Clinical trial results:
A Multicenter, Randomized, Double-blind, Parallel Group Study of CNTO 136 (sirukumab) Administered Subcutaneously as Monotherapy Compared With Adalimumab Monotherapy, in Subjects With Active Rheumatoid Arthritis

Summary

EudraCT number	2013-001417-32
Trial protocol	DE HU LT ES BG
Global end of trial date	17 August 2016

Results information

Result version number	v1 (current)
This version publication date	01 September 2017
First version publication date	01 September 2017

Trial information

Trial identification

Sponsor protocol code	CNTO136ARA3005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02019472
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International N.V.
Sponsor organisation address	920 Route 202, 08869 Raritan, NJ,, United States,
Public contact	Janssen-Cilag International N.V., Clinical Registry Group, ClinicalTrialsEU@its.jnj.com
Scientific contact	Janssen-Cilag International N.V., Clinical Registry Group, 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	17 August 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective was to demonstrate the superior efficacy of sirukumab monotherapy compared with adalimumab monotherapy in biologic naive subjects with active rheumatoid arthritis (RA) who were intolerant to methotrexate (MTX), who were considered inappropriate for treatment with MTX, or who were inadequate responders to MTX.

Protection of trial subjects:

The safety assessments included the incidence and severity of adverse events (AEs), clinical laboratory tests (hematology and serum chemistry), vital signs and physical examinations which were assessed throughout the study. This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 April 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 2
Country: Number of subjects enrolled	Chile: 10
Country: Number of subjects enrolled	Colombia: 14
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Lithuania: 36
Country: Number of subjects enrolled	Moldova, Republic of: 12
Country: Number of subjects enrolled	Mexico: 11
Country: Number of subjects enrolled	Poland: 58
Country: Number of subjects enrolled	Romania: 13
Country: Number of subjects enrolled	Russian Federation: 92
Country: Number of subjects enrolled	Serbia: 65
Country: Number of subjects enrolled	Ukraine: 118
Country: Number of subjects enrolled	United States: 88
Country: Number of subjects enrolled	South Africa: 24

Worldwide total number of subjects	559
EEA total number of subjects	125

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)	486
From 65 to 84 years	73
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 559 subjects were randomized and treated. All subjects received atleast one administration of study treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Adalimumab 40 mg

Arm description:

Subjects received 40 mg of adalimumab subcutaneously once every 2 weeks (q2w) for 52 weeks. Subjects who met early escape (EE) criteria (had less than 20 percent improvement from baseline in swollen and tender joint counts) at Week 16 received adalimumab 40 mg once every week (q1w) through Week 52.

Arm type	Active comparator
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 40 mg of adalimumab subcutaneously q2w for 52 weeks and q1w from Week 16 for subjects who met EE criteria.

Arm title	Sirukumab 50 mg

Arm description:

Subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 52 weeks and in between placebo SC injections was received at Weeks 2, 6, 10 and 14. Subjects who met EE criteria at Week 16 received 100 mg sirukumab every 2 weeks (q2w) from Week 16 through Week 52 and placebo SC injections q2w between the sirukumab injections from Week 16 through Week 50.

Arm type	Experimental
Investigational medicinal product name	Sirukumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 50 mg of sirukumab subcutaneously q4w for 52 weeks. Subjects who met EE criteria at Week 16 received 100 mg sirukumab q2w from Week 16 onwards.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received placebo SC injections at Weeks 2, 6, 10 and 14. Subjects who met EE criteria at Week 16 received placebo SC injections q4w from Week 16 through Week 50.

Arm title	Sirukumab 100 mg

Arm description:

Subjects received 100 mg of sirukumab subcutaneous injections at Weeks 0, 2, and every 2 weeks (q2w) through Week 52. Subjects who met EE criteria at Week 16 received placebo injections q2w between the sirukumab injections through Week 52.

Arm type	Experimental
Investigational medicinal product name	Sirukumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 100 mg of sirukumab subcutaneously q2w for 52 weeks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received placebo injections every week (q1w) between the sirukumab injections through Week 52.

Number of subjects in period 1	Adalimumab 40 mg	Sirukumab 50 mg	Sirukumab 100 mg
Started	186	186	187
Completed	149	134	145
Not completed	37	52	42
Adverse event, serious fatal	-	2	1
Physician decision	1	2	-
Consent withdrawn by subject	11	10	11
Adverse event, non-fatal	8	12	14
Other	3	8	6
Pregnancy	1	2	2
Adverse event, serious non-fatal	6	10	3
Lost to follow-up	-	2	1
Lack of efficacy	7	4	4

Baseline characteristics

Reporting groups	
Reporting group title	Adalimumab 40 mg
Reporting group description:	
Subjects received 40 mg of adalimumab subcutaneously once every 2 weeks (q2w) for 52 weeks. Subjects who met early escape (EE) criteria (had less than 20 percent improvement from baseline in swollen and tender joint counts) at Week 16 received adalimumab 40 mg once every week (q1w) through Week 52.	
Reporting group title	Sirukumab 50 mg
Reporting group description:	
Subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 52 weeks and in between placebo SC injections was received at Weeks 2, 6, 10 and 14. Subjects who met EE criteria at Week 16 received 100 mg sirukumab every 2 weeks (q2w) from Week 16 through Week 52 and placebo SC injections q2w between the sirukumab injections from Week 16 through Week 50.	
Reporting group title	Sirukumab 100 mg
Reporting group description:	
Subjects received 100 mg of sirukumab subcutaneous injections at Weeks 0, 2, and every 2 weeks (q2w) through Week 52. Subjects who met EE criteria at Week 16 received placebo injections q2w between the sirukumab injections through Week 52.	

Reporting group values	Adalimumab 40 mg	Sirukumab 50 mg	Sirukumab 100 mg
Number of subjects	186	186	187
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	163	159	164
From 65 to 84 years	23	27	23
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	52.6	52.5	49.8
standard deviation	± 12.15	± 12.46	± 12.31
Title for Gender Units: subjects			
Female	156	157	154
Male	30	29	33

Reporting group values	Total		
Number of subjects	559		
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	486		
From 65 to 84 years	73		
85 years and over	0		
Title for AgeContinuous Units: years			
arithmetic mean			

standard deviation	-		

Title for Gender Units: subjects			
Female	467		
Male	92		

End points

End points reporting groups

Reporting group title	Adalimumab 40 mg
Reporting group description:	
Subjects received 40 mg of adalimumab subcutaneously once every 2 weeks (q2w) for 52 weeks. Subjects who met early escape (EE) criteria (had less than 20 percent improvement from baseline in swollen and tender joint counts) at Week 16 received adalimumab 40 mg once every week (q1w) through Week 52.	

Reporting group title	Sirukumab 50 mg
Reporting group description:	
Subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 52 weeks and in between placebo SC injections was received at Weeks 2, 6, 10 and 14. Subjects who met EE criteria at Week 16 received 100 mg sirukumab every 2 weeks (q2w) from Week 16 through Week 52 and placebo SC injections q2w between the sirukumab injections from Week 16 through Week 50.	

Reporting group title	Sirukumab 100 mg
Reporting group description:	
Subjects received 100 mg of sirukumab subcutaneous injections at Weeks 0, 2, and every 2 weeks (q2w) through Week 52. Subjects who met EE criteria at Week 16 received placebo injections q2w between the sirukumab injections through Week 52.	

Primary: Change From Baseline in Disease Activity Index Score 28 (DAS28) Erythrocyte Sedimentation Rate (ESR) at Week 24

End point title	Change From Baseline in Disease Activity Index Score 28 (DAS28) Erythrocyte Sedimentation Rate (ESR) at Week 24
End point description:	
The Disease Activity Index Score 28 using ESR [DAS28 (ESR)] is a derived score combining tender joints (28 joints), swollen joints (28 joints), ESR, and Patient's Global Assessment of Disease Activity. The 28 joints evaluated for swelling and tenderness were shoulder, elbow, wrist, MCP1, MCP2, MCP3, MCP4, MCP5, PIP1, PIP2, PIP3, PIP4, PIP5 joints of the upper right and upper left extremities as well as the knee joints of the lower right and lower left extremities. The DAS28-ESR is expressed on a score range of "0-10", with the minimum score= 0 (best) to maximum score= 10 (worst). Full analysis set (FAS) was defined as all randomized participants who received at least 1 (partial or complete) dose of study agent. Participants with missing DAS28 (ESR) at baseline were excluded from the analysis.	

End point type	Primary
End point timeframe:	
Baseline and Week 24	

End point values	Adalimumab 40 mg	Sirukumab 50 mg	Sirukumab 100 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	186	185	185	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline	6.89 (± 0.851)	6.9 (± 0.881)	6.91 (± 0.863)	
Change from Baseline at Week 24	-2.19 (± 1.437)	-2.58 (± 1.524)	-2.96 (± 1.58)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Adalimumab 40 mg v Sirukumab 100 mg
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.07
upper limit	-0.46

Statistical analysis title	Statistical analysis 2
Comparison groups	Adalimumab 40 mg v Sirukumab 50 mg
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.013
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	-0.08

Primary: 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:

The ACR 50 Response is defined as greater than or equal to (>=) 50 percent (%) improvement in swollen joint count (66 joints) and tender joint count (68 joints) and >= 50% improvement in 3 of following 5 assessments: subject’s assessment of pain using Visual Analog Scale (VAS) (0-10 millimeter [mm], 0 mm=no pain and 10 mm=worst possible pain), subject’s global assessment of disease activity by using VAS (the scale ranges from 0 mm to 100 mm, [0 mm=no pain to 100 mm=worst possible pain]), 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 measured by Health Assessment Questionnaire-Disability Index (HAQ-DI) (the scale ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area) and serum C-Reactive Protein (CRP). FAS was defined as all randomized participants who received at least 1 dose of study agent.

End point type	Primary

End point timeframe:
Week 24

End point values	Adalimumab 40 mg	Sirukumab 50 mg	Sirukumab 100 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	186	186	187	
Units: percentage of Subjects				
number (not applicable)	31.7	26.9	35.3	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Adalimumab 40 mg v Sirukumab 50 mg
Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.306
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	-4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.1
upper limit	4.4

Statistical analysis title	Statistical analysis 2
Comparison groups	Adalimumab 40 mg v Sirukumab 100 mg
Number of subjects included in analysis	373
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.464
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	13.1

Secondary: Percentage of Subjects with Disease Activity Index Score 28 (DAS28) Using Erythrocyte Sedimentation Rate (ESR) Remission at Week 24

End point title	Percentage of Subjects with Disease Activity Index Score 28 (DAS28) Using Erythrocyte Sedimentation Rate (ESR) Remission at Week 24

End point description:

The Disease Activity Index Score 28 using ESR [DAS28 (ESR)] is a derived score combining tender joints (28 joints), swollen joints (28 joints), ESR, and Patient's Global Assessment of Disease Activity. The 28 joints evaluated for swelling and tenderness were shoulder, elbow, wrist, MCP1, MCP2, MCP3, MCP4, MCP5, PIP1, PIP2, PIP3, PIP4, PIP5 joints of the upper right and upper left extremities as well as the knee joints of the lower right and lower left extremities. The DAS28-ESR is expressed on a score range of "0-10", with the minimum score= 0 (best) to maximum score= 10 (worst). The DAS28 (ESR) remission is defined as a DAS28 (ESR) value of less than 2.6 at a visit. FAS was defined as all randomized participants who received at least 1 dose of study agent.

End point type	Secondary

End point timeframe:

Week 24

End point values	Adalimumab 40 mg	Sirukumab 50 mg	Sirukumab 100 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	186	186	187	
Units: Percentage of Subjects				
number (not applicable)	7.5	12.9	20.3	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Sirukumab 50 mg v Adalimumab 40 mg
Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.086
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	11.4

Statistical analysis title	Statistical analysis 2
Comparison groups	Adalimumab 40 mg v Sirukumab 100 mg

Number of subjects included in analysis	373
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	12.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.9
upper limit	19.7

Secondary: Percentage of Subjects With an American College of Rheumatology (ACR) 20 Response at Week 24

End point title	Percentage of Subjects With an American College of Rheumatology (ACR) 20 Response at Week 24

End point description:

The ACR 20 Response is defined as >= 20% improvement in swollen joint count (66 joints) and tender joint count (68 joints) and >=20% improvement in 3 of following 5 assessments: subject's assessment of pain using VAS (0-10 mm, 0 mm=no pain and 10 mm=worst possible pain), subject's global assessment of disease activity by using VAS (the scale ranges from 0 mm to 100 mm, [0 mm=no pain to 100 mm=worst possible pain]), physician's global assessment of disease activity using VAS, subject's assessment of physical function measured by HAQ-DI, defined as a 20-question instrument assessing 8 functional areas. The derived HAQ-DI 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 participants who received at least 1 dose of study agent.

End point type	Secondary

End point timeframe:

Week 24

End point values	Adalimumab 40 mg	Sirukumab 50 mg	Sirukumab 100 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	186	186	187	
Units: Percentage of Subjects				
number (not applicable)	56.5	53.8	58.8	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Adalimumab 40 mg v Sirukumab 50 mg

Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.603
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.8
upper limit	7.4

Statistical analysis title	Statistical analysis 2
Comparison groups	Adalimumab 40 mg v Sirukumab 100 mg
Number of subjects included in analysis	373
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.644
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percentage Difference
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.6
upper limit	12.3

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Screening, up to Week 68	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	Adalimumab 40 mg q2w only
Reporting group description: Subjects received 40 mg of adalimumab subcutaneously q2w for 52 weeks.	
Reporting group title	Adalimumab 40 mg q2w then 40 mg q1w
Reporting group description: Subjects received 40 mg adalimumab subcutaneously q2w until Week 16 and received 40 mg adalimumab subcutaneously weekly (q1w) (due to EE) through Week 52.	
Reporting group title	Adalimumab 40 mg
Reporting group description: Subjects received 40 mg of adalimumab subcutaneously once every 2 weeks (q2w) for 52 weeks. Subjects who met early escape (EE) criteria (had less than 20 percent improvement from baseline in swollen and tender joint counts) at Week 16 received adalimumab 40 mg once every week (q1w) through Week 52.	
Reporting group title	Sirukumab 50 mg q4w only
Reporting group description: Subjects received 50 mg of sirukumab subcutaneously every four weeks (q4w) for 52 weeks.	
Reporting group title	Sirukumab 50 mg q4w then 100 mg q2w
Reporting group description: Subjects received 50 mg sirukumab until Week 16 and received 100 mg sirukumab subcutaneously q4w (due to EE or inadvertently) through Week 52.	
Reporting group title	Sirukumab 50 mg
Reporting group description: Subjects received 50 mg of sirukumab subcutaneously every 4 weeks (q4w) for 52 weeks and in between placebo SC injections was received at Weeks 2, 6, and q4w through Week 50. Subjects who met EE criteria at Week 16 received 100 mg sirukumab every 2 weeks (q2w) from Week 16 through Week 52.	
Reporting group title	Sirukumab 100 mg
Reporting group description: Subjects received 100 mg of sirukumab subcutaneously every 2 weeks (q2w) for 52 weeks.	

Serious adverse events	Adalimumab 40 mg q2w only	Adalimumab 40 mg q2w then 40 mg q1w	Adalimumab 40 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 173 (8.67%)	1 / 13 (7.69%)	16 / 186 (8.60%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Adenocarcinoma			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma Pancreas			
subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clear Cell Renal Cell Carcinoma			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial Adenocarcinoma			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gliomatosis Cerebri			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Essential Hypertension			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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			
Pre-Eclampsia			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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			
Peripheral Swelling			
subjects affected / exposed	2 / 173 (1.16%)	0 / 13 (0.00%)	2 / 186 (1.08%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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 Fibrosis			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Failure			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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			
Mental Status Changes			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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			
Humerus Fracture			

subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint Dislocation			
subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin Wound			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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 Fracture			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary Artery Disease			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus Node Dysfunction			
subjects affected / exposed	0 / 173 (0.00%)	1 / 13 (7.69%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular Tachycardia			
subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Haemorrhagic Stroke			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar Infarction			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuralgia			
subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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			
Pancytopenia			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis Ulcerative			

subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Perforation			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis Chronic			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-Induced Liver Injury			

subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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			
Dermatitis Contact			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Petechiae			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin Ulcer			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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			
Haemarthrosis			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral Disc Protrusion			
subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Osteoarthritis			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporosis			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporotic Fracture			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid Arthritis			
subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acute Sinusitis			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis Infective			

subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Bacterial Infection			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes Ophthalmic			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious Pleural Effusion			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Streptococcal			

subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulpitis Dental			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
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 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tongue Abscess			
subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	0 / 173 (0.00%)	0 / 13 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 173 (0.58%)	0 / 13 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Sirukumab 50 mg	Sirukumab 50 mg	Sirukumab 50 mg

	q4w only	q4w then 100 mg q2w	
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 160 (14.38%)	6 / 26 (23.08%)	29 / 186 (15.59%)
number of deaths (all causes)	2	1	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Adenocarcinoma Pancreas			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clear Cell Renal Cell Carcinoma			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial Adenocarcinoma			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gliomatosis Cerebri			
subjects affected / exposed	0 / 160 (0.00%)	1 / 26 (3.85%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Essential Hypertension			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Pre-Eclampsia			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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			
Peripheral Swelling			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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 Fibrosis			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Failure			

subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Psychiatric disorders			
Mental Status Changes			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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			
Humerus Fracture			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint Dislocation			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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 Wound			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Fracture			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	2 / 160 (1.25%)	0 / 26 (0.00%)	2 / 186 (1.08%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary Artery Disease			
subjects affected / exposed	0 / 160 (0.00%)	1 / 26 (3.85%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Sinus Node Dysfunction			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular Tachycardia			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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			
Haemorrhagic Stroke			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar Infarction			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuralgia			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient Ischaemic Attack			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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			
Colitis Ulcerative			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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 / 160 (0.00%)	1 / 26 (3.85%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Perforation			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hepatobiliary disorders			
Cholecystitis Chronic			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-Induced Liver Injury			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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			
Dermatitis Contact			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Petechiae			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin Ulcer			
subjects affected / exposed	0 / 160 (0.00%)	1 / 26 (3.85%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Haemarthrosis			

subjects affected / exposed	0 / 160 (0.00%)	1 / 26 (3.85%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 160 (0.00%)	1 / 26 (3.85%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporosis			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoporotic Fracture			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid Arthritis			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	0 / 160 (0.00%)	1 / 26 (3.85%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acute Sinusitis			

subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis Infective			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 160 (1.25%)	0 / 26 (0.00%)	2 / 186 (1.08%)
occurrences causally related to treatment / all	2 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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 / 160 (0.00%)	1 / 26 (3.85%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	1 / 1
Gastrointestinal Bacterial Infection			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes Ophthalmic			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious Pleural Effusion			

subjects affected / exposed	2 / 160 (1.25%)	0 / 26 (0.00%)	2 / 186 (1.08%)
occurrences causally related to treatment / all	2 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Streptococcal			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Tuberculosis			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulpitis Dental			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	1 / 160 (0.63%)	0 / 26 (0.00%)	1 / 186 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tongue Abscess			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
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	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 160 (0.00%)	0 / 26 (0.00%)	0 / 186 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Sirukumab 100 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 187 (11.76%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma Pancreas			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clear Cell Renal Cell Carcinoma			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endometrial Adenocarcinoma			
subjects affected / exposed	1 / 187 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gliomatosis Cerebri			

subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Essential Hypertension			
subjects affected / exposed	1 / 187 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vasculitis			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Pre-Eclampsia			
subjects affected / exposed	1 / 187 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Peripheral Swelling			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleurisy			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			

subjects affected / exposed	1 / 187 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary Fibrosis				
subjects affected / exposed	0 / 187 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory Failure				
subjects affected / exposed	0 / 187 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Mental Status Changes				
subjects affected / exposed	1 / 187 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Humerus Fracture				
subjects affected / exposed	1 / 187 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Joint Dislocation				
subjects affected / exposed	0 / 187 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin Wound				
subjects affected / exposed	0 / 187 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal Fracture				
subjects affected / exposed	0 / 187 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary Artery Disease			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinus Node Dysfunction			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ventricular Tachycardia			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Haemorrhagic Stroke			
subjects affected / exposed	1 / 187 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Lacunar Infarction			
subjects affected / exposed	1 / 187 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuralgia			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Transient Ischaemic Attack			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 187 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis Ulcerative			
subjects affected / exposed	1 / 187 (0.53%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticular Perforation			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal Perforation			
subjects affected / exposed	1 / 187 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids			

subjects affected / exposed	0 / 187 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	1 / 187 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	0 / 187 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis Chronic				
subjects affected / exposed	1 / 187 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Drug-Induced Liver Injury				
subjects affected / exposed	1 / 187 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Dermatitis Contact				
subjects affected / exposed	1 / 187 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Petechiae				
subjects affected / exposed	1 / 187 (0.53%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin Ulcer				
subjects affected / exposed	0 / 187 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urticaria				

subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Haemarthrosis			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 187 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoporosis			
subjects affected / exposed	1 / 187 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoporotic Fracture			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Rheumatoid Arthritis				
subjects affected / exposed	1 / 187 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Synovitis				
subjects affected / exposed	0 / 187 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Acute Sinusitis				
subjects affected / exposed	0 / 187 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	1 / 187 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bursitis Infective				
subjects affected / exposed	0 / 187 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 187 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	1 / 187 (0.53%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 187 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal Bacterial Infection				

subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Herpes Ophthalmic			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infectious Pleural Effusion			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 187 (0.53%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia Streptococcal			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary Tuberculosis			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulpitis Dental			
subjects affected / exposed	1 / 187 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis Acute			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinusitis			

subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tongue Abscess			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection			
subjects affected / exposed	1 / 187 (0.53%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 187 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Adalimumab 40 mg q2w only	Adalimumab 40 mg q2w then 40 mg q1w	Adalimumab 40 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	71 / 173 (41.04%)	3 / 13 (23.08%)	74 / 186 (39.78%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	12 / 173 (6.94%)	0 / 13 (0.00%)	12 / 186 (6.45%)
occurrences (all)	16	0	16
Aspartate Aminotransferase Increased			
subjects affected / exposed	11 / 173 (6.36%)	0 / 13 (0.00%)	11 / 186 (5.91%)
occurrences (all)	14	0	14
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 173 (5.20%)	1 / 13 (7.69%)	10 / 186 (5.38%)
occurrences (all)	9	1	10
Nervous system disorders			

Headache			
subjects affected / exposed	9 / 173 (5.20%)	2 / 13 (15.38%)	11 / 186 (5.91%)
occurrences (all)	12	2	14
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	4 / 173 (2.31%)	0 / 13 (0.00%)	4 / 186 (2.15%)
occurrences (all)	4	0	4
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	13 / 173 (7.51%)	0 / 13 (0.00%)	13 / 186 (6.99%)
occurrences (all)	28	0	28
Injection Site Pruritus			
subjects affected / exposed	8 / 173 (4.62%)	0 / 13 (0.00%)	8 / 186 (4.30%)
occurrences (all)	12	0	12
Injection Site Swelling			
subjects affected / exposed	4 / 173 (2.31%)	0 / 13 (0.00%)	4 / 186 (2.15%)
occurrences (all)	6	0	6
Musculoskeletal and connective tissue disorders			
Rheumatoid Arthritis			
subjects affected / exposed	17 / 173 (9.83%)	0 / 13 (0.00%)	17 / 186 (9.14%)
occurrences (all)	18	0	18
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 173 (2.31%)	0 / 13 (0.00%)	4 / 186 (2.15%)
occurrences (all)	4	0	4
Nasopharyngitis			
subjects affected / exposed	16 / 173 (9.25%)	0 / 13 (0.00%)	16 / 186 (8.60%)
occurrences (all)	22	0	22
Upper Respiratory Tract Infection			
subjects affected / exposed	10 / 173 (5.78%)	0 / 13 (0.00%)	10 / 186 (5.38%)
occurrences (all)	13	0	13

Non-serious adverse events	Sirukumab 50 mg q4w only	Sirukumab 50 mg q4w then 100 mg q2w	Sirukumab 50 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 160 (49.38%)	13 / 26 (50.00%)	92 / 186 (49.46%)

Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	18 / 160 (11.25%)	3 / 26 (11.54%)	21 / 186 (11.29%)
occurrences (all)	21	4	25
Aspartate Aminotransferase Increased			
subjects affected / exposed	9 / 160 (5.63%)	4 / 26 (15.38%)	13 / 186 (6.99%)
occurrences (all)	9	4	13
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 160 (5.00%)	4 / 26 (15.38%)	12 / 186 (6.45%)
occurrences (all)	9	4	13
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 160 (6.25%)	1 / 26 (3.85%)	11 / 186 (5.91%)
occurrences (all)	17	1	18
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	16 / 160 (10.00%)	1 / 26 (3.85%)	17 / 186 (9.14%)
occurrences (all)	23	2	25
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	15 / 160 (9.38%)	2 / 26 (7.69%)	17 / 186 (9.14%)
occurrences (all)	22	5	27
Injection Site Pruritus			
subjects affected / exposed	6 / 160 (3.75%)	0 / 26 (0.00%)	6 / 186 (3.23%)
occurrences (all)	8	0	8
Injection Site Swelling			
subjects affected / exposed	3 / 160 (1.88%)	1 / 26 (3.85%)	4 / 186 (2.15%)
occurrences (all)	6	4	10
Musculoskeletal and connective tissue disorders			
Rheumatoid Arthritis			
subjects affected / exposed	17 / 160 (10.63%)	3 / 26 (11.54%)	20 / 186 (10.75%)
occurrences (all)	19	4	23
Infections and infestations			
Bronchitis			

subjects affected / exposed	8 / 160 (5.00%)	2 / 26 (7.69%)	10 / 186 (5.38%)
occurrences (all)	9	2	11
Nasopharyngitis			
subjects affected / exposed	9 / 160 (5.63%)	1 / 26 (3.85%)	10 / 186 (5.38%)
occurrences (all)	10	1	11
Upper Respiratory Tract Infection			
subjects affected / exposed	8 / 160 (5.00%)	2 / 26 (7.69%)	10 / 186 (5.38%)
occurrences (all)	12	4	16

Non-serious adverse events	Sirukumab 100 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	86 / 187 (45.99%)		
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	24 / 187 (12.83%)		
occurrences (all)	34		
Aspartate Aminotransferase Increased			
subjects affected / exposed	20 / 187 (10.70%)		
occurrences (all)	24		
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 187 (4.28%)		
occurrences (all)	8		
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 187 (6.95%)		
occurrences (all)	19		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	11 / 187 (5.88%)		
occurrences (all)	15		
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	33 / 187 (17.65%)		
occurrences (all)	156		
Injection Site Pruritus			

subjects affected / exposed	17 / 187 (9.09%)		
occurrences (all)	27		
Injection Site Swelling			
subjects affected / exposed	11 / 187 (5.88%)		
occurrences (all)	31		
Musculoskeletal and connective tissue disorders			
Rheumatoid Arthritis			
subjects affected / exposed	15 / 187 (8.02%)		
occurrences (all)	16		
Infections and infestations			
Bronchitis			
subjects affected / exposed	8 / 187 (4.28%)		
occurrences (all)	9		
Nasopharyngitis			
subjects affected / exposed	9 / 187 (4.81%)		
occurrences (all)	11		
Upper Respiratory Tract Infection			
subjects affected / exposed	9 / 187 (4.81%)		
occurrences (all)	14		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 January 2014	This amendment included the following changes: Corrected typographical errors in an inclusion criterion; Adjusted timing of biopsy and epigenetic sample collection; Clarified/corrected text throughout the protocol
30 April 2014	This amendment included the following changes: Clarified text describing pharmacogenomics and epigenetics to be studied in this trial; Clarified/corrected text throughout the protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported