Clinical trial results:
A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel Group Study of CNTO 136 (sirukumab), a Human Anti-IL-6 Monoclonal Antibody, Administered Subcutaneously, in Subjects with Active Rheumatoid Arthritis Despite DMARD Therapy

Summary

EudraCT number	2010-022242-24
Trial protocol	LT BG
Global end of trial date	06 December 2016

Results information

Result version number	v1 (current)
This version publication date	22 December 2017
First version publication date	22 December 2017

Trial information

Trial identification

Sponsor protocol code	CR100866

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01604343
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International N.V.
Sponsor organisation address	Archimedesweg 29, Leiden, Netherlands, 2333
Public contact	Clinical Registry Group, Janssen-Cilag International N.V, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International N.V, 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	06 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to assess the efficacy of sirukumab as measured by the reduction of the signs and symptoms of rheumatoid arthritis (RA) and inhibition of radiographic progression in subjects with moderately to severely active RA who were refractory to disease-modifying antirheumatic drugs (DMARDs).

Protection of trial subjects:

Safety assessment was evaluated throughout the study based on reported adverse events (AEs), clinical laboratory tests, vital sign measurements, physical examinations, and concomitant medication review.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 July 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	4 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 18
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Chile: 68
Country: Number of subjects enrolled	Colombia: 41
Country: Number of subjects enrolled	Croatia: 10
Country: Number of subjects enrolled	Japan: 168
Country: Number of subjects enrolled	Korea, Republic of: 68
Country: Number of subjects enrolled	Lithuania: 98
Country: Number of subjects enrolled	Mexico: 115
Country: Number of subjects enrolled	Malaysia: 7
Country: Number of subjects enrolled	Poland: 169
Country: Number of subjects enrolled	Romania: 15
Country: Number of subjects enrolled	Russian Federation: 201
Country: Number of subjects enrolled	Serbia: 144
Country: Number of subjects enrolled	Taiwan: 24
Country: Number of subjects enrolled	Ukraine: 152
Country: Number of subjects enrolled	United States: 261

Country: Number of subjects enrolled	South Africa: 100
Worldwide total number of subjects	1670
EEA total number of subjects	310

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)	1422
From 65 to 84 years	248
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 2746 subjects were screened of which 1670 subjects were randomized and received at least one administration of study treatment.

Period 1

Period 1 title	Prior to W52 administration(through W52)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received placebo subcutaneously (SC) every 2 weeks (q2w) from Week 0 up to Week 50. Subjects who met early escape (EE) criteria at Week 18, or late escape (LE) at Week 40, or crossover (CO) at Week 52 were re-randomized to receive sirukumab 50 or 100 mg through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

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

Dosage and administration details:

Subject received placebo subcutaneously (SC) every 2 weeks (q2w) from Week 0 up to Week 50.

Arm title	Sirukumab 50 mg q4w

Arm description:

All subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 Weeks and in between placebo SC injections was received at Weeks 2, 6, and q4w through Week 104.

Arm type	Experimental
Investigational medicinal product name	Sirukumab
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 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 weeks.

Arm title	Sirukumab 100 mg q2w

Arm description:

All subjects received 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Arm type	Experimental

Investigational medicinal product name	Sirukumab
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 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104.

Number of subjects in period 1	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Started	556	557	557
Completed	247	481	470
Not completed	309	76	87
Adverse event, serious fatal	5	3	5
Consent withdrawn by subject	19	12	16
Physician decision	4	1	2
Re-randomized at Week 18/40	211	-	-
Adverse event, non-fatal	25	40	41
Other	15	10	6
Pregnancy	1	1	-
Lost to follow-up	5	4	3
Lack of efficacy	24	5	14

Period 2

Period 2 title	Week 52 to Week 104
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	Placebo to 50 mg q4w due to EE/LE/CO

Arm description:

All subjects who were assigned to placebo group and who met EE at Week 18 or LE at Week 40 or CO at Week 52 were re- randomized to receive subcutaneous (SC) sirukumab 50 mg dose regimen q4w up to Week 104.

Arm type	Experimental

Investigational medicinal product name	Sirukumab
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 who were assigned to placebo group and who met early escape (EE) at Week 18 or LE at Week 40 or CO at Week 52 were re-randomized to receive subcutaneous (SC) sirukumab 50 mg dose regimen q4w up to Week 104.

Arm title	Sirukumab 50 mg q4w

Arm description:

All subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 weeks and in between placebo SC injections was received at Weeks 2, 6, and q4w through week 104.

Arm type	Experimental
Investigational medicinal product name	Sirukumab
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 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 weeks.

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

Arm description:

All subjects who were assigned to placebo group and who met EE at Week 18 or LE at Week 40 or CO at Week 52 were re-randomized to receive subcutaneous (SC) sirukumab 100 mg dose regimen q2w up to Week 104.

Arm type	Experimental
Investigational medicinal product name	Sirukumab
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 who were assigned to placebo group and who met EE at Week 18 or LE at Week 40 or CO at Week 52 were re-randomized to receive subcutaneous (SC) sirukumab 100 mg dose regimen q2w up to Week 104.

Arm title	Sirukumab 100 mg q2w

Arm description:

All subjects received 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104.

Arm type	Experimental
Investigational medicinal product name	Sirukumab
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 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104.

Number of subjects in period 2	Placebo to 50 mg q4w due to EE/LE/CO	Sirukumab 50 mg q4w	Placebo to 100 mg q2w due to EE/LE/CO
Started	243	481	241
Treated	242	481	241
Completed	200	414	195
Not completed	43	67	46
Adverse event, serious fatal	4	2	5
Consent withdrawn by subject	7	12	8
Physician decision	1	-	-
Adverse event, non-fatal	12	26	21
Other	11	11	6
Pregnancy	-	1	2
Lost to follow-up	2	4	2
Lack of efficacy	6	11	2

Number of subjects in period 2	Sirukumab 100 mg q2w
Started	470
Treated	470
Completed	429
Not completed	41
Adverse event, serious fatal	-
Consent withdrawn by subject	4
Physician decision	2
Adverse event, non-fatal	27
Other	3
Pregnancy	1
Lost to follow-up	1
Lack of efficacy	3

Period 3

Period 3 title	Post Treatment Safety Follow Up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes

Arm title	Placebo

Arm description:

Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

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

Dosage and administration details:

Subject received placebo subcutaneously (SC) every 2 weeks (q2w) from Week 0 up to Week 50.

Arm title	Placebo to 50 mg q4w due to EE/LE/CO

Arm description:

Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Arm type	Experimental
Investigational medicinal product name	Placebo, Sirukumab
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 who were assigned to placebo group and who met early escape (EE) at Week 18 or LE at Week 40 or CO at Week 52 were re-randomized to receive subcutaneous (SC) sirukumab 50 mg dose regimen q4w up to Week 104.

Arm title	Sirukumab 50 mg q4w

Arm description:

Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Arm type	Experimental
Investigational medicinal product name	Sirukumab
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 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 weeks.

Arm title	Placebo to Sirukumab 100 mg q2w due to EE/LE/CO

Arm description:

Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Arm type	Experimental
Investigational medicinal product name	Placebo, Sirukumab
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 who were assigned to placebo group and who met EE at Week 18 or LE at Week 40 or CO at Week 52 were re-randomized to receive subcutaneous (SC) sirukumab 100 mg dose regimen q2w up to Week 104.

Arm title	Sirukumab 100 mg q2w

Arm description:

Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Arm type	Experimental
Investigational medicinal product name	Sirukumab
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 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104.

Number of subjects in period 3	Placebo	Placebo to 50 mg q4w due to EE/LE/CO	Sirukumab 50 mg q4w
Started	109	27	105
Safety Population	109	26	105
Completed	79	20	72
Not completed	30	7	33
Consent withdrawn by subject	12	4	11
Other	15	2	20
Lost to follow-up	3	1	2

Number of subjects in period 3	Placebo to Sirukumab 100 mg q2w due to EE/LE/CO	Sirukumab 100 mg q2w
Started	36	114
Safety Population	36	114
Completed	26	85
Not completed	10	29
Consent withdrawn by subject	3	14
Other	6	14
Lost to follow-up	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo subcutaneously (SC) every 2 weeks (q2w) from Week 0 up to Week 50. Subjects who met early escape (EE) criteria at Week 18, or late escape (LE) at Week 40, or crossover (CO) at Week 52 were re-randomized to receive sirukumab 50 or 100 mg through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.	
Reporting group title	Sirukumab 50 mg q4w
Reporting group description:	
All subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 Weeks and in between placebo SC injections was received at Weeks 2, 6, and q4w through Week 104.	
Reporting group title	Sirukumab 100 mg q2w
Reporting group description:	
All subjects received 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.	

Reporting group values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w
Number of subjects	556	557	557
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	466	478	478
From 65 to 84 years	90	79	79
85 years and over	0	0	0
Title for AgeContinuous			
Units: years			
arithmetic mean	52.9	52.9	53
standard deviation	± 11.85	± 11.8	± 11.31
Title for Gender			
Units: subjects			
Female	436	447	452
Male	120	110	105

Reporting group values	Total		
Number of subjects	1670		
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	1422		
From 65 to 84 years	248		
85 years and over	0		
Title for AgeContinuous			
Units: years			
arithmetic mean			

standard deviation	-		

Title for Gender Units: subjects			
Female	1335		
Male	335		

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received placebo subcutaneously (SC) every 2 weeks (q2w) from Week 0 up to Week 50. Subjects who met early escape (EE) criteria at Week 18, or late escape (LE) at Week 40, or crossover (CO) at Week 52 were re-randomized to receive sirukumab 50 or 100 mg through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Reporting group title	Sirukumab 50 mg q4w

Reporting group description:

All subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 Weeks and in between placebo SC injections was received at Weeks 2, 6, and q4w through Week 104.

Reporting group title	Sirukumab 100 mg q2w

Reporting group description:

All subjects received 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

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

Reporting group description:

All subjects who were assigned to placebo group and who met EE at Week 18 or LE at Week 40 or CO at Week 52 were re- randomized to receive subcutaneous (SC) sirukumab 50 mg dose regimen q4w up to Week 104.

Reporting group title	Sirukumab 50 mg q4w

Reporting group description:

All subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 104 weeks and in between placebo SC injections was received at Weeks 2, 6, and q4w through week 104.

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

Reporting group description:

All subjects who were assigned to placebo group and who met EE at Week 18 or LE at Week 40 or CO at Week 52 were re-randomized to receive subcutaneous (SC) sirukumab 100 mg dose regimen q2w up to Week 104.

Reporting group title	Sirukumab 100 mg q2w

Reporting group description:

All subjects received 100 mg of sirukumab SC injections at Weeks 0, 2, and q2w through Week 104.

Reporting group title	Placebo

Reporting group description:

Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

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

Reporting group description:

Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Reporting group title	Sirukumab 50 mg q4w

Reporting group description:

Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

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

Reporting group description:

Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Reporting group title	Sirukumab 100 mg q2w

Reporting group description:

Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Primary: Percentage of Subjects With an American College of Rheumatology (ACR) 20 Response at Week 16

End point title	Percentage of Subjects With an American College of Rheumatology (ACR) 20 Response at Week 16

End point description:

ACR 20 response is defined as greater than or equal to (>=) 20 percent (%) improvement in both tender joint count (TJC, 68 joints) and swollen joint count (SJC, 66 joints) and >= 20% improvement in 3 of following 5 assessments: Subject's assessment of pain using visual analog scale (VAS) (0-10 scale, 0=no pain and 10=worst possible pain), Subject's global assessment of disease activity by using VAS (scale ranges from 0 to 10, [0=very well to 10=very poor]), Physician's global assessment of disease activity using VAS (scale ranges from 0 to 10, [0=no arthritis activity to 10=extremely active arthritis]), Subject's assessment of physical function as measured by Health Assessment Questionnaire-Disability Index (HAQ-DI) (scale ranges from 0-no difficulty, to 3-inability to perform a task in that area), and Serum C-reactive protein (CRP). Full analysis set included all randomized subjects. Subjects were set to non-responders if meeting TF criteria prior to week 16 or having data missing.

End point type	Primary

End point timeframe:

Week 16

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)	26.4	54.8	53.5	

Statistical analyses

Statistical analysis title	Statistical Analysis-1
Comparison groups	Placebo v Sirukumab 50 mg q4w
Number of subjects included in analysis	1113
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	28.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.8
upper limit	33.8

Statistical analysis title	Statistical Analysis-2

Comparison groups	Placebo v Sirukumab 100 mg q2w
Number of subjects included in analysis	1113
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	27.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.6
upper limit	32.6

Primary: Change from Baseline in van der Heijde-modified Sharp (vdH-S) Score at Week 52

End point title	Change from Baseline in van der Heijde-modified Sharp (vdH-S) Score at Week 52

End point description:

vdH-S score is sum of joint erosion score and joint space narrowing (JSN) score. Joint erosion assessment is scored according to the surface area involved, from 0 to 5, with 0 indicating no erosion and 5 indicating complete collapse of bone whereas the JSN assessment including subluxation, is scored from 0 (normal) to 4 (bony ankylosis or complete luxation). Total score ranges from 0 (best) to 448 (worst) with higher scores indicating more joint damage. Efficacy FAS for radiographic assessment includes all randomized subjects who received at least 1 (partial or complete) dose of study agent and who had non-missing baseline vdH-S score. Subjects were analyzed according to randomized treatments they were assigned to, regardless of the treatment groups they actually received. This score was based on imputed value by EE Rules (set scores after EE to missing for placebo arm) and then missing data rules in all treatment groups (imputed using linear extrapolation method).

End point type	Primary

End point timeframe:

Baseline, Week 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	553	551	
Units: Units on a Scale				
arithmetic mean (standard deviation)	3.69 (± 9.245)	0.50 (± 2.961)	0.46 (± 3.258)	

Statistical analyses

Statistical analysis title	Statistical Analysis-2
Comparison groups	Placebo v Sirukumab 100 mg q2w

Number of subjects included in analysis	1101
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	van der waerden ANOVA

Statistical analysis title	Statistical Analysis-1
Comparison groups	Placebo v Sirukumab 50 mg q4w
Number of subjects included in analysis	1103
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	van der waerden ANOVA

Secondary: Change from Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score at Week 24

End point title	Change from Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score at Week 24

End point description:

The HAQ-DI score is an evaluation of the functional status for a subject. The 20- question instrument assesses the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and activities of daily living). Responses in each functional area are scored from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range: 0-3 where 0 = least difficulty and 3 = extreme difficulty. Full analysis set included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. Last Observation at or prior EE was used to replace the data after EE for subjects who met EE criteria.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Units on Scale				
arithmetic mean (standard deviation)	-0.2179 (± 0.53081)	-0.4262 (± 0.57631)	-0.4610 (± 0.56784)	

Statistical analyses

Statistical analysis title	Statistical Analysis-1
Comparison groups	Placebo v Sirukumab 50 mg q4w

Number of subjects included in analysis	1113
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least Square (LS) mean difference
Point estimate	-0.226
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	-0.17

Statistical analysis title	Statistical Analysis-2
Comparison groups	Placebo v Sirukumab 100 mg q2w
Number of subjects included in analysis	1113
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.256
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	-0.2

Secondary: Percentage of Subjects With an American College of Rheumatology (ACR) 50 Response at Week 24

End point title	Percentage of Subjects With an American College of Rheumatology (ACR) 50 Response at Week 24

End point description:

ACR 50 response is defined as >= 50% improvement in both TJC (68 joints) and SJC (66 joints) and >= 50% improvement in 3 of the following 5 assessments: Subject's assessment of pain using VAS (0-10 scale, 0=no pain and 10=worst possible pain), Subject's global assessment of disease activity by using VAS (the scale ranges from 0 to 10, [0 =very well to 10 =very poor]), Physician's global assessment of disease activity using VAS (the scale ranges from 0 to 10, [0=no arthritis activity to 10=extremely active arthritis]), Subject's assessment of physical function as measured by HAQ-DI (the scale ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area), and Serum CRP. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders if meeting EE or TF criteria prior to week 24 or having data missing.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)	12.4	30.2	33.2	

Statistical analyses

Statistical analysis title	Statistical Analysis-1
Comparison groups	Placebo v Sirukumab 50 mg q4w
Number of subjects included in analysis	1113
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	17.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.1
upper limit	22.4

Statistical analysis title	Statistical Analysis-2
Comparison groups	Placebo v Sirukumab 100 mg q2w
Number of subjects included in analysis	1113
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	20.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.1
upper limit	25.6

Secondary: Percentage of Subjects With Disease Activity Index Score 28 (DAS28) (C-reactive protein [CRP]) Remission at Week 24

End point title	Percentage of Subjects With Disease Activity Index Score 28 (DAS28) (C-reactive protein [CRP]) Remission at Week 24

End point description:

The DAS28 based on C-Reactive Protein (CRP) is a statistically derived index combining tender joints (28 joints), swollen joints (28 joints), CRP and patient's global assessment of disease activity. The set of 28 joint count is based on evaluation of the shoulder, elbow, wrist, metacarpophalangeal (MCP) MCP1 to MCP5, proximal interphalangeal (PIP) PIP1 to PIP5 joints of both the upper right extremity and the upper left extremity as well as the knee joints of lower right and lower left extremities. The values are 0=best to 10=worst. The Disease Activity Index Score 28 (DAS28) C-reactive protein (CRP) remission is defined as a DAS28 (CRP) value of less than 2.6 at a visit. Full analysis set included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to not achieving DAS28 remission if meeting EE or TF criteria prior to week 24 or having data missing.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)	5.6	26.0	25.5	

Statistical analyses

Statistical analysis title	Statistical Analysis-1
Comparison groups	Placebo v Sirukumab 50 mg q4w
Number of subjects included in analysis	1113
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	20.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.4
upper limit	24.6

Statistical analysis title	Statistical Analysis-2
Comparison groups	Placebo v Sirukumab 100 mg q2w

Number of subjects included in analysis	1113
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	19.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.8
upper limit	24

Secondary: Percentage of Subjects With Major Clinical Response (MCR) at Week 52

End point title	Percentage of Subjects With Major Clinical Response (MCR) at Week 52

End point description:

MCR was defined as subject achieving ACR 70 response for 6 continuous months (24 weeks) in study period (i.e., through Week 52). An ACR 70 response is defined as >= 70% improvement in both TJC (68 joints) and SJC (66 joints) and >= 70% improvement in 3 of following 5 assessments Subject's assessment of pain using VAS, Subject's global assessment of disease activity by using VAS, Physician's global assessment of disease activity using VAS, Subject's assessment of physical function as measured by HAQ-DI and Serum CRP. FAS was defined as all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders if meeting EE, LE or TF criteria prior to week 52 or having data missing.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)	1.8	5.4	9.0	

Statistical analyses

Statistical analysis title	Statistical Analysis-1
Comparison groups	Placebo v Sirukumab 50 mg q4w

Number of subjects included in analysis	1113
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	508

Statistical analysis title	Statistical Analysis-2
Comparison groups	Placebo v Sirukumab 100 mg q2w
Number of subjects included in analysis	1113
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	7.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.6
upper limit	9.8

Secondary: Percentage of Subjects With an American College of Rheumatology (ACR) 20 Response Through Week 52

End point title	Percentage of Subjects With an American College of Rheumatology (ACR) 20 Response Through Week 52

End point description:

ACR 20 response is defined as >=20% improvement in both TJC(68 joints) and SJC(66 joints) and >=20% improvement in 3 of the following 5 assessments: Subject’s assessment of pain using VAS 0-10 scale, 0=no pain and 10=worst possible pain), Subject’s global assessment of disease activity by using VAS(scale ranges from 0 to 10, [0=very well to 10=very poor]), Physician’s global assessment of disease activity using VAS (scale ranges from 0 to 10, [0=no arthritis activity to 10=extremely active arthritis]), Subject’s assessment of physical function as measured by HAQ-DI (scale ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area), and Serum CRP. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 18, 20, 24, 28, 32, 36, 40, 44, 48, and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)				
Week 2	7.4	18.3	15.4	
Week 4	14.2	36.3	33.8	
Week 6	20.3	45.8	46.9	
Week 8	25.9	47.2	51.3	
Week 12	27.3	53.1	53.3	
Week 18	29.3	54.4	56.9	
Week 20	29.5	53.7	52.8	
Week 24	27.0	53.7	56.0	
Week 28	31.5	53.1	57.3	
Week 32	29.5	53.3	56.7	
Week 36	28.4	54.0	58.2	
Week 40	28.8	53.3	53.3	
Week 44	27.7	49.2	54.0	
Week 48	26.8	50.1	54.8	
Week 52	26.6	49.9	54.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With an American College of Rheumatology (ACR) 50 Response

End point title	Percentage of Subjects With an American College of Rheumatology (ACR) 50 Response

End point description:

ACR 50 response is defined as >=50% improvement in both TJC(68 joints) and SJC(66 joints) and >=50% improvement in 3 of the following 5 assessments: Subject’s assessment of pain using VAS(0-10 scale, 0=no pain and 10=worst possible pain), Subject’s global assessment of disease activity by using VAS(scale ranges from 0 to 10,[0=very well to 10=very poor]), Physician’s global assessment of disease activity using VAS (scale ranges from 0 to 10, [0=no arthritis activity to 10=extremely active arthritis]), Subject’s assessment of physical function as measured by HAQ-DI(scale ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area) and Serum CRP. FAS was defined as all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)				
Week 2	1.1	3.2	2.0	
Week 4	2.5	9.2	9.9	
Week 6	4.1	15.6	14.0	
Week 8	7.7	20.3	18.9	
Week 12	10.1	24.6	28.0	
Week 16	10.8	30.0	26.2	
Week 18	11.7	31.2	31.2	
Week 20	13.5	32.7	33.4	
Week 28	15.1	31.6	33.0	
Week 32	14.0	33.6	35.0	
Week 36	12.2	33.4	34.5	
Week 40	13.3	31.1	33.4	
Week 44	14.2	31.4	33.9	
Week 48	14.4	32.9	34.8	
Week 52	13.8	30.3	35.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With an American College of Rheumatology (ACR) 70 Response Through Week 52

End point title	Percentage of Subjects With an American College of Rheumatology (ACR) 70 Response Through Week 52

End point description:

ACR 70 response is defined as >=70% improvement in both TJC(68 joints) and SJC(66 joints) and >=70% improvement in 3 of the following 5 assessments: Subject's assessment of pain using VAS(0-10 scale, 0=no pain and 10=worst possible pain), Subject's global assessment of disease activity by using VAS (scale ranges from 0 to 10,[0=very well to 10=very poor]), Physician's global assessment of disease activity using VAS (scale ranges from 0 to 10,[0=no arthritis activity to 10=extremely active arthritis]), Subject's assessment of physical function as measured by HAQ-DI(scale ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area) and Serum CRP. FAS was defined as all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)				
Week 2	0.4	0.7	0.4	
Week 4	0.5	2.0	3.1	
Week 6	1.6	4.7	4.5	
Week 8	1.6	7.2	7.2	
Week 12	3.1	10.4	10.6	
Week 16	4.0	13.5	13.5	
Week 18	4.3	12.6	14.7	
Week 20	4.0	13.1	16.0	
Week 24	3.4	14.9	16.3	
Week 28	5.2	16.0	16.5	
Week 32	4.7	17.4	17.2	
Week 36	4.7	15.8	16.2	
Week 40	5.0	16.9	17.6	
Week 44	5.2	16.3	17.1	
Week 48	6.8	18.5	17.8	
Week 52	5.4	16.5	18.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With an American College of Rheumatology (ACR) 90 Response Through Week 52

End point title	Percentage of Subjects With an American College of Rheumatology (ACR) 90 Response Through Week 52

End point description:

ACR 90 response is defined as >=90% improvement in both TJC(68 joints) and SJC(66 joints) and >=90% improvement in 3 of the following 5 assessments: Subject’s assessment of pain using VAS(0-10 scale, 0=no pain and 10=worst possible pain), Subject’s global assessment of disease activity by using VAS(scale ranges from 0 to 10, [0=very well to 10=very poor]), Physician’s global assessment of disease activity using VAS(scale ranges from 0 to 10,[0=no arthritis activity to 10=extremely active arthritis]), Subject’s assessment of physical function as measured by HAQ-DI (scale ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area) and Serum CRP. FAS was defined as all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)				
Week 2	0	0	0	
Week 4	0	0.2	0.2	
Week 6	0.2	0.2	0.2	
Week 8	0.2	1.1	0.5	
Week 12	0.5	2.2	1.8	
Week 16	0.9	2.5	2.9	
Week 18	1.1	2.5	2.5	
Week 20	0.5	3.6	4.1	
Week 24	0.5	3.4	5.2	
Week 28	0.4	4.5	4.7	
Week 32	1.1	4.1	5.7	
Week 36	0.9	4.8	5.4	
Week 40	0.7	5.4	6.1	
Week 44	0.5	5.0	6.6	
Week 48	0.7	4.7	6.3	
Week 52	1.3	4.5	5.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Disease Activity Index Score 28 (DAS28) C-reactive Protein (CRP) Response Through Week 52

End point title	Percentage of Subjects With Disease Activity Index Score 28 (DAS28) C-reactive Protein (CRP) Response Through Week 52

End point description:

DAS28 based on CRP is a statistically derived index combining tender joints (28 joints), swollen joints (28 joints), CRP and patient's global assessment of disease activity. The values are 0=best to 10=worst. Good responders: improvement from baseline greater than (>) 1.2 with DAS28 less than or equal to (<=) 3.2; moderate responders: improvement from baseline >1.2 with DAS28 >3.2 to <=5.1 or improvement from baseline >0.6 to <=1.2 with DAS28 <=5.1; non-responders: improvement from baseline <=0.6 or improvement from baseline >0.6 and <=1.2 with DAS28 >5.1. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to non-responders after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)				
Week 2	18.5	72.0	72.4	
Week 4	28.1	80.1	78.3	
Week 6	36.7	82.4	80.3	
Week 8	38.5	81.7	81.3	
Week 12	43.7	83.3	81.3	
Week 16	42.6	80.4	79.5	
Week 18	41.5	79.7	79.4	
Week 20	41.5	73.8	72.5	
Week 24	37.9	71.5	72.2	
Week 28	41.2	69.7	72.2	
Week 32	41.4	68.2	70.6	
Week 36	39.7	67.7	69.8	
Week 40	39.2	66.8	67.9	
Week 44	37.6	63.2	64.6	
Week 48	36.7	61.9	64.6	
Week 52	35.6	62.5	64.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Disease Activity Index Score 28 (DAS28) C-reactive Protein (CRP) Through Week 52

End point title	Change From Baseline in Disease Activity Index Score 28 (DAS28) C-reactive Protein (CRP) Through Week 52

End point description:

DAS28 based on C-Reactive Protein (CRP) is a statistically derived index combining tender joints (28 joints), swollen joints (28 joints), CRP and patient's global assessment of disease activity. The values are 0=best to 10=worst. A negative change from baseline in DAS28 (CRP) (that is, a decrease from baseline) indicates improvement from baseline. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Change at Week 2	-0.319 (± 0.7677)	-1.316 (± 0.7776)	-1.284 (± 0.7605)	
Change at Week 4	-0.515 (± 0.9287)	-1.638 (± 0.9759)	-1.627 (± 0.9529)	
Change at Week 6	-0.707 (± 1.0599)	-1.886 (± 1.0622)	-1.888 (± 1.0340)	
Change at Week 8	-0.754 (± 1.1013)	-2.016 (± 1.1183)	-2.031 (± 1.1138)	
Change at Week 12	-0.881 (± 1.1727)	-2.187 (± 1.1995)	-2.185 (± 1.1950)	
Change at Week 16	-0.908 (± 1.2834)	-2.264 (± 1.2443)	-2.282 (± 1.2283)	
Change at Week 18	-0.895 (± 1.2986)	-2.286 (± 1.2690)	-2.335 (± 1.2314)	
Change at Week 20	-0.920 (± 1.2973)	-2.367 (± 1.3368)	-2.380 (± 1.3158)	
Change at Week 24	-0.912 (± 1.3180)	-2.356 (± 1.3599)	-2.402 (± 1.3048)	
Change at Week 28	-0.979 (± 1.3752)	-2.417 (± 1.4068)	-2.440 (± 1.3245)	
Change at Week 32	-1.010 (± 1.3904)	-2.451 (± 1.4141)	-2.479 (± 1.3304)	
Change at Week 36	-1.019 (± 1.4020)	-2.461 (± 1.3951)	-2.497 (± 1.3231)	
Change at Week 40	-0.985 (± 1.4054)	-2.462 (± 1.4180)	-2.459 (± 1.3901)	
Change at Week 44	-0.994 (± 1.4117)	-2.442 (± 1.4364)	-2.477 (± 1.4381)	
Change at Week 48	-1.026 (± 1.4755)	-2.482 (± 1.4630)	-2.488 (± 1.3783)	
Change at Week 52	-0.992 (± 1.4431)	-2.491 (± 1.4305)	-2.476 (± 1.4109)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Disease Activity Index Score 28 (DAS28) (C-reactive protein [CRP]) Remission Through Week 52

End point title	Percentage of Subjects with Disease Activity Index Score 28 (DAS28) (C-reactive protein [CRP]) Remission Through Week 52

End point description:

DAS28 based on C-Reactive Protein (CRP) is a statistically derived index combining tender joints (28 joints), swollen joints (28 joints), CRP and patient's global assessment of disease activity. The set of 28 joint count is based on evaluation of the shoulder, elbow, wrist, metacarpophalangeal (MCP) MCP1 to MCP5, proximal interphalangeal (PIP) PIP1 to PIP5 joints of both the upper right extremity and the upper left extremity as well as the knee joints of lower right and lower left extremities. The values are 0=best to 10=worst. DAS28 (CRP) remission is defined as a DAS28 (CRP) value of less than 2.6 at a visit. Full analysis set included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to not achieving DAS28 remission after meeting EE, LE or TF criteria (whichever is earliest) or

if having data missing.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)				
Week 2	0.5	2.5	2.7	
Week 4	1.6	7.9	9.3	
Week 6	3.1	10.2	12.6	
Week 8	3.2	13.6	17.8	
Week 12	4.3	18.3	19.6	
Week 16	5.8	21.2	21.9	
Week 18	6.1	22.8	23.7	
Week 20	5.8	26.4	25.5	
Week 24	5.6	26.0	25.5	
Week 28	7.7	27.5	27.1	
Week 32	7.7	29.6	28.4	
Week 36	8.5	29.1	28.0	
Week 40	7.2	27.8	27.3	
Week 44	8.5	28.2	27.5	
Week 48	9.0	29.6	30.2	
Week 52	8.8	30.0	29.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Simplified Disease Activity Index (SDAI) Score Through Week 52

End point title	Change From Baseline in Simplified Disease Activity Index (SDAI) Score Through Week 52

End point description:

SDAI score is a derived score combining tender joints (28 joints), swollen joints (28 joints), patient's global assessment of disease activity, physician's global assessments of disease activity, and CRP. The total score range is from 0 to 86 with a lower score indicating less disease activity. A negative change from baseline indicates an improvement and a positive change from baseline indicates a worsening. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Change at Week 2	-4.5129 (± 9.68032)	-9.1095 (± 9.64598)	-7.9649 (± 9.58765)	
Change at Week 4	-7.3134 (± 11.87959)	-13.3976 (± 12.00410)	-12.2156 (± 11.65262)	
Change at Week 6	-9.5833 (± 13.15531)	-16.1013 (± 12.80166)	-15.4404 (± 12.18642)	
Change at Week 8	-10.0752 (± 13.54599)	-17.6624 (± 12.98109)	-17.1302 (± 12.92830)	
Change at Week 12	-11.5975 (± 14.53181)	-19.6639 (± 13.67016)	-19.0635 (± 13.63444)	
Change at Week 16	-11.3507 (± 15.72864)	-20.3221 (± 14.14177)	-20.0652 (± 13.85171)	
Change at Week 18	-10.6805 (± 16.31549)	-20.1215 (± 14.75683)	-20.4858 (± 13.72370)	
Change at Week 20	-11.0425 (± 16.42770)	-20.8300 (± 15.31245)	-20.8508 (± 14.44400)	
Change at Week 24	-11.1443 (± 16.37909)	-20.7459 (± 15.48312)	-21.0858 (± 14.57962)	
Change at Week 28	-11.7828 (± 17.04652)	-21.3535 (± 15.98762)	-21.5524 (± 14.69362)	
Change at Week 32	-12.0835 (± 17.11297)	-21.8176 (± 16.15549)	-21.8530 (± 14.58393)	
Change at Week 36	-12.2107 (± 17.24703)	-21.9077 (± 15.95251)	-22.1040 (± 14.54871)	
Change at Week 40	-11.9185 (± 17.32206)	-21.7862 (± 16.12260)	-21.6692 (± 15.33635)	
Change at Week 44	-11.8730 (± 17.41934)	-21.4843 (± 16.33985)	-21.5514 (± 15.78476)	
Change at Week 48	-11.9055 (± 17.91398)	-21.7238 (± 16.45520)	-21.7991 (± 15.34514)	
Change at Week 52	-11.7647 (± 17.61074)	-21.9130 (± 16.32611)	-21.7344 (± 15.64620)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Disease Activity Index (CDAI) Score Through Week 52

End point title	Change From Baseline in Clinical Disease Activity Index (CDAI) Score Through Week 52

End point description:

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. 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. FAS included all randomized subjects. Subjects were analyzed according

to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Change at Week 2	-4.38 (± 9.210)	-6.82 (± 9.350)	-5.65 (± 9.014)	
Change at Week 4	-7.09 (± 11.241)	-11.13 (± 11.699)	-9.88 (± 11.166)	
Change at Week 6	-9.24 (± 12.407)	-13.79 (± 12.416)	-13.10 (± 11.599)	
Change at Week 8	-9.72 (± 12.714)	-15.37 (± 12.593)	-14.79 (± 12.438)	
Change at Week 12	-11.19 (± 13.625)	-17.36 (± 13.223)	-16.74 (± 13.098)	
Change at Week 16	-10.86 (± 14.716)	-18.04 (± 13.651)	-17.75 (± 13.261)	
Change at Week 18	-10.24 (± 15.245)	-17.82 (± 14.291)	-18.17 (± 13.204)	
Change at Week 20	-10.57 (± 15.338)	-18.53 (± 14.809)	-18.57 (± 13.910)	
Change at Week 24	-10.68 (± 15.302)	-18.45 (± 14.936)	-18.80 (± 14.075)	
Change at Week 28	-11.27 (± 15.926)	-19.06 (± 15.395)	-19.27 (± 14.168)	
Change at Week 32	-11.55 (± 15.950)	-19.57 (± 15.549)	-19.56 (± 14.095)	
Change at Week 36	-11.70 (± 16.099)	-19.66 (± 15.455)	-19.80 (± 14.084)	
Change at Week 40	-11.46 (± 16.236)	-19.54 (± 15.640)	-19.3 (± 14.833)	
Change at Week 44	-11.41 (± 16.126)	-19.24 (± 15.888)	-19.26 (± 15.264)	
Change at Week 48	-11.47 (± 16.594)	-19.47 (± 15.951)	-19.50 (± 14.871)	
Change at Week 52	-11.38 (± 16.348)	-19.67 (± 15.834)	-19.44 (± 15.115)	

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 Through Week 52

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 Through Week 52

End point description:

SDAI-based ACR/EULAR remission in subject at visit if SDAI score of <= 3.3. SDAI score is derived by combining 5 disease assessments: tender joint (28 joints), swollen joint (28 joints) counts, PGA of disease activity by using VAS (scale ranges from 0 to 10 [0 = very well to 10 = very poor]), PhGA of disease activity using VAS (scale ranges from 0 to 10 [0=no arthritis to 10=extremely active arthritis]) and CRP. Change from baseline measures change in disease activity, negative change shows improvement and positive change shows worsening. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to not achieving SDAI-based remission after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)				
Week 2	0.2	0	0	
Week 4	0.4	0.2	1.3	
Week 6	0.4	1.6	2.3	
Week 8	0.7	2.9	2.9	
Week 12	1.6	4.8	5.2	
Week 16	2.2	5.4	6.6	
Week 18	1.6	6.3	6.8	
Week 20	1.6	7.5	7.7	
Week 24	2.3	8.1	9.5	
Week 28	2.3	9.0	8.4	
Week 32	2.9	9.7	10.2	
Week 36	1.8	10.1	10.6	
Week 40	2.5	11.5	11.5	
Week 44	2.5	9.7	11.7	
Week 48	3.8	11.3	10.4	
Week 52	3.2	11.5	10.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Boolean-based American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) Remission Through Week 52

End point title	Percentage of Subjects With Boolean-based American College

	of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) Remission Through Week 52

End point description:

A subject was considered as having achieved the Boolean-based American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) remission at a visit if all of the following 4 criteria were met at that visit: Tender joint count (68 joints) less than or equal to (<=) 1; Swollen joint count (66 joints) <=1; CRP <=1 milligram per deciliter (mg/dL); Patient's Global Assessment of Disease Activity <=1 on a 0 (very well) to 10 (very poor) VAS. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. Subjects were set to not achieving Boolean-based remission after meeting EE, LE or TF criteria (whichever is earliest) or if having data missing.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)				
Week 2	0.2	0.4	0	
Week 4	0.2	0.4	0.7	
Week 6	0	0.9	0.9	
Week 8	0.2	1.3	1.8	
Week 12	1.3	2.9	3.1	
Week 16	1.6	3.2	4.7	
Week 18	0.7	3.6	4.7	
Week 20	1.3	4.3	5.6	
Week 24	0.9	4.3	7.0	
Week 28	1.1	5.2	6.1	
Week 32	2.3	5.0	6.5	
Week 36	1.3	7.0	7.9	
Week 40	0.9	5.9	7.9	
Week 44	1.4	5.7	7.9	
Week 48	1.8	7.0	7.0	
Week 52	2.2	7.0	5.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score Through Week 52

End point title	Change from Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score Through Week 52

End point description:

The HAQ-DI score is an evaluation of the functional status for a subject. The 20- question instrument assesses the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and activities of daily living). Responses in each

functional area are scored from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range: 0-3 where 0 = least difficulty and 3 = extreme difficulty. Full analysis set included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. LOCF method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 6, 8, 12, 16, 18, 20, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Change at Week 2	-0.075 (± 0.3809)	-0.139 (± 0.3744)	-0.128 (± 0.3939)	
Change at Week 4	-0.130 (± 0.4444)	-0.244 (± 0.4498)	-0.254 (± 0.4184)	
Change at Week 6	-0.170 (± 0.4657)	-0.318 (± 0.4989)	-0.360 (± 0.4910)	
Change at Week 8	-0.172 (± 0.4824)	-0.362 (± 0.5163)	-0.388 (± 0.5163)	
Change at Week 12	-0.191 (± 0.5055)	-0.387 (± 0.5512)	-0.399 (± 0.5364)	
Change at Week 16	-0.201 (± 0.5439)	-0.409 (± 0.5736)	-0.433 (± 0.5489)	
Change at Week 18	-0.217 (± 0.5266)	-0.431 (± 0.5744)	-0.464 (± 0.5496)	
Change at Week 20	-0.209 (± 0.5275)	-0.429 (± 0.6074)	-0.474 (± 0.5797)	
Change at Week 28	-0.232 (± 0.5515)	-0.438 (± 0.5837)	-0.471 (± 0.5763)	
Change at Week 32	-0.225 (± 0.5462)	-0.441 (± 0.6017)	-0.483 (± 0.5886)	
Change at Week 36	-0.226 (± 0.5585)	-0.444 (± 0.5961)	-0.461 (± 0.5810)	
Change at Week 40	-0.230 (± 0.5586)	-0.447 (± 0.5900)	-0.431 (± 0.5921)	
Change at Week 44	-0.228 (± 0.5601)	-0.442 (± 0.6182)	-0.456 (± 0.5956)	
Change at Week 48	-0.227 (± 0.5727)	-0.447 (± 0.6207)	-0.481 (± 0.6043)	
Change at Week 52	-0.225 (± 0.5693)	-0.453 (± 0.6127)	-0.470 (± 0.5959)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve (AUC) of Change from Baseline in HAQ-DI Score

From Week 0 Through Week 24 and From Week 0 Through Week 52

End point title	Area Under the Curve (AUC) of Change from Baseline in HAQ-DI Score From Week 0 Through Week 24 and From Week 0 Through Week 52

End point description:

AUC of change from baseline in HAQ-DI score is AUC of change from baseline in HAQ-DI score versus the time. AUC was calculated based on measurement at scheduled visits using trapezoidal rule. Functional status was determined as cumulative measure of HAQ-DI over 1 year by using AUC of change from baseline in HAQ-DI score through week 52. Decreases in AUC of change from baseline in HAQ-DI indicate a greater average improvement in physical function over time. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. LOCF method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

End point type	Secondary

End point timeframe:

Week 0 Through Week 24 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Units on a Scale*Day				
arithmetic mean (standard deviation)				
Week 0 Through Week 24	-28.85 (± 69.783)	-57.99 (± 76.384)	-61.71 (± 75.189)	
Week 0 Through Week 52	-73.55 (± 170.636)	-145.30 (± 184.630)	-153.03 (± 180.633)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Health Assessment Questionnaire-Disability Index (HAQ-DI) Response Through Week 52

End point title	Percentage of Subjects With Health Assessment Questionnaire-Disability Index (HAQ-DI) Response Through Week 52

End point description:

HAQ-DI response was defined as change of less than -0.22 from baseline in HAQ-DI score. HAQ-DI score is a 20-question instrument assesses the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and activities of daily living). Responses in each functional area are scored from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range 0-3 where 0 = least difficulty and 3 = extreme difficulty. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. LOCF method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)				
Week 2	34.4	40.6	37.0	
Week 4	38.1	49.2	52.2	
Week 6	42.4	56.2	58.0	
Week 8	44.1	56.2	61.0	
Week 12	44.6	60.1	60.9	
Week 16	45.5	60.9	61.9	
Week 18	45.9	62.7	65.4	
Week 20	46.2	61.4	65.4	
Week 24	46.9	63.0	65.4	
Week 28	47.8	64.8	63.4	
Week 32	46.9	62.8	63.7	
Week 36	47.3	63.9	63.7	
Week 40	47.3	63.7	61.8	
Week 44	47.3	62.1	63.2	
Week 48	47.3	61.8	64.6	
Week 52	47.1	63.4	64.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Health Assessment Questionnaire-Disability Index (HAQ-DI) Score of Less Than or Equal to 0.5

End point title	Percentage of Subjects With Health Assessment Questionnaire-Disability Index (HAQ-DI) Score of Less Than or Equal to 0.5

End point description:

HAQ-DI score is an evaluation of the functional status for a subject. The 20- question instrument assesses the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and activities of daily living). Responses in each functional area are scored from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range 0-3 where 0 = least difficulty and 3 = extreme difficulty. FAS included all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of the treatments they actually received. LOCF method was used to impute missing values. Last Observation at or prior EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

End point type	Secondary

End point timeframe:

Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)				
Week 2	7.9	12.2	11.5	
Week 4	9.9	15.6	16.3	
Week 6	9.5	18.3	21.2	
Week 8	10.6	21.7	21.0	
Week 12	12.2	22.8	23.3	
Week 16	13.3	24.6	26.8	
Week 18	13.7	24.6	25.9	
Week 20	13.1	26.0	27.5	
Week 24	13.1	25.9	27.5	
Week 28	13.8	26.2	28.7	
Week 32	13.7	26.0	28.7	
Week 36	13.7	27.5	27.5	
Week 40	13.7	27.3	26.2	
Week 44	13.1	27.8	27.6	
Week 48	13.8	28.2	30.0	
Week 52	12.4	27.5	29.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in van der Heijde-modified Sharp (vdH-S) Score at Week 24

End point title	Change from Baseline in van der Heijde-modified Sharp (vdH-S) Score at Week 24

End point description:

vdH-S score is sum of joint erosion score and joint space narrowing (JSN) score. Joint erosion assessment is scored according to the surface area involved, from 0 to 5, with 0 indicating no erosion and 5 indicating complete collapse of bone whereas the JSN assessment including subluxation, is scored from 0 (normal) to 4 (bony ankylosis or complete luxation). Total score ranges from 0 (best) to 448 (worst) with higher scores indicating more joint damage. Efficacy FAS for radiographic assessment includes all randomized subjects who received at least 1 (partial or complete) dose of study agent and who had non-missing baseline vdH-S score. Subjects were analyzed according to randomized treatments they were assigned to, regardless of the treatment groups they actually received. This score was based on imputed value by EE Rules (set scores after EE to missing for placebo arm) and then missing data rules (imputed using linear extrapolation method).

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	553	551	
Units: Units on a Scale				
arithmetic mean (standard deviation)	1.96 (± 5.390)	0.35 (± 2.149)	0.30 (± 2.165)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in van der Heijde-modified Sharp (vdH-S) Sub-score by Type of Damage (erosion or JSN) at Week 24 and 52

End point title	Change From Baseline in van der Heijde-modified Sharp (vdH-S) Sub-score by Type of Damage (erosion or JSN) at Week 24 and 52

End point description:

vdH-S score measures structural damage progression as sum of JE and JSN scores(S).JE is summary of erosion severity in 32 of hands(H) and 12 of feet(F) joints,scored as per surface area-from 0 (no erosion) to 5 (complete(CM) collapse of bone). Maximum (MAX) JES for H-160 (32*5) and MAX JES for F-120 (12*10 [5*2 sides of foot]). MAX JES is 280 whereas JSN is summary of severity of 30 of H and 12 of F joints, scored to subluxation from 0(normal) to 4(bony ankylosis or CM luxation). MAX JSNS for H-120(30*4), and MAX JSS for F-48(12*4). MAX JSNS is 168.Thus MAX JES-280 combined with MAX JSNS-168 gives worst possible vdH-SS of 448.Efficacy FAS population for radiographic assessments included here. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Imputed value based on EE Rules (set scores after EE to missing for placebo arm) and then missing data rules in all treatment groups (using linear extrapolation method).

End point type	Secondary

End point timeframe:

Baseline, Week 24 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	553	551	
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Erosion Score: Change at Week 24	1.21 (± 3.348)	0.10 (± 1.306)	0.08 (± 1.321)	
JSN Score: Change at Week 24	0.76 (± 2.540)	0.24 (± 1.404)	0.21 (± 1.537)	
Erosion Score: Change at Week 52	2.23 (± 5.903)	0.12 (± 1.809)	0.08 (± 2.005)	
JSN Score: Change at Week 52	1.46 (± 4.311)	0.38 (± 1.839)	0.38 (± 2.184)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in van der Heijde-modified Sharp (vdH-S) Sub-

score by Region Hand or Feet and Type Erosion or JSN at Week 24 and 52	
End point title	Change from Baseline in van der Heijde-modified Sharp (vdH-S) Sub-score by Region Hand or Feet and Type Erosion or JSN at Week 24 and 52

End point description:

vdH-S score measures structural damage progression as sum of JE and JSN scores(S).JE is summary of erosion severity in 32 of hands(H) and 12 of feet(F) joints,scored as per surface area-from 0 (no erosion) to 5 (complete(CM) collapse of bone). Maximum (MAX) JES for H-160 (32*5) and MAX JES for F-120 (12*10 [5*2 sides of foot]). MAX JES is 280 whereas JSN is summary of severity of 30 of H and 12 of F joints, scored to subluxation from 0(normal) to 4(bony ankylosis or CM luxation). MAX JSNS for H-120(30*4), and MAX JSS for F-48(12*4). MAX JSNS is 168.Thus MAX JES-280 combined with MAX JSNS-168 gives worst possible vdH-SS of 448.Efficacy FAS population for radiographic assessments included here. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Imputed value based on EE Rules (set scores after EE to missing for placebo arm) and then missing data rules in all treatment groups (using linear extrapolation method).

End point type	Secondary

End point timeframe:

Baseline, Week 24 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	553	551	
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Change in Hand Erosion Score at Week 24	0.74 (± 2.406)	0.07 (± 0.920)	0.03 (± 0.966)	
Change in Hand JSN Score at Week 24	0.51 (± 1.818)	0.16 (± 1.025)	0.16 (± 1.021)	
Change in Foot Erosion Score at Week 24	0.46 (± 1.459)	0.03 (± 0.682)	0.05 (± 0.754)	
Change in Foot JSN Score at Week 24	0.25 (± 1.207)	0.09 (± 0.722)	0.06 (± 1.152)	
Change in Hand Erosion Score at Week 52	1.43 (± 4.378)	0.09 (± 1.296)	0.03 (± 1.312)	
Change in Hand JSN Score at Week 52	0.98 (± 3.196)	0.25 (± 1.378)	0.28 (± 1.808)	
Change in Foot Erosion Score at Week 52	0.80 (± 2.460)	0.03 (± 0.955)	0.06 (± 1.302)	
Change in Foot JSN Score at Week 52	0.48 (± 2.013)	0.13 (± 0.929)	0.10 (± 1.171)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Change From Baseline in van der Heijde Modified Sharp Score (vdH-S Score) Greater Than Smallest Detectable Change (SDC) at Weeks 24 and 52	
End point title	Percentage of Subjects With Change From Baseline in van der Heijde Modified Sharp Score (vdH-S Score) Greater Than Smallest Detectable Change (SDC) at Weeks 24 and 52

End point description:

vdH-S score measures structural damage progression as sum of JE and JSNS.JE is summary of erosion(E) severity in 32 of hand(H) and 12 of feet(F) joints, scored as per the surface area- 0(no E) to 5

(complete(CM) collapse of bone); JSN-summary of severity of 30 of H12 of F joints, scored as per sub-luxation(L) from 0(normal) to 4(bony ankylosis or CML). SDC is smallest change in S to be assessed correctly as per limits of agreement. SDC for change from baseline in vdH-SS is determined as:SDC=1.96*SD/(root 2*root k), here SD=standard deviation of difference between 2 readers; k= number of readers. Efficacy FAS population for radiographic assessments included here. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. This score was based on imputed value by EE Rules (set scores after EE to missing for placebo arm) and then missing data rules in all treatment groups (imputed using linear extrapolation

End point type	Secondary

End point timeframe:

Weeks 24 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	553	551	
Units: Percentage of Subjects				
number (not applicable)				
Week 24	25.3	8.3	7.6	
Week 52	35.5	12.1	12.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Change of Less Than or Equal to 0 From Baseline in van der Heijde Modified Sharp (vdH-S) Score at Weeks 24 and 52

End point title	Percentage of Subjects With a Change of Less Than or Equal to 0 From Baseline in van der Heijde Modified Sharp (vdH-S) Score at Weeks 24 and 52

End point description:

vdH-S score measures structural damage progression as sum of JE and JSN scores(S).JE is summary of erosion severity in 32 of hands(H) and 12 of feet(F) joints,scored as per surface area-from 0 (no erosion) to 5 (complete(CM) collapse of bone). Maximum (MAX) JES for H-160 (32*5) and MAX JES for F-120 (12*10 [5*2 sides of foot]). MAX JES is 280 whereas JSN is summary of severity of 30 of H and 12 of F joints, scored to subluxation from 0(normal) to 4(bony ankylosis or CM luxation). MAX JSNS for H-120(30*4), and MAX JSS for F-48(12*4). MAX JSNS is 168.Thus MAX JES-280 combined with MAX JSNS-168 gives worst possible vdH-SS of 448.Efficacy FAS population for radiographic assessments included here. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Imputed value based on EE Rules (set scores after EE to missing for placebo arm) and then missing data rules in all treatment groups (using linear extrapolation method).

End point type	Secondary

End point timeframe:

Week 24 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	553	551	
Units: Percentage of Subjects				
number (not applicable)				
Week 24	48.4	65.8	68.8	
Week 52	45.5	59.0	62.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in van der Heijde Modified Sharp Score (vdH-S Score) by Reader at Weeks 24 and 52

End point title	Change From Baseline in van der Heijde Modified Sharp Score (vdH-S Score) by Reader at Weeks 24 and 52

End point description:

vdH-S score measures structural damage progression as sum of JE and JSN scores(S).JE is summary of erosion severity in 32 of hands(H) and 12 of feet(F) joints,scored as per surface area-from 0 (no erosion) to 5 (complete(CM) collapse of bone). Maximum (MAX) JES for H-160 (32*5) and MAX JES for F-120 (12*10 [5*2 sides of foot]). MAX JES is 280 whereas JSN is summary of severity of 30 of H and 12 of F joints, scored to subluxation from 0(normal) to 4(bony ankylosis or CM luxation). MAX JSNS for H-120(30*4), and MAX JSS for F-48(12*4). MAX JSNS is 168.Thus MAX JES-280 combined with MAX JSNS-168 gives worst possible vdH-SS of 448.Efficacy FAS population for radiographic assessments included here. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Imputed value based on EE Rules (set scores after EE to missing for placebo arm) then missing data rules in all treatment groups (using linear extrapolation method).

End point type	Secondary

End point timeframe:

Baseline, Weeks 24 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	550	553	551	
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Reader 1 at Week 24 (n= 550, 551, 550)	2.06 (± 5.616)	0.21 (± 2.495)	0.20 (± 2.773)	
Reader 2 at Week 24 (n= 550, 553, 551)	1.65 (± 5.053)	0.38 (± 1.969)	0.33 (± 1.830)	
Reader 1 at Week 52 (n= 447, 459, 467)	2.99 (± 7.940)	0.54 (± 3.285)	0.29 (± 3.325)	
Reader 2 at Week 52 (n= 447, 460, 467)	2.65 (± 7.331)	0.54 (± 2.660)	0.35 (± 2.184)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum C-reactive protein (CRP) Levels Through Week 52

End point title	Change From Baseline in Serum C-reactive protein (CRP) Levels Through Week 52

End point description:

Serum CRP is a marker of systemic inflammation. A negative change from baseline in CRP represents improvement. FAS included all randomized subjects. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. The last observation at or prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Milligram per Deciliter				
arithmetic mean (standard deviation)				
Baseline	2.5148 (± 3.38577)	2.4145 (± 2.62179)	2.3952 (± 2.64241)	
Change at Week 2	-0.1339 (± 2.86946)	-2.2867 (± 2.44604)	-2.3198 (± 2.64772)	
Change at Week 4	-0.2209 (± 2.94279)	-2.2707 (± 2.41525)	-2.3406 (± 2.64584)	
Change at Week 6	-0.3432 (± 2.96865)	-2.3124 (± 2.44604)	-2.3451 (± 2.64678)	
Change at Week 8	-0.3561 (± 3.05281)	-2.2919 (± 2.41368)	-2.3392 (± 2.65864)	
Change at Week 12	-0.4099 (± 3.22085)	-2.3038 (± 2.43828)	-2.3274 (± 2.67383)	
Change at Week 16	-0.4890 (± 3.17554)	-2.2841 (± 2.43707)	-2.3166 (± 2.65115)	
Change at Week 18	-0.4375 (± 3.48359)	-2.3030 (± 2.45255)	-2.3114 (± 2.65919)	
Change at Week 20	-0.4682 (± 3.21483)	-2.2973 (± 2.44855)	-2.2798 (± 2.74939)	
Change at Week 24	-0.4610 (± 3.31445)	-2.2974 (± 2.45343)	-2.2891 (± 2.73480)	
Change at Week 28	-0.5108 (± 3.34288)	-2.2937 (± 2.45419)	-2.2820 (± 2.73435)	
Change at Week 32	-0.5332 (± 3.39542)	-2.2474 (± 2.63824)	-2.2907 (± 2.73375)	
Change at Week 36	-0.5128 (± 3.36374)	-2.2515 (± 2.62647)	-2.3085 (± 2.73396)	
Change at Week 40	-0.4623 (± 3.46179)	-2.2429 (± 2.64450)	-2.3032 (± 2.73402)	
Change at Week 44	-0.4631 (± 4.00446)	-2.2398 (± 2.65898)	-2.2895 (± 2.75035)	
Change at Week 48	-0.4372 (± 4.15311)	-2.2561 (± 2.62491)	-2.2944 (± 2.75776)	
Change at Week 52	-0.3854 (± 3.96633)	-2.2399 (± 2.64267)	-2.2976 (± 2.73878)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Duration of Morning Stiffness Through Week 52

End point title	Change From Baseline in the Duration of Morning Stiffness Through Week 52

End point description:

Duration of morning stiffness was defined as the time elapsed when subject woke up in the morning and was able to resume normal activities without stiffness in minutes (If none was present = 0; If morning stiffness was continuing at the time of assessment or was unusual compared to the recent past, average of duration of stiffness over the past 3 days was reported; If stiffness persisted the entire day, 1440 minutes was recorded). Negative values for this outcome measure represent improvement, i.e. shortening of duration of morning stiffness. FAS was defined as all randomized subjects. Subjects were analyzed according to randomized treatment groups they were assigned to, regardless of treatment they actually received. Here 'N'(number of subject analyzed) signifies subject who were evaluable for this outcome measure. LOCF method was used to impute missing values. The last observation at or prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 6, 8, 12, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	552	552	555	
Units: Minutes				
arithmetic mean (standard deviation)				
Change at Week 2	-22.5 (± 184.96)	-35.2 (± 212.94)	-24.0 (± 177.41)	
Change at Week 4	-27.2 (± 202.02)	-61.6 (± 213.09)	-45.1 (± 181.13)	
Change at Week 6	-35.3 (± 190.54)	-81.0 (± 207.07)	-70.3 (± 206.41)	
Change at Week 8	-41.7 (± 171.05)	-84.1 (± 232.34)	-79.6 (± 213.42)	
Change at Week 12	-53.2 (± 179.24)	-88.1 (± 220.03)	-89.4 (± 217.48)	
Change at Week 16	-52.2 (± 173.24)	-82.2 (± 241.75)	-84.1 (± 224.72)	
Change at Week 18	-60.2 (± 191.68)	-84.6 (± 239.43)	-88.5 (± 223.95)	
Change at Week 20	-62.0 (± 193.64)	-93.5 (± 234.10)	-90.0 (± 229.08)	
Change at Week 24	-63.7 (± 195.58)	-96.7 (± 228.31)	-95.5 (± 234.19)	
Change at Week 28	-68.3 (± 195.42)	-95.2 (± 230.36)	-98.0 (± 235.03)	

Change at Week 32	-68.9 (± 196.31)	-96.5 (± 230.46)	-96.5 (± 231.25)	
Change at Week 36	-68.8 (± 196.90)	-96.5 (± 228.71)	-95.2 (± 226.37)	
Change at Week 40	-68.7 (± 68.7)	-95.7 (± 243.78)	-95.9 (± 233.28)	
Change at Week 44	-69.9 (± 197.38)	-96.6 (± 232.42)	-97.0 (± 234.63)	
Change at Week 48	-69.6 (± 195.50)	-97.8 (± 238.36)	-97.0 (± 230.66)	
Change at Week 52	-67.3 (± 196.98)	-99.1 (± 233.82)	-97.7 (± 231.53)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physical and Mental Component Summary (MCS) Scores of 36-Item Short Form Health Survey (SF-36) at Weeks 24 and 52

End point title	Change From Baseline in Physical and Mental Component Summary (MCS) Scores of 36-Item Short Form Health Survey (SF-36) at Weeks 24 and 52

End point description:

SF-36(36 questions),consists of 8 multi-item scales:Limitations(LIM) in physical (PHY) functioning due to health (HEL) problems;LIM in usual role activities due to PHY HEL problems;Bodily pain;General mental HEL(psychological distress/well-being);LIM in usual role activities due to personal/emotional problems;LIM in social functioning due to PHY/mental HEL problems;Vitality;General HEL perception.All 8 scales scored from 0- 100(higher scores(S)=better HEL) Based on scale S,summary S,physical component score (PCS)/MCS will be derived.Scoring is based on algorithm provided by developer.Summary MCS/PCS score is also scaled from 0-100(higher S indicating better HEL).FAS included all randomized subjects.Subjects analyzed according to randomized treatment groups they were assigned to,regardless of treatments they actually received.LOCF method was used to impute missing values.The last observation at/prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria

End point type	Secondary

End point timeframe:

Baseline, Week 24 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Units on a Scale				
arithmetic mean (standard deviation)				
PCS :Change at Week 24	2.290 (± 6.2790)	5.358 (± 7.3312)	5.850 (± 7.0677)	
PCS :Change at Week 52	2.423 (± 6.8069)	5.661 (± 7.7405)	6.162 (± 7.2277)	
MCS :Change at Week 24	2.892 (± 9.1766)	4.898 (± 9.6508)	4.216 (± 9.4819)	
MCS :Change at Week 52	2.690 (± 9.5698)	5.351 (± 9.6397)	4.767 (± 9.7991)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Greater Than or Equal to 4-Point Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Score at Week 8, 16, 24, 36 and 52

End point title	Percentage of Subjects With Greater Than or Equal to 4-Point Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Score at Week 8, 16, 24, 36 and 52

End point description:

Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) is a questionnaire that assesses self-reported tiredness, weakness, and difficulty conducting usual activities due to fatigue. The questionnaire consists of 13 questions that assess a subject's level of fatigue and tiredness over the last 7 days. Each question is graded on a 5-point scale (0 - 4); and accordingly, the total FACIT Fatigue scores can range from 0 to 52, with lower score reflecting more fatigue and higher scores reflecting less fatigue. FAS was defined as all randomized subjects. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. The last observation at or prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

End point type	Secondary

End point timeframe:

Week 8, 16, 24, 36 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Percentage of Subjects				
number (not applicable)				
Week 8	41.0	55.8	54.9	
Week 16	42.4	58.0	58.9	
Week 24	43.9	61.4	59.4	
Week 36	39.7	57.8	56.2	
Week 52	41.0	59.1	60.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Total Scores of Work Limitations Questionnaire (WLQ) Week 8, 16, 24, 36 and 52

End point title	Change from Baseline in Total Scores of Work Limitations

	Questionnaire (WLQ) Week 8, 16, 24, 36 and 52

End point description:

The Work Limitations Questionnaire (WLQ) was used to measure the impairment in work-related productivity, with reference to the previous two weeks. Each work-related question is scored from 0 to 4 and the total score ranges from 0-100, with lower scores signifying fewer limitations at work. FAS was defined as all randomized subjects. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Here 'N'(number of subjects analyzed) signifies subjects who were evaluable for this outcome measure. Last Observation Carried Forward (LOCF) method was used to impute missing values. The last observation at or prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

End point type	Secondary

End point timeframe:

Baseline, Week 8, 16, 24, 36 and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	227	223	223	
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Week 8	-0.812 (± 3.6230)	-1.946 (± 3.8040)	-2.202 (± 3.8437)	
Week 16	-0.840 (± 4.6414)	-2.406 (± 4.1403)	-2.600 (± 4.3066)	
Week 24	-1.019 (± 4.5328)	-2.765 (± 4.4381)	-2.884 (± 4.5873)	
Week 36	-0.940 (± 4.7982)	-2.921 (± 4.4205)	-2.952 (± 4.5640)	
Week 52	-0.732 (± 5.0288)	-3.057 (± 4.5290)	-2.936 (± 4.3940)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EuroQol Health State Visual Analogue Scale (EQ VAS)

End point title	Change From Baseline in EuroQol Health State Visual Analogue Scale (EQ VAS)

End point description:

The EuroQol Health State Visual Analogue Scale (EQ VAS) records the respondent’s self-rated health on a vertical line, VAS where the endpoints are labeled as 0= ‘Worst imaginable health state’ and 100= ‘Best imaginable health state’. The EQ VAS can be used as a quantitative measure of health outcome as judged by the individual respondents. FAS included all randomized subjects. Here 'N'(number of subjects analyzed) signifies subjects who were evaluable for this outcome measure. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. Last Observation Carried Forward (LOCF) method was used to impute missing values. The last observation at or prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

End point type	Secondary

End point timeframe:

Baseline, Week 8, 16, 24, and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	554	557	556	
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Change at Week 8	5.61 (± 24.415)	11.64 (± 26.979)	12.24 (± 26.025)	
Change at Week 16	5.83 (± 26.177)	14.09 (± 28.581)	14.36 (± 27.884)	
Change at Week 24	6.71 (± 26.520)	14.86 (± 28.747)	16.41 (± 28.830)	
Change at Week 36	8.30 (± 26.144)	16.80 (± 28.595)	17.14 (± 28.329)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EuroQol EQ-5D-3L Descriptive System

End point title	Change From Baseline in EuroQol EQ-5D-3L Descriptive System

End point description:

The EQ-5D-3L Descriptive System comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is assessed on a 3-point ordinal scale (1=no problems, 2=some problems, 3=extreme problems). The responses to the five EQ-5D dimensions were scored using a utility-weighted algorithm to derive an EQ-5D health status index score between 0 to 1, with 1.00 indicating "full health" and 0 representing dead. FAS included all randomized subjects. Subjects analyzed according to randomized treatment they were assigned to, regardless of treatments they actually received. LOCF method was used to impute missing values. The last observation at or prior to EE/LE was used to replace the data after EE/LE for subjects who met EE/LE criteria.

End point type	Secondary

End point timeframe:

Baseline, Week 8, 16, 24, and 52

End point values	Placebo	Sirukumab 50 mg q4w	Sirukumab 100 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	556	557	557	
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Change at Week 8	0.1041 (± 0.31794)	0.1734 (± 0.32473)	0.1647 (± 0.30146)	
Change at Week 16	0.1131 (± 0.33788)	0.1831 (± 0.34875)	0.1899 (± 0.31149)	
Change at Week 24	0.1263 (± 0.33539)	0.1885 (± 0.33867)	0.2057 (± 0.32081)	
Change at Week 52	0.1255 (± 0.34312)	0.1950 (± 0.33448)	0.2007 (± 0.32895)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Screening up to Week 120

Adverse event reporting additional description:

Safety population included all subjects who received at least 1 partial or complete dose of study agent, analysed in treatment received overtime, regardless randomization.One subject inadvertently received Sirukumab 100 mg instead of Sirukumab 50 mg and therefore reported in Sirukumab 100 mg arm (558) instead of Sirukumab 50 mg (556 subjects).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	W0 to W120-Placebo to Sirukumab 50 mg q4w due to EE/LE or CO

Reporting group description:

Subjects who received placebo in the placebo controlled period were rerandomized (due to EE at Week 18 or LE at Week 40 or CO at Week 52) to receive subcutaneous (SC) sirukumab 50 mg q4w dose regimen up to Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Reporting group title	Week 0 to Week 120-Placebo

Reporting group description:

Subjects received matching placebo from week 0 to week 52, every 2 weeks (q2w) until either early escape (EE) at Week 18 or late escape (LE) at Week 40 or crossover (CO) at Week 52 and were rerandomized to subcutaneous (SC) sirukumab 50 mg q4w or sirukumab 100 mg q2w dose regimens up to Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Reporting group title	W0 to W120- Placebo to Sirukumab 100 mg q2w Due to EE/LE or CO

Reporting group description:

Subjects who received placebo in the placebo controlled period were rerandomized (due to EE at Week 18 or LE at Week 40 or CO at Week 52) to receive subcutaneous (SC) sirukumab 100 mg q2w dose up to Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Reporting group title	W0 to W120-Sirukumab 100 mg q2w

Reporting group description:

Subjects received 100 mg of sirukumab SC injections at Weeks 0, 2 and q2w throught Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Reporting group title	W0 to W120- Sirukumab 50 mg q4w

Reporting group description:

Subjects received 50 mg of sirukumab SC injections at Weeks 0, 4, and q4w through Week 104. Subjects who completed study agent administration up to Week 104 and did not elect for long term extension (LTE) were followed up for safety from Week 104 up to Week 120.

Serious adverse events	W0 to W120-Placebo to Sirukumab 50 mg q4w due to EE/LE or CO	Week 0 to Week 120-Placebo	W0 to W120-Placebo to Sirukumab 100 mg q2w Due to EE/LE or CO
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 242 (12.40%)	40 / 556 (7.19%)	35 / 241 (14.52%)

number of deaths (all causes) number of deaths resulting from adverse events	5	1	6
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute Myeloid Leukaemia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenal Adenoma			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal Cell Carcinoma			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign Neoplasm of Thyroid Gland			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Bladder Cancer			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder Transitional Cell Carcinoma			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast Cancer			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon Cancer Metastatic			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric Cancer			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
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 Stromal Tumour			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma Multiforme			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Intraductal Papilloma of Breast			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive Ductal Breast Carcinoma			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leiomyoma			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Cancer Metastatic			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Meningioma			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Metastases to Bone			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to Central Nervous System			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine Carcinoma			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oropharyngeal Squamous Cell Carcinoma			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian Clear Cell Carcinoma			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Teratoma			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Cancer			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Leiomyoma			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Vascular disorders			
Aortic Aneurysm			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic Dissection			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Axillary Vein Thrombosis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Deep Vein Thrombosis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Extremity Necrosis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			

subjects affected / exposed	1 / 242 (0.41%)	1 / 556 (0.18%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Labile Hypertension			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrosis Ischaemic			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Arterial Occlusive Disease			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Peripheral Ischaemia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subclavian Vein Thrombosis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Thrombosed Varicose Vein			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Venous Thrombosis Limb			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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			
Asthenia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest Pain			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Death			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Influenza Like Illness			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Inflammation			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serositis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Sudden Cardiac Death			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug Hypersensitivity			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast Mass			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Cystocele			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Endometriosis			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian Cyst			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectocele			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Vaginal Haemorrhage			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Distress Syndrome			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Acute Respiratory Failure			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			

subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Dyspnoea			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial Lung Disease			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Lung Disorder			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural Effusion			
subjects affected / exposed	1 / 242 (0.41%)	1 / 556 (0.18%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Aspiration			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax Spontaneous			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Pulmonary Embolism			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	2 / 241 (0.83%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Mass			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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 Necrosis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Failure			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Mental Status Changes			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	2 / 241 (0.83%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood Bilirubin Increased			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	2 / 241 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest X-Ray Abnormal			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Hepatic Enzyme Increased			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver Function Test Increased			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight Decreased			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Abdominal Injury			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chemical Peritonitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Contusion			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiphyseal Fracture			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial Bones Fracture			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Femoral Neck Fracture			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur Fracture			
subjects affected / exposed	1 / 242 (0.41%)	1 / 556 (0.18%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot Fracture			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand Fracture			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip Fracture			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Humerus Fracture			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Joint Capsule Rupture			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Joint Dislocation			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney Rupture			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Laceration			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower Limb Fracture			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Vertebral Fracture			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus Injury			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple Fractures			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Rupture			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Post Procedural Complication			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative Wound Complication			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural Haemorrhage			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural Pain			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius Fracture			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Rib Fracture			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Road Traffic Accident			
subjects affected / exposed	2 / 242 (0.83%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Spinal Compression Fracture			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon Injury			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon Rupture			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna Fracture			

subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Upper Limb Fracture			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound Dehiscence			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Cardiac disorders			
Acute Left Ventricular Failure			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Angina Pectoris			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Atrial Fibrillation			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Bradycardia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Failure Congestive			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary Failure			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial Infarction			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Sinus Bradycardia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carpal Tunnel Syndrome			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Infarction			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Cerebral Ischaemia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular Accident			
subjects affected / exposed	2 / 242 (0.83%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	3 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Cervical Myelopathy			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical Radiculopathy			

subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Haemorrhagic Stroke			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 242 (0.41%)	1 / 556 (0.18%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive Encephalopathy			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Aneurysm			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic Stroke			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Lumbar Radiculopathy			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyramidal Tract Syndrome			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculopathy			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reversible Cerebral Vasoconstriction Syndrome			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient Ischaemic Attack			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trigeminal Neuralgia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulnar Nerve Palsy			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebrobasilar Insufficiency			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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			
Amaurosis Fugax			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal Detachment			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scleritis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulcerative Keratitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal Strangulated Hernia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular Perforation			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocele			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Erosive Duodenitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric Perforation			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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 Polyps			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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 Ulcer			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric Ulcer Haemorrhage			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis Erosive			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Hypomotility			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Necrosis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Gastrointestinal Perforation			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal Haemorrhage			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated Inguinal Hernia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal Obstruction			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic Fistula			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Pancreatitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal Haemorrhage			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis Acute			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder Perforation			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic Cyst			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Hepatic Steatosis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice Cholestatic			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Alcoholic Steatohepatitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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			
Angioedema			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Decubitus Ulcer			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Allergic			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Contact			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage Subcutaneous			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkeratosis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Exfoliation			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin Ulcer			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Stevens-Johnson Syndrome			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			

subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus Urinary			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Hydronephrosis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Nephrolithiasis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Ureterolithiasis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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 Obstruction			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Basedow's Disease			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Goitre			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atlantoaxial Instability			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back Pain			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Bursitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Chondromalacia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula Discharge			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot Deformity			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral Disc Disorder			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Spinal Stenosis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Musculoskeletal Chest Pain			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Osteoarthritis			
subjects affected / exposed	1 / 242 (0.41%)	1 / 556 (0.18%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid Arthritis			
subjects affected / exposed	0 / 242 (0.00%)	6 / 556 (1.08%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	6 / 6	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid Nodule			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Rotator Cuff Syndrome			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Pain			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal Abscess			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Sepsis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Abscess			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Soft Tissue			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Appendicitis Perforated			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis Bacterial			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Bacterial Food Poisoning			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial Sepsis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Cellulitis			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	2 / 241 (0.83%)
occurrences causally related to treatment / all	0 / 0	1 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis Staphylococcal			

subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Cytomegalovirus Colitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue Fever			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Related Infection			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Endophthalmitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epididymitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia Bacteraemia			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extradural Abscess			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Infection Fungal			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Herpes Zoster			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Bite			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Infectious Pleural Effusion			
subjects affected / exposed	1 / 242 (0.41%)	1 / 556 (0.18%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective Spondylitis			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral Discitis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised Infection			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Abscess			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphangitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Necrotising Fasciitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis Chronic			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal Abscess			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	2 / 242 (0.83%)	1 / 556 (0.18%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	2 / 2	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar Abscess			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pneumonia Bacterial			
subjects affected / exposed	1 / 242 (0.41%)	1 / 556 (0.18%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Necrotising			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Post Procedural Infection			

subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative Wound Infection			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Tuberculosis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis Acute			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyoderma			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyonephrosis			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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
Salpingitis			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salpingo-Oophoritis			

subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	2 / 242 (0.83%)	1 / 556 (0.18%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	2 / 2	1 / 1	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Septic Shock			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Infection			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 Infection			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous Abscess			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
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 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis E			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 242 (0.00%)	1 / 556 (0.18%)	0 / 241 (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
Diabetes Mellitus			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 242 (0.00%)	0 / 556 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 242 (0.41%)	0 / 556 (0.00%)	0 / 241 (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

Serious adverse events	W0 to W120-Sirukumab 100 mg q2w	W0 to W120-Sirukumab 50 mg q4w	
Total subjects affected by serious adverse events			
subjects affected / exposed	97 / 558 (17.38%)	111 / 556 (19.96%)	
number of deaths (all causes)	5	7	
number of deaths resulting from			

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute Myeloid Leukaemia			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Adrenal Adenoma			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal Cell Carcinoma			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign Neoplasm of Thyroid Gland			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder Cancer			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Bladder Transitional Cell Carcinoma			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast Cancer			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon Cancer Metastatic			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastric Cancer			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Stromal Tumour			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioblastoma Multiforme			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal Papilloma of Breast			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive Ductal Breast Carcinoma			
subjects affected / exposed	2 / 558 (0.36%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leiomyoma			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Cancer Metastatic			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Lung Neoplasm Malignant			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			

subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to Bone			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to Central Nervous System			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine Carcinoma			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal Squamous Cell Carcinoma			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian Clear Cell Carcinoma			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Teratoma			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine Cancer			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine Leiomyoma			

subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic Aneurysm			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic Dissection			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Axillary Vein Thrombosis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep Vein Thrombosis			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity Necrosis			
subjects affected / exposed	1 / 558 (0.18%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Hypotension			

subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Labile Hypertension			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrosis Ischaemic			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral Arterial Occlusive Disease			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral Ischaemia			
subjects affected / exposed	1 / 558 (0.18%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian Vein Thrombosis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosed Varicose Vein			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis			

subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous Thrombosis Limb			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest Pain			
subjects affected / exposed	2 / 558 (0.36%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Influenza Like Illness			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical Device Site Joint Inflammation			

subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Serositis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden Cardiac Death			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Immune system disorders			
Drug Hypersensitivity			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast Mass			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystocele			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometriosis			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ovarian Cyst			
subjects affected / exposed	1 / 558 (0.18%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectocele			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal Haemorrhage			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Distress Syndrome			
subjects affected / exposed	2 / 558 (0.36%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Acute Respiratory Failure			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 558 (0.00%)	3 / 556 (0.54%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dyspnoea			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial Lung Disease			
subjects affected / exposed	0 / 558 (0.00%)	4 / 556 (0.72%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Disorder			
subjects affected / exposed	1 / 558 (0.18%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural Effusion			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Aspiration			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax Spontaneous			

subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Embolism			
subjects affected / exposed	2 / 558 (0.36%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Mass			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Necrosis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Failure			
subjects affected / exposed	1 / 558 (0.18%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental Status Changes			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal Ideation			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

Alanine Aminotransferase Increased			
subjects affected / exposed	3 / 558 (0.54%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood Bilirubin Increased			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest X-Ray Abnormal			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Enzyme Increased			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver Function Test Increased			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight Decreased			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Abdominal Injury			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chemical Peritonitis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiphyseal Fracture			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial Bones Fracture			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral Neck Fracture			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur Fracture			
subjects affected / exposed	0 / 558 (0.00%)	2 / 556 (0.36%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot Fracture			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand Fracture			

subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip Fracture			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus Fracture			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint Capsule Rupture			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint Dislocation			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney Rupture			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament Sprain			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Limb Fracture			

subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar Vertebral Fracture			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus Injury			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple Fractures			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle Rupture			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post Procedural Complication			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative Wound Complication			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural Haemorrhage			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural Pain			

subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius Fracture			
subjects affected / exposed	5 / 558 (0.90%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	5 / 5	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib Fracture			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road Traffic Accident			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Compression Fracture			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon Injury			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon Rupture			
subjects affected / exposed	1 / 558 (0.18%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna Fracture			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Limb Fracture			

subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound Dehiscence			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute Left Ventricular Failure			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina Pectoris			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial Fibrillation			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Failure Congestive			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary Failure			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial Infarction			

subjects affected / exposed	1 / 558 (0.18%)	3 / 556 (0.54%)	
occurrences causally related to treatment / all	1 / 1	4 / 4	
deaths causally related to treatment / all	1 / 1	0 / 0	
Sinus Bradycardia			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carpal Tunnel Syndrome			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral Infarction			
subjects affected / exposed	1 / 558 (0.18%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Cerebral Ischaemia			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular Accident			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical Myelopathy			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical Radiculopathy			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic Stroke			

subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive Encephalopathy			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial Aneurysm			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic Stroke			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar Radiculopathy			
subjects affected / exposed	0 / 558 (0.00%)	2 / 556 (0.36%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyramidal Tract Syndrome			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reversible Cerebral Vasoconstriction Syndrome			

subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient Ischaemic Attack			
subjects affected / exposed	2 / 558 (0.36%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal Neuralgia			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulnar Nerve Palsy			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar Insufficiency			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 558 (0.36%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	2 / 558 (0.36%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Amaurosis Fugax			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	1 / 558 (0.18%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratitis			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal Detachment			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scleritis			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcerative Keratitis			
subjects affected / exposed	0 / 558 (0.00%)	2 / 556 (0.36%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Strangulated Hernia			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			

subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular Perforation			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocele			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erosive Duodenitis			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Perforation			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Polyps			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Ulcer			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Ulcer Haemorrhage			

subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis Erosive			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Hypomotility			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Necrosis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Perforation			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal Haemorrhage			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated Inguinal Hernia			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Obstruction			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic Fistula			

subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal Haemorrhage			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	3 / 558 (0.54%)	2 / 556 (0.36%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis Acute			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	3 / 558 (0.54%)	2 / 556 (0.36%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder Perforation			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Cyst			

subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Steatosis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice Cholestatic			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Alcoholic Steatohepatitis			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus Ulcer			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis Allergic			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis Bullous			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis Contact			

subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage Subcutaneous			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkeratosis			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Exfoliation			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Necrosis			
subjects affected / exposed	2 / 558 (0.36%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Ulcer			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stevens-Johnson Syndrome			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute Kidney Injury			

subjects affected / exposed	1 / 558 (0.18%)	2 / 556 (0.36%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus Urinary			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 558 (0.18%)	3 / 556 (0.54%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Obstruction			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Basedow's Disease			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atlantoaxial Instability			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back Pain			
subjects affected / exposed	1 / 558 (0.18%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondromalacia			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula Discharge			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot Deformity			
subjects affected / exposed	2 / 558 (0.36%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral Disc Disorder			

subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar Spinal Stenosis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	2 / 558 (0.36%)	4 / 556 (0.72%)	
occurrences causally related to treatment / all	2 / 2	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid Arthritis			
subjects affected / exposed	5 / 558 (0.90%)	5 / 556 (0.90%)	
occurrences causally related to treatment / all	5 / 5	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid Nodule			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Pain			

subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal Abscess			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Sepsis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess Limb			
subjects affected / exposed	4 / 558 (0.72%)	3 / 556 (0.54%)	
occurrences causally related to treatment / all	4 / 4	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess Soft Tissue			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			

subjects affected / exposed	2 / 558 (0.36%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis Perforated			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis Bacterial			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial Food Poisoning			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial Sepsis			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	5 / 558 (0.90%)	7 / 556 (1.26%)	
occurrences causally related to treatment / all	6 / 6	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis Staphylococcal			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus Colitis			

subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue Fever			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device Related Infection			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 558 (0.00%)	4 / 556 (0.72%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endophthalmitis			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 558 (0.18%)	2 / 556 (0.36%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia Bacteraemia			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural Abscess			

subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye Infection Fungal			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes Zoster			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected Bite			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious Pleural Effusion			
subjects affected / exposed	0 / 558 (0.00%)	2 / 556 (0.36%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective Spondylitis			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral Discitis			

subjects affected / exposed	1 / 558 (0.18%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised Infection			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Abscess			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangitis			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising Fasciitis			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Osteomyelitis			
subjects affected / exposed	2 / 558 (0.36%)	2 / 556 (0.36%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis Chronic			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal Abscess			

subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 558 (0.00%)	3 / 556 (0.54%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Peritonsillar Abscess			
subjects affected / exposed	1 / 558 (0.18%)	2 / 556 (0.36%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	10 / 558 (1.79%)	11 / 556 (1.98%)	
occurrences causally related to treatment / all	12 / 12	11 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Bacterial			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Necrotising			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post Procedural Infection			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative Wound Infection			

subjects affected / exposed	1 / 558 (0.18%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Tuberculosis			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis Acute			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyonephrosis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salpingitis			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salpingo-Oophoritis			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	5 / 558 (0.90%)	3 / 556 (0.54%)	
occurrences causally related to treatment / all	5 / 5	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Septic Shock			
subjects affected / exposed	1 / 558 (0.18%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Skin Infection			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft Tissue Infection			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous Abscess			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			
subjects affected / exposed	3 / 558 (0.54%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	4 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Varicella			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound Infection			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis E			

subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes Mellitus			
subjects affected / exposed	0 / 558 (0.00%)	1 / 556 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 558 (0.18%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 558 (0.00%)	0 / 556 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	W0 to W120-Placebo to Sirukumab 50 mg q4w due to EE/LE or CO	Week 0 to Week 120-Placebo	W0 to W120-Placebo to Sirukumab 100 mg q2w Due to EE/LE or CO
Total subjects affected by non-serious adverse events			
subjects affected / exposed	113 / 242 (46.69%)	213 / 556 (38.31%)	128 / 241 (53.11%)
Investigations			

Alanine Aminotransferase Increased			
subjects affected / exposed	34 / 242 (14.05%)	23 / 556 (4.14%)	41 / 241 (17.01%)
occurrences (all)	45	28	57
Aspartate Aminotransferase Increased			
subjects affected / exposed	20 / 242 (8.26%)	17 / 556 (3.06%)	23 / 241 (9.54%)
occurrences (all)	26	18	30
Vascular disorders			
Hypertension			
subjects affected / exposed	14 / 242 (5.79%)	21 / 556 (3.78%)	11 / 241 (4.56%)
occurrences (all)	15	23	11
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 242 (3.31%)	22 / 556 (3.96%)	9 / 241 (3.73%)
occurrences (all)	9	30	11
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	12 / 242 (4.96%)	7 / 556 (1.26%)	8 / 241 (3.32%)
occurrences (all)	13	9	11
Neutropenia			
subjects affected / exposed	9 / 242 (3.72%)	5 / 556 (0.90%)	8 / 241 (3.32%)
occurrences (all)	11	5	12
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	11 / 242 (4.55%)	6 / 556 (1.08%)	31 / 241 (12.86%)
occurrences (all)	27	8	126
Injection Site Pruritus			
subjects affected / exposed	3 / 242 (1.24%)	1 / 556 (0.18%)	14 / 241 (5.81%)
occurrences (all)	5	1	33
Injection Site Swelling			
subjects affected / exposed	3 / 242 (1.24%)	0 / 556 (0.00%)	13 / 241 (5.39%)
occurrences (all)	5	0	38
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 242 (0.83%)	21 / 556 (3.78%)	9 / 241 (3.73%)
occurrences (all)	2	26	9
Musculoskeletal and connective tissue disorders			

Rheumatoid Arthritis			
subjects affected / exposed	9 / 242 (3.72%)	36 / 556 (6.47%)	10 / 241 (4.15%)
occurrences (all)	11	39	12
Infections and infestations			
Bronchitis			
subjects affected / exposed	17 / 242 (7.02%)	27 / 556 (4.86%)	13 / 241 (5.39%)
occurrences (all)	22	29	14
Nasopharyngitis			
subjects affected / exposed	16 / 242 (6.61%)	53 / 556 (9.53%)	19 / 241 (7.88%)
occurrences (all)	26	67	24
Pharyngitis			
subjects affected / exposed	5 / 242 (2.07%)	13 / 556 (2.34%)	8 / 241 (3.32%)
occurrences (all)	9	16	14
Upper Respiratory Tract Infection			
subjects affected / exposed	28 / 242 (11.57%)	63 / 556 (11.33%)	20 / 241 (8.30%)
occurrences (all)	37	76	31
Urinary Tract Infection			
subjects affected / exposed	8 / 242 (3.31%)	13 / 556 (2.34%)	13 / 241 (5.39%)
occurrences (all)	10	15	15

Non-serious adverse events	W0 to W120-Sirukumab 100 mg q2w	W0 to W120-Sirukumab 50 mg q4w	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	353 / 558 (63.26%)	355 / 556 (63.85%)	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	124 / 558 (22.22%)	108 / 556 (19.42%)	
occurrences (all)	192	149	
Aspartate Aminotransferase Increased			
subjects affected / exposed	84 / 558 (15.05%)	63 / 556 (11.33%)	
occurrences (all)	132	90	
Vascular disorders			
Hypertension			
subjects affected / exposed	45 / 558 (8.06%)	32 / 556 (5.76%)	
occurrences (all)	55	39	
Nervous system disorders			

Headache			
subjects affected / exposed	28 / 558 (5.02%)	38 / 556 (6.83%)	
occurrences (all)	46	47	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	39 / 558 (6.99%)	37 / 556 (6.65%)	
occurrences (all)	67	62	
Neutropenia			
subjects affected / exposed	34 / 558 (6.09%)	40 / 556 (7.19%)	
occurrences (all)	61	86	
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	70 / 558 (12.54%)	50 / 556 (8.99%)	
occurrences (all)	413	169	
Injection Site Pruritus			
subjects affected / exposed	34 / 558 (6.09%)	12 / 556 (2.16%)	
occurrences (all)	135	40	
Injection Site Swelling			
subjects affected / exposed	27 / 558 (4.84%)	15 / 556 (2.70%)	
occurrences (all)	66	26	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	23 / 558 (4.12%)	28 / 556 (5.04%)	
occurrences (all)	28	31	
Musculoskeletal and connective tissue disorders			
Rheumatoid Arthritis			
subjects affected / exposed	29 / 558 (5.20%)	46 / 556 (8.27%)	
occurrences (all)	37	59	
Infections and infestations			
Bronchitis			
subjects affected / exposed	36 / 558 (6.45%)	48 / 556 (8.63%)	
occurrences (all)	46	62	
Nasopharyngitis			
subjects affected / exposed	67 / 558 (12.01%)	70 / 556 (12.59%)	
occurrences (all)	99	123	
Pharyngitis			

subjects affected / exposed	24 / 558 (4.30%)	30 / 556 (5.40%)	
occurrences (all)	28	38	
Upper Respiratory Tract Infection			
subjects affected / exposed	72 / 558 (12.90%)	76 / 556 (13.67%)	
occurrences (all)	122	123	
Urinary Tract Infection			
subjects affected / exposed	23 / 558 (4.12%)	30 / 556 (5.40%)	
occurrences (all)	31	42	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 November 2012	Clarified that in the event of clinically significant decreases in neutrophils or platelet counts, MTX should be temporarily or permanently discontinued
18 February 2014	Increased the total number of subjects to be enrolled to approximately 1,650 with approximately 550 subjects in each of the 3 treatment groups. The sample size of CNTO136ARA3002 was increased to ensure that the overall safety database size of the Phase 3 RA program for sirukumab was maintained despite a reduction in enrollment in CNTO136ARA3003. Along with the increase in subject enrollment, there was an increase in power of the study.
07 May 2014	Added acute diverticulitis requiring antibiotic treatment and GI perforation to the list of conditions that would result in the permanent discontinuation of study agent administrations. Power calculations were revised due to an increase in sample size.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The short pure placebo-controlled period (through Week 18) and the EE at Week 18 and LE at Week 40 for subjects in the placebo group might have affected the ability to directly compare safety between sirukumab and placebo groups through Week 52.

Notes: