0	25.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Boolean-Based American College of Rheumatology (ACR) or European League Against Rheumatism (EULAR) Remission Through Week 260

End point title	Percentage of Subjects with Boolean-Based American College of Rheumatology (ACR) or European League Against Rheumatism (EULAR) Remission Through Week 260

End point description:

Boolean based ACR/EULAR remission is achieved if all of the following 4 criteria at that visit are met: tender joint count (68 joints) <=1; swollen joint count (66 joints) <=1; CRP <=1 milligram per deciliter (mg/dL); and patient's global assessment of disease activity on visual analog scale (VAS) <=1 on a 0 (very well) to 10 (extremely bad) scale. Higher scores indicates worst health condition. Subjects were analyzed for efficacy according to the assigned treatment groups from the primary studies, regardless of the treatments they actually received. Population included all subjects who were enrolled in this study. For "Placebo to 50mg" and "Placebo to 100mg" groups, only efficacy data collected after escape or CO (after Week 18) to sirukumab was planned to be reported, with exception of baseline data. Here 'n' signifies the number of subjects analyzed at the specified time point.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48, 52, 76, 80, 104, 128, 132, 156, 180, 208, 232 and 260

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	305	291	606	618
Units: Percentage of subject				
number (not applicable)				
At week 2 (n = 0, 0, 604, 616)	99999	99999	0.2	0.2
At week 4 (n = 0, 0, 603, 616)	99999	99999	0.5	0.6
At week 6 (n = 0, 0, 511, 527)	99999	99999	0.8	1.5

At week 8 (n = 0, 0, 603, 611)	99999	99999	603	611
At week 12 (n = 0, 0, 602, 614)	99999	99999	3.2	4.9
At week 16 (n = 0, 0, 603, 614)	99999	99999	3.3	5.7
At week 18 (n = 0, 0, 603, 613)	99999	99999	4.3	5.4
At week 20 (n = 111, 106, 604, 611)	99999	99999	4.5	5.9
At week 24 (n = 112, 106, 604, 611)	0.9	0.9	5.3	8.1
At week 28 (n = 180, 174, 602, 613)	2.8	2.9	6.0	6.2
At week 32 (n = 180, 170, 601, 613)	2.2	4.1	4.8	7.7
At week 36 (n = 178, 174, 603, 611)	2.8	4.0	7.8	9.7
At week 40 (n = 177, 173, 596, 613)	4.0	6.4	7.2	9.0
At week 44 (n = 187, 180, 598, 610)	4.3	6.1	7.4	9.7
At week 48 (n = 187, 180, 598, 610)	4.3	7.3	9.8	9.0
At week 52 (n = 190, 181, 604, 618)	6.8	6.6	9.3	7.1
At week 76 (n = 196, 183, 402, 411)	9.7	7.1	10.7	9.2
At week 80 (n = 91, 87, 180, 189)	6.6	8.0	7.8	6.3
At week 104 (n = 283, 270, 573, 578)	10.6	11.1	12.6	10.2
At week 128 (n = 76, 74, 158, 157)	2.6	8.1	10.8	8.9
At week 132 (n = 177, 168, 360, 373)	12.4	11.3	10.8	10.2
At week 156 (n = 244, 229, 503, 508)	9.4	8.7	10.9	11.8
At week 180 (n = 187, 177, 386, 395)	11.8	10.7	14.2	13.9
At week 208 (n = 111, 95, 201, 219)	12.6	13.7	11.4	19.2
At week 232 (n = 34, 28, 66, 66)	11.8	17.9	18.2	9.1
At week 260 (n = 4, 3, 11, 5)	0	0	18.2	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Disease Activity Index Score 28 (DAS28) (CRP) Remission Through Week 260

End point title	Percentage of Subjects With Disease Activity Index Score 28 (DAS28) (CRP) Remission Through Week 260

End point description:

DAS28 based on CRP is statistically derived index combining tender joints (28 joints), swollen joints (28 joints), CRP and patient's global assessment (PGA) of disease activity. Set of 28 joint count is based on evaluation of shoulder, elbow, wrist, metacarpophalangeal (MCP) MCP1 to MCP5, proximal interphalangeal (PIP) PIP1 to PIP5 joints of both upper right extremity and upper left extremity also knee joints of lower right and lower left extremities. Values are 0=best to 10=worst. DAS28 (CRP) remission is DAS28 (CRP) value of less than (<) 2.6 at any study visit. Subjects analyzed for efficacy as per assigned treatment groups from primary studies, regardless of treatments received. Population included all subjects enrolled in study. For "Placebo to 50mg" and "Placebo to 100mg" groups, only efficacy data collected after escape or CO (after Week 18) to sirukumab was planned to be reported, with exception of baseline data. 'n': number of subjects analyzed at specified time point.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48, 52, 76, 80, 104, 128, 132, 156, 180, 208, 232 and 260

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	305	291	606	618
Units: Percentage of subjects				
number (not applicable)				
At week 2 (n = 0, 0, 601, 609)	99999	99999	2.7	2.6
At week 4 (n = 0, 0, 599, 611)	99999	99999	7.5	9.0
At week 6 (n = 0, 0, 502, 524)	99999	99999	10.2	13.4
At week 8 (n = 0, 0, 601, 608)	99999	99999	15.0	18.8
At week 12 (n = 0, 0, 598, 614)	99999	99999	20.4	23.5
At week 16 (n = 0, 0, 602, 612)	99999	99999	23.8	24.0
At week 18 (n = 0, 0, 589, 606)	99999	99999	25.6	25.4
At week 20 (n = 110, 106, 600, 605)	1.8	0	29.8	30.1
At week 24 (n = 111, 106, 603, 610)	7.2	7.5	30.8	32.1
At week 28 (n = 180, 173, 595, 608)	17.8	20.8	33.8	32.7
At week 32 (n = 177, 170, 597, 609)	24.9	24.7	35.3	36.9
At week 36 (n = 178, 174, 596, 610)	21.3	30.5	35.1	35.4
At week 40 (n = 174, 172, 594, 608)	29.9	32.0	34.5	34.9
At week 44 (n = 184, 178, 595, 607)	34.2	30.9	36.0	35.4
At week 48 (n = 184, 179, 592, 605)	33.2	31.3	38.7	38.3
At week 52 (n = 189, 181, 601, 610)	30.7	32.6	38.8	37.4
At week 76 (n = 195, 183, 399, 408)	44.6	44.3	47.6	45.8
At week 80 (n = 90, 84, 175, 184)	38.9	39.3	38.3	38.6
At week 104 (n = 279, 266, 571, 573)	44.8	47.4	42.6	46.6
At week 128 (n = 73, 72, 156, 154)	43.8	43.1	45.5	43.5
At week 132 (n = 169, 165, 350, 365)	41.4	47.3	48.0	49.0
At week 156 (n = 235, 233, 486, 500)	43.0	47.1	46.5	49.6
At week 180 (n = 180, 170, 376, 388)	48.9	48.8	50.5	53.9
At week 208 (n = 109, 93, 197, 213)	55.0	54.8	54.3	60.1
At week 232 (n = 27, 25, 56, 57)	59.3	52.0	57.1	59.6
At week 260 (n = 3, 2, 9, 4)	66.7	100.0	77.8	25.0

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Disease Activity Index (CDAI) Score Through Week 260

End point title	Change From Baseline in Clinical Disease Activity Index (CDAI) Score Through Week 260

End point description:

The CDAI score is a derived score of 4 components: tender joints (28 joints), swollen joints (28 joints), patient's global assessment of disease activity, and physician's global assessments of disease activity. The total score ranges from 0 to 76 with a lower score indicating less disease activity. A negative change in CDAI score indicates an improvement in disease activity and a positive change in score indicates a worsening of disease activity. Subjects were analyzed for efficacy according to the assigned treatment groups from the primary studies, regardless of the treatments they actually received. Population included all subjects who were enrolled in this study. For "Placebo to 50mg" and "Placebo to 100mg" groups, only efficacy data collected after escape or CO (after Week 18) to sirukumab was planned to be reported, with exception of baseline data. Here 'n' signifies the number of subjects analyzed at specified time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0 of primary studies), Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48, 52, 76, 80, 104, 128, 132, 156, 180, 208, 232 and 260

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	305	291	606	614
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Week 2 (n = 0, 0, 602, 614)	99999 (± 99999)	99999 (± 99999)	-6.54 (± 9.464)	-6.10 (± 9.295)
Change at Week 4 (n = 0, 0, 598, 614)	99999 (± 99999)	99999 (± 99999)	-11.09 (± 11.257)	-10.73 (± 11.469)
Change at Week 6 (n = 0, 0, 510, 524)	99999 (± 99999)	99999 (± 99999)	-13.79 (± 12.198)	-14.05 (± 11.613)
Change at Week 8 (n = 0, 0, 602, 611)	99999 (± 99999)	99999 (± 99999)	-15.56 (± 12.736)	-15.74 (± 12.333)
Change at Week 12 (0, 0, 600, 612)	99999 (± 99999)	99999 (± 99999)	-17.79 (± 13.955)	-17.89 (± 13.636)
Change at Week 16 (0, 0, 600, 612)	99999 (± 99999)	99999 (± 99999)	-18.50 (± 13.956)	-18.65 (± 13.584)
Change at Week 18 (n = 0, 0, 599, 613)	99999 (± 99999)	99999 (± 99999)	-18.93 (± 14.459)	-18.40 (± 13.524)
Change at Week 20 (n = 109, 106, 601, 610)	-7.19 (± 12.051)	-7.01 (± 11.666)	-20.72 (± 14.077)	-19.96 (± 13.678)
Change at Week 24 (n = 111, 106, 605, 615)	-15.08 (± 11.697)	-12.78 (± 11.654)	-21.20 (± 13.625)	-21.06 (± 13.888)
Change at Week 28 (n = 179, 172, 600, 612)	-19.69 (± 13.518)	-19.58 (± 12.578)	-21.85 (± 14.000)	-21.33 (± 13.655)
Change at Week 32 (n = 179, 169, 600, 612)	-20.36 (± 14.238)	-20.69 (± 12.754)	-22.37 (± 13.935)	-22.17 (± 13.462)
Change at Week 36 (n = 177, 174, 600, 611)	-21.49 (± 12.343)	-22.53 (± 12.609)	-22.64 (± 13.750)	-22.79 (± 13.220)
Change at Week 40 (n = 176, 173, 593, 609)	-22.67 (± 13.374)	-22.36 (± 13.208)	-23.09 (± 13.890)	-22.49 (± 14.268)
Change at Week 44 (n = 186, 178, 596, 608)	-22.80 (± 14.390)	-22.31 (± 13.062)	-23.19 (± 14.214)	23.04 (± 13.484)
Change at Week 48 (n = 185, 179, 599, 606)	-23.74 (± 13.685)	-22.56 (± 13.229)	-23.22 (± 14.281)	-23.20 (± 13.008)
Change at Week 52 (n = 190, 183, 603, 617)	-24.09 (± 13.629)	-23.17 (± 13.280)	-24.50 (± 13.930)	-23.61 (± 12.664)
Change at Week 76 (n = 196, 185, 402, 410)	-27.49 (± 12.763)	-25.91 (± 13.537)	-25.98 (± 14.077)	-24.83 (± 12.664)
Change at Week 80 (n = 85, 84, 174, 180)	-23.31 (± 14.840)	-22.67 (± 12.546)	-23.27 (± 15.372)	-23.70 (± 14.755)
Change at Week 104 (n = 280, 267, 569, 573)	-26.85 (± 13.261)	-26.08 (± 12.872)	-25.75 (± 13.931)	-25.60 (± 13.596)
Change at Week 128 (n = 74, 74, 154, 156)	-24.55 (± 13.797)	-25.12 (± 12.102)	-25.06 (± 15.496)	-2614 (± 14.810)
Change at Week 132 (n = 172, 165, 347, 366)	-27.24 (± 12.671)	-26.62 (± 13.334)	-26.06 (± 13.661)	-24.61 (± 13.391)
Change at Week 156 (n = 238, 225, 489, 503)	-26.53 (± 14.998)	-26.85 (± 13.999)	-25.59 (± 14.641)	-25.60 (± 13.196)

Change at Week 180 (n = 180, 168, 375, 388)	-27.21 (± 14.370)	-27.07 (± 13.969)	-26.95 (± 13.671)	-25.88 (± 13.910)
Change at Week 208 (n = 109, 92, 197, 211)	-27.54 (± 12.054)	-27.06 (± 15.579)	-27.01 (± 12.968)	-27.12 (± 13.008)
Change at Week 232 (n = 34, 28, 67, 69)	-26.61 (± 13.420)	-26.25 (± 17.509)	-26.06 (± 16.858)	-27.23 (± 14.636)
Change at Week 260 (n = 3, 2, 10, 4)	-34.70 (± 4.776)	-26.60 (± 20.789)	-20.73 (± 11.983)	-19.03 (± 18.823)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Simplified Disease Activity Index Based (SDAI-based) American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) Remission

End point title	Percentage of Subjects With Simplified Disease Activity Index Based (SDAI-based) American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) Remission

End point description:

SDAI derived by combining 5 disease assessments: tender joint (28), swollen joint (28) counts, PGA of disease activity using VAS (0 to 10 [0 =very well to 10 = very poor]), PGA of disease activity using VAS (0 to 10 [0=no arthritis to 10=extremely active arthritis]) and CRP. 28 joints evaluated for swelling and tenderness are same set of 28 joints used in DAS28 includes shoulder, elbow, wrist, MCP1, MCP2, MCP3, MCP4, MCP5, PIP1, PIP2, PIP3, PIP4, PIP5 joints of upper right and left extremities and knee joints of lower right and left extremities. Subjects analyzed for efficacy as per assigned treatment groups from primary studies, regardless of treatments received. Population included subjects enrolled in study. For "Placebo to 50mg" and "Placebo to 100mg" groups, only efficacy data collected after escape or CO (after Week 18) to sirukumab was planned to be reported, with exception of baseline data. 'n': number of subjects analyzed at specified time point.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48, 52, 76, 80, 104, 128, 132, 156, 180, 208, 232 and 260

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	305	291	606	618
Units: Percentage of subjects				
number (not applicable)				
At week 2 (n = 0, 0, 600, 609)	99999	99999	0.2	0.2
At week 4 (n = 0, 0, 596, 610)	99999	99999	0.8	1.1
At week 6 (n = 0, 0, 502, 522)	99999	99999	1.2	2.9
At week 8 (n = 0, 0, 601, 608)	99999	99999	2.8	3.9
At week 12 (n = 0, 0, 598, 612)	99999	99999	4.5	6.4
At week 16 (n = 0, 0, 600, 611)	99999	99999	5.2	8.0
At week 18 (n = 0, 0, 587, 606)	99999	99999	7.5	7.1
At week 20 (n = 110, 106, 600, 604)	0	0	8.0	9.3
At week 24 (n = 111, 106, 603, 610)	1.8	1.9	9.8	10.7
At week 28 (n = 180, 172, 595, 608)	3.9	6.4	10.4	9.2

At week 32 (n = 177, 169, 596, 607)	4.0	7.1	9.9	12.4
At week 36 (n = 178, 174, 596, 609)	4.5	7.5	11.7	13.0
At week 40 (n = 174, 172, 592, 605)	7.5	11.0	13.7	13.7
At week 44 (n = 184, 176, 595, 605)	8.7	10.2	11.8	13.5
At week 48 (n = 183, 179, 591, 603)	8.2	12.3	14.9	12.8
At week 52 (n = 189, 179, 1591, 603)	9.05	8.8	15.0	12.5
At week 76 (n = 195, 183, 399, 408)	16.9	13.7	16.8	14.2
At week 80 (n = 86, 83, 174, 180)	9.3	10.8	12.6	11.1
At week 104 (n = 2789, 264, 568, 571)	14.3	18.2	17.8	19.8
At week 128 (n = 73, 72, 155, 154)	8.2	15.3	16.1	13.6
At week 132 (n = 169, 165, 347, 364)	18.3	15.8	20.5	19.0
At week 156 (n = 235, 223, 483, 499)	17.9	14.8	17.8	19.4
At week 180 (n = 180, 167, 374, 387)	18.3	20.4	22.5	24.0
At week 208 (n = 108, 92, 196, 211)	21.3	20.7	22.4	30.3
At week 232 (n = 27, 25, 55, 57)	25.39	20.2	27.3	29.8
At week 260 (N = 3, 2, 9, 4)	33.3	50.0	55.6	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score Through Week 260

End point title	Change From Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score Through Week 260

End point description:

HAQ-DI score is an evaluation of functional status for a subject. 20-question instrument assesses degree of difficulty person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, activities of daily living). Responses in each functional area scored from 0(no difficulty), to 3, (inability to perform a task in that area. Overall score was sum of domain scores and divided by number of domains answered. Total score: 0-3, 0 = least difficulty and 3 = extreme difficulty. Subjects were analyzed for efficacy according to assigned treatment groups from the primary studies, regardless of treatments actually received. Population included all subjecs enrolled in this study. For "Placebo to 50mg" and "Placebo to 100mg" groups, only efficacy data collected after the escape or CO (after Week 18) to sirukumab was planned to be reported, with exception of baseline data. 'n':number of subjects analyzed at specified time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0 of primary studies), Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48, 52, 76, 80, 104, 128, 132, 156, 180, 208, 232 and 260

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	305	291	606	618
Units: Units on Scale				
arithmetic mean (standard deviation)				
Change at Week 2 (n = 0, 0, 603, 616)	99999 (± 99999)	99999 (± 99999)	-0.1136 (± 0.3455)	-0.1230 (± 0.3741)

Change at Week 4 (n = 0, 0, 602, 616)	99999 (± 99999)	99999 (± 99999)	-0.2307 (± 0.4173)	-0.2417 (± 0.4034)
Change at Week 6 (n = 0, 0, 511, 526)	99999 (± 99999)	99999 (± 99999)	-0.3112 (± 0.4944)	-0.3683 (± 0.4823)
Change at Week 8 (n = 0, 0, 602, 611)	99999 (± 99999)	99999 (± 99999)	-0.3499 (± 0.5077)	-0.3914 (± 0.5022)
Change at Week 12 (n = 0, 0, 601, 613)	99999 (± 99999)	99999 (± 99999)	-0.3866 (± 0.5421)	-0.4121 (± 0.5270)
Change at Week 16 (n = 0, 0, 606, 614)	99999 (± 99999)	99999 (± 99999)	-0.3991 (± 0.5611)	-0.4414 (± 0.5430)
Change at Week 18 (n = 0, 0, 602, 614)	99999 (± 99999)	99999 (± 99999)	-0.4365 (± 0.5476)	-0.4621 (± 0.5325)
Change at Week 20 (n = 111, 106, 602, 611)	-0.1363 (± 0.4947)	-0.2005 (± 0.4987)	-0.4425 (± 0.5826)	-0.4920 (± 0.5582)
Change at Week 24 (n = 112, 106, 605, 615)	-0.3192 (± 0.5279)	-0.3267 (± 0.4739)	-0.4506 (± 0.5665)	-0.4876 (± 0.5622)
Change at Week 28 (n = 180, 174, 601, 612)	-0.3722 (± 0.5683)	-0.3836 (± 0.4741)	-0.4736 (± 0.5696)	-0.4912 (± 0.5626)
Change at Week 32 (n = 180, 170, 601, 614)	-0.3847 (± 0.5651)	-0.4015 (± 0.5532)	-0.4769 (± 0.5880)	-0.5307 (± 0.5740)
Change at Week 36 (n = 178, 174, 602, 611)	-0.3862 (± 0.5474)	-0.4339 (± 0.5432)	-0.4850 (± 0.5764)	-0.5176 (± 0.5688)
Change at Week 40 (n = 177, 173, 593, 613)	-0.4138 (± 0.5778)	-0.4509 (± 0.4988)	-0.4850 (± 0.5894)	-0.5039 (± 0.5735)
Change at Week 44 (n = 187, 181, 597, 610)	-0.4231 (± 0.5809)	-0.4461 (± 0.5206)	-0.4906 (± 0.6088)	-0.5297 (± 0.5777)
Change at Week 48 (n = 187, 179, 601, 609)	-0.4392 (± 0.5911)	-0.4567 (± 0.5254)	-0.4890 (± 0.6242)	-0.5470 (± 0.5942)
Change at Week 52 (n = 191, 182, 604, 618)	-0.4228 (± 0.5752)	-0.4609 (± 0.5455)	-0.4946 (± 0.6021)	-0.5374 (± 0.5881)
Change at Week 76 (n = 196, 185, 402, 411)	-0.5816 (± 0.6313)	-0.5351 (± 0.5605)	-0.5628 (± 0.6089)	-0.6128 (± 0.5992)
Change at Week 80 (n = 91, 87, 179, 187)	-0.2074 (± 0.5333)	-0.3980 (± 0.5579)	-0.3834 (± 0.5685)	-0.5579 (± 0.5913)
Change at Week 104 (n = 282, 269, 573, 579)	-0.4778 (± 0.6569)	-0.4476 (± 0.5263)	-0.3615 (± 0.6227)	-0.4506 (± 0.5227)
Change at Week 128 (n = 76, 74, 157, 157)	-0.2664 (± 0.5963)	-0.4476 (± 0.5263)	-0.3615 (± 0.6227)	-0.4506 (± 0.5527)
Change at Week 132 (n = 178, 169, 362, 375)	-0.4831 (± 0.6979)	-0.4815 (± 0.6656)	-0.5045 (± 0.6542)	-0.5310 (± 0.6240)
Change at Week 156 (n = 243, 231, 503, 505)	-0.4614 (± 0.6610)	-0.4984 (± 0.6520)	-0.4719 (± 0.6604)	-0.4998 (± 0.6109)
Change at Week 180 (n = 187, 276, 384, 393)	-0.4505 (± 0.7024)	-0.4957 (± 0.5969)	-0.5072 (± 0.6492)	-0.5258 (± 0.6167)
Change at Week 208 (n = 109, 276, 384, 393)	-0.4622 (± 0.6898)	-0.4973 (± 0.6032)	-0.5031 (± 0.6701)	-0.5588 (± 0.6023)
Change at Week 232 (n = 34, 29, 67, 69)	-0.4191 (± 0.7410)	-0.4655 (± 0.6477)	-0.5877 (± 0.8312)	-0.6069 (± 0.6262)
Change at Week 260 (n = 3, 2, 9, 3)	-0.5417 (± 0.8323)	-0.3750 (± 1.0607)	-0.2083 (± 0.6702)	-0.5000 (± 0.4507)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Health Assessment Questionnaire-Disability Index (HAQ-DI) Response Through Week 260

End point title	Percentage of Subjects With Health Assessment Questionnaire-

	Disability Index (HAQ-DI) Response Through Week 260

End point description:

HAQ-DI score is an evaluation of functional status for a subject. 20-question instrument assesses degree of difficulty person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, activities of daily living). Responses in each functional area scored from 0(no difficulty), to 3, (inability to perform a task in that area. Overall score was sum of domain scores and divided by number of domains answered. Total score: 0-3, 0 = least difficulty and 3 = extreme difficulty. Subjects were analyzed for efficacy according to assigned treatment groups from the primary studies, regardless of treatments actually received. Population included all subjecs enrolled in this study. For "Placebo to 50mg" and "Placebo to 100mg" groups, only efficacy data collected after the escape or CO (after Week 18) to sirukumab was planned to be reported, with exception of baseline data. 'n':number of subjects analyzed at specified time point.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48, 52, 76, 80, 104, 128, 132, 156, 180, 208, 232 and 260

End point values	Placebo to 50 mg q4w Due to EE/LE/CO	Placebo to 100 mg q2w Due to EE/LE/CO	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	305	291	606	618
Units: Percentage of subjects				
number (not applicable)				
At week 2 (n = 0, 0, 603, 616)	99999	99999	36.3	36.4
At week 4 (n = 0, 0, 602, 616)	99999	99999	48.3	51.3
At week 6 (n = 0, 0, 511, 526)	99999	99999	56.4	57.6
At week 8 (n = 0, 0, 602, 611)	99999	99999	58.0	62.5
At week 12 (n = 0, 0, 601, 613)	99999	99999	60.4	62.3
At week 16 (n = 0, 0, 602, 614)	99999	99999	62.0	63.2
At week 18 (n = 0, 0, 602, 614)	99999	99999	63.0	66.0
At week 20 (n = 111, 106, 602, 611)	40.5	45.3	64.0	67.1
At week 24 (n = 112, 106, 605, 615)	54.5	54.7	64.3	67.0
At week 28 (n = 180, 174, 601, 612)	58.3	61.5	66.7	66.8
At week 36 (n = 178, 174, 602, 611)	61.2	64.9	67.1	67.9
At week 40 (n = 177, 174, 602, 611)	61.0	67.1	65.4	66.6
At week 44 (n = 187, 181, 597, 610)	62.6	65.2	65.8	67.9
At week 48 (n = 187, 181, 597, 610)	61.5	65.9	65.6	70.1
At week 52 (N = 191, 182, 604, 618)	60.7	65.9	65.6	68.9
At week 76 (n = 191, 182, 604, 618)	70.4	69.2	68.4	73.7
At week 80 (n = 91, 87, 179, 187)	40.7	58.6	58.1	62.0
At week 104 (n = 282, 269, 573, 579)	64.2	68.4	66.1	68.0
At week 128 (n = 76, 74, 157, 157)	51.3	64.9	54.8	61.1
At week 132 (n = 178, 169, 362, 375)	65.2	63.3	66.3	69.9
At week 156 (n = 243, 231, 503, 505)	62.6	64.5	65.0	66.9
At week 180 (n = 187, 231, 503, 505)	61.0	69.3	66.4	72.3
At week 208 (n = 109, 94, 201, 217)	65.1	69.1	71.1	72.4
At week 232 (n = 34, 29, 67, 69)	67.6	69.0	65.7	72.5
At week 280 (n = 66.7, 50.0, 44.4, 66.7)	66.7	50.0	44.4	66.7

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline of this LTE study through up to 4.3 years

Adverse event reporting additional description:

Population included all subjects enrolled. 1subject mistakenly took sirukumab 100mg, originally assigned to sirukumab 50mg, analyzed in sirukumab 100mg group for safety analyses. Treatment group 'Placebo to 100 mg q2w due to EE/LE/CO, 6 deaths happened in ARA3004 study. 1 additional death reported in this group after subject discontinued study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Placebo to 50 mg q4w due to EE/LE or CO

Reporting group description:

Subjects initially randomized to placebo, then at early escape (EE), late escape (LE), or cross over (CO) randomized to sirukumab 50 milligram (mg) every 4 weeks (q4w) during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen (sirukumab 50 mg q4w) upon entering this long-term extension (LTE) study.

Reporting group title	Sirukumab 50 mg q4w Start

Reporting group description:

Subjects initially randomized to sirukumab 50 mg q4w during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen upon entering this LTE study.

Reporting group title	Placebo to 100 mg q2w due to EE/LE or CO

Reporting group description:

Subjects initially randomized to placebo, then at EE, LE, or CO randomized to sirukumab 100 mg every two weeks (q2w) during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen upon entering this LTE study.

Reporting group title	Sirukumab 100 mg q2w Start

Reporting group description:

Subjects initially randomized to sirukumab 100 mg q2w during the primary studies CNTO136ARA3002 and CNTO136ARA3003, and then continued to receive the same regimen upon entering this LTE study.

Serious adverse events	Placebo to 50 mg q4w due to EE/LE or CO	Sirukumab 50 mg q4w Start	Placebo to 100 mg q2w due to EE/LE or CO
Total subjects affected by serious adverse events			
subjects affected / exposed	65 / 305 (21.31%)	160 / 605 (26.45%)	81 / 291 (27.84%)
number of deaths (all causes)	5	13	7
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute promyelocytic leukaemia			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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

Basal cell carcinoma			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign ovarian tumour			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Bladder cancer			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Central nervous system lymphoma			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
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 adenoma			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammatory pseudotumour			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipoma			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 neoplasm malignant			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Lymphoproliferative disorder			
subjects affected / exposed	0 / 305 (0.00%)	2 / 605 (0.33%)	0 / 291 (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
Malignant melanoma			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoclonal gammopathy			

subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Myelofibrosis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Rectal cancer			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer stage III			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schwannoma			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
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 pharynx			

subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Tonsil cancer			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Uterine cancer			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Vaginal cancer			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Aortic dissection			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic stenosis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			

subjects affected / exposed	1 / 305 (0.33%)	2 / 605 (0.33%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 305 (0.00%)	3 / 605 (0.50%)	0 / 291 (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
Malignant hypertension			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Penetrating aortic ulcer			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Peripheral vascular disorder			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose vein			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Vasculitis			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 necrotising			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 305 (0.33%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 305 (0.33%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Implant site haematoma			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 organ dysfunction syndrome			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Non-cardiac chest pain			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Peripheral swelling			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue inflammation			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden cardiac death			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Reproductive system and breast disorders			
Cervical polyp			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometriosis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Genital haemorrhage			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metrorrhagia			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst ruptured			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic prolapse			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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			
Acute respiratory failure			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 305 (0.00%)	2 / 605 (0.33%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diaphragmatic disorder			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Dyspnoea			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Hypoxia			

subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Interstitial lung disease			
subjects affected / exposed	1 / 305 (0.33%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
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 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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	1 / 305 (0.33%)	1 / 605 (0.17%)	2 / 291 (0.69%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			

subjects affected / exposed	1 / 305 (0.33%)	1 / 605 (0.17%)	0 / 291 (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
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Alcohol abuse			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conversion disorder			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Depression			
subjects affected / exposed	0 / 305 (0.00%)	3 / 605 (0.50%)	0 / 291 (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
Depression suicidal			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Disorientation			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Persistent depressive disorder			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Suicide attempt			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 305 (0.00%)	2 / 605 (0.33%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device loosening			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Transaminases increased			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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

Injury, poisoning and procedural complications			
Acetabulum fracture			
subjects affected / exposed	1 / 305 (0.33%)	1 / 605 (0.17%)	0 / 291 (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
Ankle fracture			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Comminuted fracture			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dislocation of vertebra			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	2 / 305 (0.66%)	2 / 605 (0.33%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	2 / 305 (0.66%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fractured sacrum			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Hand fracture			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hip fracture			
subjects affected / exposed	1 / 305 (0.33%)	1 / 605 (0.17%)	0 / 291 (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
Humerus fracture			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	1 / 305 (0.33%)	2 / 605 (0.33%)	2 / 291 (0.69%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament rupture			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament sprain			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 305 (0.00%)	2 / 605 (0.33%)	0 / 291 (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
Lumbar vertebral fracture			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 injuries			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle injury			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle rupture			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patella fracture			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Pelvic fracture			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periprosthetic fracture			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Pneumothorax traumatic			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural fistula			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Postoperative thrombosis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 injury			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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	0 / 305 (0.00%)	2 / 605 (0.33%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic rupture			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			

subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Synovial rupture			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Tendon rupture			
subjects affected / exposed	2 / 305 (0.66%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	2 / 291 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound necrosis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	1 / 305 (0.33%)	1 / 605 (0.17%)	0 / 291 (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
Cardiac disorders			
Acute left ventricular failure			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 305 (0.33%)	3 / 605 (0.50%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 305 (0.00%)	2 / 605 (0.33%)	0 / 291 (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
Angina unstable			
subjects affected / exposed	0 / 305 (0.00%)	3 / 605 (0.50%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 305 (0.33%)	2 / 605 (0.33%)	0 / 291 (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
Atrial flutter			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bradycardia			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Cardiac arrest			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Cardiac failure congestive			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Cardio-respiratory arrest			
subjects affected / exposed	1 / 305 (0.33%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery insufficiency			

subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hypertensive heart disease			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Mitral valve incompetence			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Sinus node dysfunction			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Amnesia			

subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Carpal tunnel syndrome			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar infarction			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Cerebral artery embolism			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Cerebral haematoma			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cerebral infarction			
subjects affected / exposed	0 / 305 (0.00%)	4 / 605 (0.66%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 305 (0.33%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cubital tunnel syndrome			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 postural			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Facial paresis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Hemiparesis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Hypertensive encephalopathy			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IIIrd nerve paralysis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial mass			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Lumbar radiculopathy			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Mononeuropathy multiplex			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Myxoedema coma			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Spondylitic myelopathy			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 / 305 (0.00%)	1 / 605 (0.17%)	2 / 291 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulnar tunnel syndrome			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Bone marrow failure			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic anaemia			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Hypochromic anaemia			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Iron deficiency anaemia			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Leukopenia			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Lymphadenitis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 305 (0.00%)	3 / 605 (0.50%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Inner ear disorder			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Meniere's disease			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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			
Blindness			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	1 / 305 (0.33%)	3 / 605 (0.50%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corneal perforation			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keratitis			

subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Retinal detachment			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Scleritis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Ulcerative keratitis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Anal fissure			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	2 / 291 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Diverticular perforation			

subjects affected / exposed	1 / 305 (0.33%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Duodenal ulcer			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric volvulus			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Gastritis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal angiodysplasia haemorrhagic			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids thrombosed			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 intestine perforation			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	2 / 291 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric vein thrombosis			

subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pancreatic cyst			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Pancreatitis acute			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 305 (0.00%)	2 / 605 (0.33%)	0 / 291 (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
Cholelithiasis			
subjects affected / exposed	1 / 305 (0.33%)	1 / 605 (0.17%)	2 / 291 (0.69%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sphincter of Oddi dysfunction			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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			

Cutaneous vasculitis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decubitus ulcer			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis bullous			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic foot			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Hypersensitivity vasculitis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 necrosis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	0 / 305 (0.00%)	5 / 605 (0.83%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	2 / 5	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous emphysema			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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			

Acute kidney injury			
subjects affected / exposed	0 / 305 (0.00%)	2 / 605 (0.33%)	0 / 291 (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
Calculus urethral			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Calculus urinary			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis interstitial			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerulonephritis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Hydronephrosis			
subjects affected / exposed	0 / 305 (0.00%)	2 / 605 (0.33%)	0 / 291 (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
IgA nephropathy			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incontinence			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lupus nephritis			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 / 305 (0.00%)	3 / 605 (0.50%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal haematoma			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Stag horn calculus			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Ureterolithiasis			
subjects affected / exposed	0 / 305 (0.00%)	3 / 605 (0.50%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 305 (0.66%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Arthritis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	2 / 291 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atlantoaxial instability			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis			
subjects affected / exposed	2 / 305 (0.66%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Finger deformity			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Foot deformity			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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 / 305 (0.00%)	1 / 605 (0.17%)	2 / 291 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			

subjects affected / exposed	0 / 305 (0.00%)	3 / 605 (0.50%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mixed connective tissue disease			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	2 / 305 (0.66%)	3 / 605 (0.50%)	9 / 291 (3.09%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteochondrosis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Osteonecrosis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Pathological fracture			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudarthrosis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Rheumatoid arthritis			
subjects affected / exposed	0 / 305 (0.00%)	6 / 605 (0.99%)	2 / 291 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Spondylolisthesis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Synovitis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Abscess intestinal			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	2 / 305 (0.66%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Appendicitis			
subjects affected / exposed	0 / 305 (0.00%)	2 / 605 (0.33%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	1 / 305 (0.33%)	2 / 605 (0.33%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Bacterial pyelonephritis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Breast abscess			

subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Breast cellulitis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Bursitis infective staphylococcal			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Cellulitis			
subjects affected / exposed	3 / 305 (0.98%)	12 / 605 (1.98%)	4 / 291 (1.37%)
occurrences causally related to treatment / all	2 / 3	7 / 12	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic abscess			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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			
subjects affected / exposed	0 / 305 (0.00%)	2 / 605 (0.33%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis infected			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Device related infection			

subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	2 / 305 (0.66%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	1 / 2	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 305 (0.00%)	4 / 605 (0.66%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extradural abscess			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Gangrene			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Gastroenteritis salmonella			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma infection			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis E			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster disseminated			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Infected seroma			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected skin ulcer			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Infectious pleural effusion			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Infective tenosynovitis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Intervertebral discitis			

subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Klebsiella infection			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	2 / 305 (0.66%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastitis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device site joint infection			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis pneumococcal			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	1 / 305 (0.33%)	2 / 605 (0.33%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ophthalmic herpes zoster			

subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Osteomyelitis			
subjects affected / exposed	2 / 305 (0.66%)	2 / 605 (0.33%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	2 / 2	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal cyst			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	4 / 305 (1.31%)	9 / 605 (1.49%)	8 / 291 (2.75%)
occurrences causally related to treatment / all	3 / 4	5 / 9	5 / 8
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 1
Pneumonia bacterial			
subjects affected / exposed	1 / 305 (0.33%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Postoperative wound infection			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoas abscess			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Pyelonephritis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 305 (0.00%)	2 / 605 (0.33%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyomyositis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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	1 / 305 (0.33%)	3 / 605 (0.50%)	6 / 291 (2.06%)
occurrences causally related to treatment / all	1 / 1	2 / 3	3 / 6
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 2
Septic shock			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	3 / 291 (1.03%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 3
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 2
Soft tissue infection			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord infection			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal abscess			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	1 / 291 (0.34%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Staphylococcal skin infection			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal abscess			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal endocarditis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth abscess			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Urinary tract infection			
subjects affected / exposed	0 / 305 (0.00%)	2 / 605 (0.33%)	0 / 291 (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
Urosepsis			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulval abscess			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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 infection			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	2 / 291 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	1 / 305 (0.33%)	1 / 605 (0.17%)	0 / 291 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 305 (0.00%)	1 / 605 (0.17%)	0 / 291 (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
Hyperlipidaemia			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Hypokalaemia			
subjects affected / exposed	1 / 305 (0.33%)	0 / 605 (0.00%)	0 / 291 (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
Hypoproteinaemia			
subjects affected / exposed	0 / 305 (0.00%)	0 / 605 (0.00%)	0 / 291 (0.00%)
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	Sirukumab 100 mg q2w Start		
Total subjects affected by serious adverse events			
subjects affected / exposed	143 / 619 (23.10%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute promyelocytic leukaemia			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Basal cell carcinoma				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Benign ovarian tumour				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bladder cancer				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Breast cancer				
subjects affected / exposed	3 / 619 (0.48%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Central nervous system lymphoma				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colon adenoma				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Colon cancer				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diffuse large B-cell lymphoma				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Inflammatory pseudotumour				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Intraductal proliferative breast lesion				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Invasive ductal breast carcinoma				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lipoma				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung neoplasm malignant				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lymphoma				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphoproliferative disorder				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Monoclonal gammopathy				

subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myelofibrosis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-Hodgkin's lymphoma				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Papillary thyroid cancer				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal cancer				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal cancer stage III				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Schwannoma				
subjects affected / exposed	0 / 619 (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	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of pharynx				

subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsil cancer				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterine cancer				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterine leiomyoma				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vaginal cancer				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Aortic aneurysm				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic dissection				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic stenosis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				

subjects affected / exposed	2 / 619 (0.32%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypertensive crisis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant hypertension				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Penetrating aortic ulcer				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral vascular disorder				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombophlebitis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Varicose vein				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vasculitis				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vasculitis necrotising				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest pain				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Implant site haematoma				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral swelling				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Soft tissue inflammation				

subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sudden cardiac death				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Reproductive system and breast disorders				
Cervical polyp				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endometriosis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Genital haemorrhage				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metrorrhagia				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian cyst				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian cyst ruptured				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic prolapse				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Uterine polyp				
subjects affected / exposed	2 / 619 (0.32%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	2 / 619 (0.32%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 1			
Asthma				
subjects affected / exposed	3 / 619 (0.48%)			
occurrences causally related to treatment / all	3 / 5			
deaths causally related to treatment / all	0 / 0			
Bronchospasm				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	2 / 619 (0.32%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Diaphragmatic disorder				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	3 / 619 (0.48%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pleurisy				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	2 / 619 (0.32%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary fibrosis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary hypertension				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Psychiatric disorders				
Acute psychosis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alcohol abuse				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Conversion disorder				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression suicidal				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disorientation				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mental status changes				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Persistent depressive disorder				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device dislocation				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device loosening				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transaminases increased				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Injury, poisoning and procedural complications			
Acetabulum fracture			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Comminuted fracture			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dislocation of vertebra			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fractured sacrum			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hand fracture			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hip fracture				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Joint dislocation				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Joint injury				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ligament rupture				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ligament sprain				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Limb injury				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lumbar vertebral fracture				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple injuries				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscle injury				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscle rupture				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Patella fracture				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic fracture				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Periprosthetic fracture				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax traumatic				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural fistula				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postoperative thrombosis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin injury				
subjects affected / exposed	0 / 619 (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 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Splenic rupture				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haemorrhage				

subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Synovial rupture				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ulna fracture				
subjects affected / exposed	0 / 619 (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 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular pseudoaneurysm				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound necrosis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				

subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute left ventricular failure			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	3 / 619 (0.48%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	6 / 619 (0.97%)		
occurrences causally related to treatment / all	2 / 7		
deaths causally related to treatment / all	0 / 0		
Atrial flutter			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Bradycardia			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac tamponade			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiomyopathy			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery insufficiency			

subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive heart disease				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mitral valve incompetence				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial ischaemia				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus node dysfunction				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus tachycardia				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Amnesia				

subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Carpal tunnel syndrome				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebellar infarction				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral artery embolism				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haematoma				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	3 / 619 (0.48%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Cubital tunnel syndrome				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness postural				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Facial paresis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive encephalopathy				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
IIIrd nerve paralysis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intracranial mass				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				

subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbar radiculopathy				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mononeuropathy multiplex				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myxoedema coma				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spondylitic myelopathy				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ulnar tunnel syndrome				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				

subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone marrow failure				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Disseminated intravascular coagulation				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic anaemia				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypochromic anaemia				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Iron deficiency anaemia				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphadenitis				
subjects affected / exposed	2 / 619 (0.32%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Neutropenia				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Inner ear disorder				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meniere's disease				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Blindness				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cataract				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Corneal perforation				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Keratitis				

subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal detachment				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Scleritis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ulcerative keratitis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal hernia				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal fissure				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis ischaemic				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticular perforation				

subjects affected / exposed	3 / 619 (0.48%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Diverticulum intestinal haemorrhagic				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer haemorrhage				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric volvulus				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal angiodysplasia haemorrhagic				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal reflux disease				

subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhoidal haemorrhage			
subjects affected / exposed	2 / 619 (0.32%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids thrombosed			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal ischaemia			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Mesenteric vein thrombosis			

subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatic cyst				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Biliary colic				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sphincter of Oddi dysfunction				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				

Cutaneous vasculitis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Decubitus ulcer				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dermatitis bullous				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic foot				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypersensitivity vasculitis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Skin necrosis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin ulcer				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subcutaneous emphysema				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				

Acute kidney injury				
subjects affected / exposed	5 / 619 (0.81%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 0			
Calculus urethral				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Calculus urinary				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cystitis interstitial				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Glomerulonephritis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hydronephrosis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
IgA nephropathy				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Incontinence				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lupus nephritis				

subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	2 / 619 (0.32%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal haematoma			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stag horn calculus			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ureterolithiasis			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 619 (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	2 / 619 (0.32%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Arthritis			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atlantoaxial instability			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bursitis			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Finger deformity			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Foot deformity			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc disorder			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lumbar spinal stenosis			

subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mixed connective tissue disease				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal pain				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	9 / 619 (1.45%)			
occurrences causally related to treatment / all	0 / 9			
deaths causally related to treatment / all	0 / 0			
Osteochondrosis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pseudarthrosis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rheumatoid arthritis				
subjects affected / exposed	5 / 619 (0.81%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Rotator cuff syndrome				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal osteoarthritis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spondylolisthesis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Synovitis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abscess				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess intestinal				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abscess limb				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthritis bacterial				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial pyelonephritis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Beta haemolytic streptococcal infection				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Breast abscess				

subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Breast cellulitis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bursitis infective staphylococcal				
subjects affected / exposed	2 / 619 (0.32%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	10 / 619 (1.62%)			
occurrences causally related to treatment / all	7 / 10			
deaths causally related to treatment / all	0 / 0			
Colonic abscess				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dermatitis infected				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	2 / 619 (0.32%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	5 / 619 (0.81%)			
occurrences causally related to treatment / all	4 / 5			
deaths causally related to treatment / all	0 / 0			
Extradural abscess				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gangrene				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis salmonella				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematoma infection				

subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis E			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes zoster disseminated			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infected seroma			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infected skin ulcer			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infectious pleural effusion			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infective tenosynovitis			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral discitis			

subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Klebsiella infection				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Localised infection				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mastitis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Medical device site joint infection				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meningitis pneumococcal				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Necrotising fasciitis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ophthalmic herpes zoster				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	3 / 619 (0.48%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pilonidal cyst				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumococcal sepsis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	19 / 619 (3.07%)			
occurrences causally related to treatment / all	11 / 22			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia pneumococcal				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia viral				

subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural infection			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative wound infection			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psoas abscess			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyomyositis			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			

subjects affected / exposed	5 / 619 (0.81%)			
occurrences causally related to treatment / all	3 / 5			
deaths causally related to treatment / all	0 / 1			
Septic shock				
subjects affected / exposed	2 / 619 (0.32%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Soft tissue infection				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal cord infection				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Staphylococcal abscess				
subjects affected / exposed	2 / 619 (0.32%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Staphylococcal infection				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal sepsis				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal skin infection				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Streptococcal abscess				

subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Streptococcal endocarditis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tooth abscess				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tuberculosis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	2 / 619 (0.32%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vulval abscess				
subjects affected / exposed	1 / 619 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	0 / 619 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				

subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 619 (0.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperlipidaemia			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 619 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoproteinaemia			
subjects affected / exposed	1 / 619 (0.16%)		
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 to 50 mg q4w due to EE/LE or CO	Sirukumab 50 mg q4w Start	Placebo to 100 mg q2w due to EE/LE or CO
Total subjects affected by non-serious adverse events			
subjects affected / exposed	139 / 305 (45.57%)	268 / 605 (44.30%)	135 / 291 (46.39%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	27 / 305 (8.85%)	35 / 605 (5.79%)	29 / 291 (9.97%)
occurrences (all)	30	50	39

Aspartate aminotransferase increased			
subjects affected / exposed	16 / 305 (5.25%)	22 / 605 (3.64%)	18 / 291 (6.19%)
occurrences (all)	17	32	22
Vascular disorders			
Hypertension			
subjects affected / exposed	14 / 305 (4.59%)	31 / 605 (5.12%)	14 / 291 (4.81%)
occurrences (all)	16	33	15
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	5 / 305 (1.64%)	23 / 605 (3.80%)	14 / 291 (4.81%)
occurrences (all)	8	30	17
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	10 / 305 (3.28%)	16 / 605 (2.64%)	17 / 291 (5.84%)
occurrences (all)	29	85	58
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	35 / 305 (11.48%)	80 / 605 (13.22%)	30 / 291 (10.31%)
occurrences (all)	52	117	42
Infections and infestations			
Bronchitis			
subjects affected / exposed	29 / 305 (9.51%)	32 / 605 (5.29%)	20 / 291 (6.87%)
occurrences (all)	30	42	24
Upper respiratory tract infection			
subjects affected / exposed	30 / 305 (9.84%)	52 / 605 (8.60%)	35 / 291 (12.03%)
occurrences (all)	41	77	55
Urinary tract infection			
subjects affected / exposed	11 / 305 (3.61%)	24 / 605 (3.97%)	15 / 291 (5.15%)
occurrences (all)	14	29	21
Viral upper respiratory tract infection			
subjects affected / exposed	37 / 305 (12.13%)	73 / 605 (12.07%)	36 / 291 (12.37%)
occurrences (all)	56	139	58

Non-serious adverse events	Sirukumab 100 mg q2w Start		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	281 / 619 (45.40%)		

Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	 47 / 619 (7.59%) 65 35 / 619 (5.65%) 50		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	 31 / 619 (5.01%) 35		
Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all)	 33 / 619 (5.33%) 46		
General disorders and administration site conditions Injection site erythema subjects affected / exposed occurrences (all)	 26 / 619 (4.20%) 245		
Musculoskeletal and connective tissue disorders Rheumatoid arthritis subjects affected / exposed occurrences (all)	 65 / 619 (10.50%) 86		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	 41 / 619 (6.62%) 60 62 / 619 (10.02%) 97 17 / 619 (2.75%) 30 80 / 619 (12.92%) 154		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 March 2013	The amendment included the following important changes 1) Details on the study design, study design rationale, primary and secondary objectives, duration of blinded/open-label treatment, phases, dose regimen, treatment duration (related to the overall sirukumab exposure for a subject from the start of the primary study to the end of his/her LTE study participation), and description on study assessments were updated for clarity, 2) A summary of the PFS-AI and instructions on training to use the PFS-AI were added, 3) Birth control measures were revised. The rationale for cautious coadministration of sirukumab with CYP3A4 substrate drugs was added.
01 May 2014	The amendment included the following important changes 1) Efficacy assessments at Week 180 were added, 2) Statement of PK and immunogenicity analyses to be performed in subjects enrolled from the study CNTO136ARA3002 was updated to reflect the number of subjects (750) instead of the percent (50%) previously specified, 3) Tofacitinib and any other biologic therapy for RA were added as prohibited medications during the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to the study’s early termination, the full intended length of observation and amount of safety and efficacy data collected for subjects receiving sirukumab treatment was not achieved.

Notes: