Clinical trial results:
A Randomized, Controlled Study of Sarilumab and Methotrexate (MTX) Versus Etanercept and MTX in Patients with Rheumatoid Arthritis (RA) and an Inadequate Response to 4 Months of Treatment with Adalimumab and MTX

Summary

EudraCT number	2012-001984-66
Trial protocol	GB DE HU CZ ES GR LT FI LV IT NO
Global end of trial date	12 January 2015

Results information

Result version number	v1 (current)
This version publication date	24 July 2016
First version publication date	24 July 2016

Trial information

Trial identification

Sponsor protocol code	EFC11574

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01764997
WHO universal trial number (UTN)	U1111-1131-6653

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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	11 February 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 January 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the combination of sarilumab and MTX was superior to the combination of etanercept and MTX for the improvement (reduction) of Disease Activity Score for 28 joints C-reactive protein (DAS28-CRP) score at Week 24, compared to the randomization treatment phase baseline evaluation, in subjects with RA and an inadequate response to 4 months of treatment with adalimumab and MTX.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.
Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy:

A stable dose of MTX was administered during the study.

Evidence for comparator: -

Actual start date of recruitment	09 May 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 91
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Czech Republic: 43
Country: Number of subjects enrolled	Finland: 9
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Greece: 2
Country: Number of subjects enrolled	Hungary: 6
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Latvia: 6
Country: Number of subjects enrolled	Lithuania: 11
Country: Number of subjects enrolled	Argentina: 6

Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Brazil: 2
Country: Number of subjects enrolled	Chile: 58
Country: Number of subjects enrolled	Colombia: 22
Country: Number of subjects enrolled	Ecuador: 5
Country: Number of subjects enrolled	Israel: 20
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Malaysia: 21
Country: Number of subjects enrolled	Mexico: 61
Country: Number of subjects enrolled	New Zealand: 11
Country: Number of subjects enrolled	Peru: 38
Country: Number of subjects enrolled	Romania: 8
Country: Number of subjects enrolled	Russian Federation: 105
Country: Number of subjects enrolled	South Africa: 23
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	Thailand: 5
Country: Number of subjects enrolled	Ukraine: 95
Country: Number of subjects enrolled	United States: 77
Worldwide total number of subjects	776
EEA total number of subjects	212

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)	0
From 65 to 84 years	668
85 years and over	108

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 228 sites in 31 countries. A total of 1949 subjects were screened between 09 May 2013 and 07 Aug 2014, of which 1173 subjects were screen failures and a total of 776 subjects entered in the adalimumab run-in phase of the study.

Pre-assignment

Screening details:

Of 776 subjects, 365 completed adalimumab run-in phase, of whom 43 non-responders were randomized(1:1:1) in double-blind fashion to receive sarilumab 150 mg, sarilumab 200 mg or etanercept 50 mg; and 322 responders entered in open label sub-study. 373 subjects did not proceed into randomized phase or sub-study and 38 discontinued from run-in phase.

Period 1

Period 1 title	Run-In Period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Adalimumab Open Label Run-in

Arm description:

Adalimumab 40 mg every 2 weeks (Q2W) for 16 weeks added to stable dose of methotrexate (MTX).

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

Dosage and administration details:

Adalimumab 40 mg subcutaneous (SC) injection in lower abdomen and front of thigh or as per local labeling requirements.

Number of subjects in period 1	Adalimumab Open Label Run-in
Started	776
Completed	738
Not completed	38
Other than specified above	17
Poor compliance to protocol	1
Adverse Events	15
Lack of efficacy	5

Period 2

Period 2 title	Study Drug Treatment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Etanercept + MTX (Randomized)

Arm description:

Etanercept 50 mg in combination with Placebo for sarilumab Q2W and etanercept 50 mg on alternating weeks for 24 weeks added to stable dose of MTX.

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

Dosage and administration details:

Etanercept 50 mg SC injection in lower abdomen, front and side of thigh and upper arm.

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

Dosage and administration details:

Placebo matched to sarilumab SC injection in lower abdomen, front and side of thigh and upper arm.

Arm title	Sarilumab 150 mg + MTX (Randomized)

Arm description:

Sarilumab 150 mg in combination with placebo for etanercept Q2W and placebo for etanercept on alternating weeks for 24 weeks added to stable dose of MTX.

Arm type	Experimental
Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191 (REGN88)
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Sarilumab 150 mg SC injection in lower abdomen, front and side of thigh and upper arm.

Investigational medicinal product name	Placebo (for Etanercept)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo matched to etanercept SC injection in lower abdomen, front and side of thigh and upper arm.

Arm title	Sarilumab 200 mg + MTX (Randomized)

Arm description:

Sarilumab 200 mg in combination with placebo for etanercept Q2W and placebo for etanercept on alternating weeks for 24 weeks added to stable dose of MTX.

Arm type	Experimental

Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191 (REGN88)
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Sarilumab 200 mg SC injection in lower abdomen, front and side of thigh and upper arm.

Investigational medicinal product name	Placebo (for Etanercept)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo matched to etanercept SC injection in lower abdomen, front and side of thigh and upper arm.

Arm title	Sarilumab 150 mg + MTX Open Label Sub-study

Arm description:

Sarilumab 150 mg Q2W for 52 weeks added to stable dose of MTX.

Arm type	Experimental
Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191 (REGN88)
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Sarilumab 150 mg SC injection in lower abdomen, front and side of thigh and upper arm.

Number of subjects in period 2[1]	Etanercept + MTX (Randomized)	Sarilumab 150 mg + MTX (Randomized)	Sarilumab 200 mg + MTX (Randomized)
Started	17	13	13
Completed	16	13	13
Not completed	1	0	0
Other than specified above	-	-	-
Adverse Events	1	-	-
Lack of efficacy	-	-	-

Number of subjects in period 2[1]	Sarilumab 150 mg + MTX Open Label Sub-study
Started	322
Completed	286
Not completed	36
Other than specified above	10
Adverse Events	24
Lack of efficacy	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 43 subjects proceeded to randomized treatment; 322 proceeded to open-label sub-study; 373 did not proceeded into the randomized phase or sub-study and 38 discontinued from run-in phase.

Baseline characteristics

Reporting groups	
Reporting group title	Adalimumab Open Label Run-in
Reporting group description:	
Adalimumab 40 mg every 2 weeks (Q2W) for 16 weeks added to stable dose of methotrexate (MTX).	

Reporting group values	Adalimumab Open Label Run-in	Total	
Number of subjects	776	776	
Age categorical Units: Subjects			
Adults (18-64 years)	668	668	
From 65-84 years	108	108	
Gender categorical Units: Subjects			
Female	637	637	
Male	139	139	

End points

End points reporting groups

Reporting group title	Adalimumab Open Label Run-in
Reporting group description:	
Adalimumab 40 mg every 2 weeks (Q2W) for 16 weeks added to stable dose of methotrexate (MTX).	
Reporting group title	Etanercept + MTX (Randomized)
Reporting group description:	
Etanercept 50 mg in combination with Placebo for sarilumab Q2W and etanercept 50 mg on alternating weeks for 24 weeks added to stable dose of MTX.	
Reporting group title	Sarilumab 150 mg + MTX (Randomized)
Reporting group description:	
Sarilumab 150 mg in combination with placebo for etanercept Q2W and placebo for etanercept on alternating weeks for 24 weeks added to stable dose of MTX.	
Reporting group title	Sarilumab 200 mg + MTX (Randomized)
Reporting group description:	
Sarilumab 200 mg in combination with placebo for etanercept Q2W and placebo for etanercept on alternating weeks for 24 weeks added to stable dose of MTX.	
Reporting group title	Sarilumab 150 mg + MTX Open Label Sub-study
Reporting group description:	
Sarilumab 150 mg Q2W for 52 weeks added to stable dose of MTX.	

Primary: Change From Baseline in DAS28-CRP Score at Week 24

End point title	Change From Baseline in DAS28-CRP Score at Week 24[1]
End point description:	
End point type	Primary
End point timeframe:	
Baseline, Week 24	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the study was terminated due to small number of subjects entering randomization, efficacy endpoints were not analyzed.

End point values	Etanercept + MTX (Randomized)	Sarilumab 150 mg + MTX (Randomized)	Sarilumab 200 mg + MTX (Randomized)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: Units on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[2] - Due to small number of subjects entering randomization, efficacy endpoints were not analyzed.

[3] - Due to small number of subjects entering randomization, efficacy endpoints were not analyzed.

[4] - Due to small number of subjects entering randomization, efficacy endpoints were not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With at Least 20% Improvement in American College of Rheumatology (ACR20), at Least 50% Improvement in ACR (ACR50) and at Least 70% Improvement in ACR (ACR70) Efficacy Response Rates at Week 12 and Week 24

End point title	Number of Subjects With at Least 20% Improvement in American College of Rheumatology (ACR20), at Least 50% Improvement in ACR (ACR50) and at Least 70% Improvement in ACR (ACR70) Efficacy Response Rates at Week 12 and Week 24

End point description:

End point type	Secondary

End point timeframe:

Week 12 and Week 24

End point values	Etanercept + MTX (Randomized)	Sarilumab 150 mg + MTX (Randomized)	Sarilumab 200 mg + MTX (Randomized)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[5]	0[6]	0[7]	
Units: Subjects				

Notes:

[5] - Due to small number of subjects entering randomization, efficacy endpoints were not analyzed.

[6] - Due to small number of subjects entering randomization, efficacy endpoints were not analyzed.

[7] - Due to small number of subjects entering randomization, efficacy endpoints were not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Clinical Remission Score (DAS28-CRP) <2.6 at Week 12 and Week 24

End point title	Percentage of Subjects Achieving Clinical Remission Score (DAS28-CRP) <2.6 at Week 12 and Week 24

End point description:

End point type	Secondary

End point timeframe:

Week 12 and Week 24

End point values	Etanercept + MTX (Randomized)	Sarilumab 150 mg + MTX (Randomized)	Sarilumab 200 mg + MTX (Randomized)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[8]	0[9]	0[10]	
Units: Percentage of Subjects				
number (not applicable)				

Notes:
[8] - Due to small number of subjects entering randomization, efficacy endpoints were not analyzed.
[9] - Due to small number of subjects entering randomization, efficacy endpoints were not analyzed.
[10] - Due to small number of subjects entering randomization, efficacy endpoints were not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in DAS28-CRP Score at Week 12

End point title	Change From Baseline in DAS28-CRP Score at Week 12

End point description:

End point type	Secondary

End point timeframe:
Baseline, Week 12

End point values	Etanercept + MTX (Randomized)	Sarilumab 150 mg + MTX (Randomized)	Sarilumab 200 mg + MTX (Randomized)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[11]	0[12]	0[13]	
Units: Units on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:
[11] - Due to small number of subjects entering randomization, efficacy endpoints were not analyzed.
[12] - Due to small number of subjects entering randomization, efficacy endpoints were not analyzed.
[13] - Due to small number of subjects entering randomization, efficacy endpoints were not analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (Week 16 for run-in period and Week 58 for treatment period) regardless of seriousness or relationship to investigational product

Adverse event reporting additional description:

Reported AEs are treatment-emergent AEs that is AEs that developed/worsened during the 'on-treatment period' (the time from the first dose of adalimumab to the end of follow-up period). All subjects who entered open-label run-in period were included for safety assessment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Adalimumab Open Label Run-in

Reporting group description:

Adalimumab 40 mg Q2W for 16 weeks added to stable dose of MTX. AEs in this group were those collected from signature of the informed consent form up to the end of Adalimumab treatment (Week 16).

Reporting group title	Etanercept + MTX (Randomized)

Reporting group description:

Etanercept 50 mg in combination with Placebo for sarilumab Q2W and etanercept 50 mg on alternating weeks for 24 weeks added to stable dose of MTX. AEs in this group were those collected post randomization up to the final visit (Week 30).

Reporting group title	Sarilumab 150 mg + MTX (Randomized)

Reporting group description:

Sarilumab 150 mg in combination with placebo for etanercept Q2W and placebo for etanercept on alternating weeks for 24 weeks added to stable dose of MTX. AEs in this group were those collected post randomization up to the final visit (Week 30).

Reporting group title	Sarilumab 200 mg + MTX (Randomized)

Reporting group description:

Sarilumab 200 mg in combination with placebo for etanercept Q2W and placebo for etanercept on alternating weeks for 24 weeks added to stable dose of MTX. AEs in this group were those collected post randomization up to the final visit (Week 30).

Reporting group title	Sarilumab 150 mg + MTX Open Label Sub-study

Reporting group description:

Sarilumab 150 mg Q2W for 52 weeks added to stable dose of MTX. AEs in this group were those collected from enrollment in the sub-study up to the final visit (Week 58).

Serious adverse events	Adalimumab Open Label Run-in	Etanercept + MTX (Randomized)	Sarilumab 150 mg + MTX (Randomized)
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 776 (3.22%)	2 / 17 (11.76%)	0 / 13 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder Cancer			

subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal Proliferative Breast Lesion			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm Malignant			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous Cell Carcinoma Of Skin			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
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			
Haematoma			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive Crisis			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemia			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Pleural Effusion			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Embolism			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
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			
Suicide Attempt			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza B Virus Test Positive			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver Function Test Abnormal			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Postoperative Respiratory Failure			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
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 Compression Fracture			

subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
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	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon Rupture			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
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			
Angina Unstable			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial Fibrillation			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
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			
Syncope			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
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 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Blindness			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
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			
Gastroduodenitis			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal Haemorrhage			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity Vasculitis			
subjects affected / exposed	0 / 776 (0.00%)	1 / 17 (5.88%)	0 / 13 (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 and connective tissue disorders			
Bursitis			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			

subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid Arthritis			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Arthritis Bacterial			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis Infective			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic Abscess			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
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	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia Pyelonephritis			

subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Histoplasmosis Disseminated			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral Herpes			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculous Pleurisy			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	0 / 776 (0.00%)	1 / 17 (5.88%)	0 / 13 (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
Viral Parotitis			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Sarilumab 200 mg + MTX (Randomized)	Sarilumab 150 mg + MTX Open Label Sub-study	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	11 / 322 (3.42%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder Cancer			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal Proliferative Breast Lesion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm Malignant			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous Cell Carcinoma Of Skin			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive Crisis			

subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural Effusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (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	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide Attempt			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (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	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza B Virus Test Positive			

subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver Function Test Abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Postoperative Respiratory Failure			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Compression Fracture			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Fracture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon Rupture			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina Unstable			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial Fibrillation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Blindness			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastroduodenitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal Haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			

subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity Vasculitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (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	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid Arthritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (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			
Arthritis Bacterial			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (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	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cholecystitis Infective			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic Abscess			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia Pyelonephritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Histoplasmosis Disseminated			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral Herpes			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculous Pleurisy			

subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral Parotitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (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 / 13 (0.00%)	0 / 322 (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	Adalimumab Open Label Run-in	Etanercept + MTX (Randomized)	Sarilumab 150 mg + MTX (Randomized)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	132 / 776 (17.01%)	7 / 17 (41.18%)	7 / 13 (53.85%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	5 / 776 (0.64%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	5	0	0
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blood Creatinine Increased			
subjects affected / exposed	0 / 776 (0.00%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Neutrophil Count Decreased			

subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	24 / 776 (3.09%)	0 / 17 (0.00%)	3 / 13 (23.08%)
occurrences (all)	24	0	3
Chillblains			
subjects affected / exposed	0 / 776 (0.00%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Sunburn			
subjects affected / exposed	0 / 776 (0.00%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Tremor			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 776 (0.26%)	1 / 17 (5.88%)	1 / 13 (7.69%)
occurrences (all)	3	1	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 776 (0.39%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	3	0	0
Injection Site Erythema			
subjects affected / exposed	9 / 776 (1.16%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	17	0	0
Injection Site Pain			
subjects affected / exposed	9 / 776 (1.16%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	15	0	0
Injection Site Pruritus			
subjects affected / exposed	5 / 776 (0.64%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	6	2	0
Injection Site Rash			
subjects affected / exposed	6 / 776 (0.77%)	0 / 17 (0.00%)	1 / 13 (7.69%)
occurrences (all)	10	0	2

Injection Site Swelling			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Peripheral Swelling			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	7 / 776 (0.90%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	7	0	0
Gastrointestinal disorders			
Abdominal Tenderness			
subjects affected / exposed	0 / 776 (0.00%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	10 / 776 (1.29%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	11	0	0
Food Poisoning			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	8 / 776 (1.03%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	10	1	0
Tooth Disorder			
subjects affected / exposed	0 / 776 (0.00%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Paranasal Sinus Hypersecretion			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Sinus Congestion			

subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis Allergic			
subjects affected / exposed	4 / 776 (0.52%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	4	1	0
Pruritus			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 776 (0.64%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	5	1	0
Musculoskeletal Pain			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Costochondritis			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pain In Extremity			
subjects affected / exposed	2 / 776 (0.26%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	3	0	0
Osteoporotic Fracture			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Tenosynovitis Stenosans			
subjects affected / exposed	0 / 776 (0.00%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Body Tinea			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Hordeolum			
subjects affected / exposed	2 / 776 (0.26%)	0 / 17 (0.00%)	1 / 13 (7.69%)
occurrences (all)	2	0	2
Onychomycosis			

subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	7 / 776 (0.90%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	8	0	0
Pharyngitis Streptococcal			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	7 / 776 (0.90%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	8	0	0
Rash Pustular			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	1 / 13 (7.69%)
occurrences (all)	2	0	1
Tinea Versicolour			
subjects affected / exposed	1 / 776 (0.13%)	0 / 17 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Urinary Tract Infection			
subjects affected / exposed	16 / 776 (2.06%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	19	1	0
Upper Respiratory Tract Infection			
subjects affected / exposed	27 / 776 (3.48%)	1 / 17 (5.88%)	1 / 13 (7.69%)
occurrences (all)	30	1	1
Viral Pharyngitis			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 776 (0.00%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Vitamin D Deficiency			
subjects affected / exposed	0 / 776 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Sarilumab 200 mg + MTX (Randomized)	Sarilumab 150 mg + MTX Open Label Sub-study	
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	8 / 13 (61.54%)	104 / 322 (32.30%)	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	2 / 13 (15.38%)	11 / 322 (3.42%)	
occurrences (all)	2	11	
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 13 (7.69%)	3 / 322 (0.93%)	
occurrences (all)	1	3	
Blood Creatinine Increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences (all)	0	0	
Neutrophil Count Decreased			
subjects affected / exposed	0 / 13 (0.00%)	4 / 322 (1.24%)	
occurrences (all)	0	4	
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 13 (0.00%)	14 / 322 (4.35%)	
occurrences (all)	0	15	
Chillblains			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences (all)	0	0	
Sunburn			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Tremor			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 13 (15.38%)	33 / 322 (10.25%)	
occurrences (all)	4	45	
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	1 / 13 (7.69%)	2 / 322 (0.62%)	
occurrences (all)	1	2	
Injection Site Erythema			
subjects affected / exposed	1 / 13 (7.69%)	15 / 322 (4.66%)	
occurrences (all)	2	33	
Injection Site Pain			
subjects affected / exposed	1 / 13 (7.69%)	3 / 322 (0.93%)	
occurrences (all)	2	3	
Injection Site Pruritus			
subjects affected / exposed	0 / 13 (0.00%)	9 / 322 (2.80%)	
occurrences (all)	0	19	
Injection Site Rash			
subjects affected / exposed	1 / 13 (7.69%)	7 / 322 (2.17%)	
occurrences (all)	1	10	
Injection Site Swelling			
subjects affected / exposed	1 / 13 (7.69%)	2 / 322 (0.62%)	
occurrences (all)	1	14	
Peripheral Swelling			
subjects affected / exposed	1 / 13 (7.69%)	0 / 322 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 322 (0.31%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Abdominal Tenderness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	1 / 13 (7.69%)	5 / 322 (1.55%)	
occurrences (all)	1	5	
Food Poisoning			
subjects affected / exposed	1 / 13 (7.69%)	1 / 322 (0.31%)	
occurrences (all)	1	1	

Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	1 / 13 (7.69%)	3 / 322 (0.93%)	
occurrences (all)	1	4	
Tooth Disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Paranasal Sinus Hypersecretion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 322 (0.00%)	
occurrences (all)	1	0	
Sinus Congestion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 322 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dermatitis Allergic			
subjects affected / exposed	0 / 13 (0.00%)	2 / 322 (0.62%)	
occurrences (all)	0	2	
Pruritus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 13 (0.00%)	4 / 322 (1.24%)	
occurrences (all)	0	4	
Musculoskeletal Pain			
subjects affected / exposed	0 / 13 (0.00%)	2 / 322 (0.62%)	
occurrences (all)	0	2	
Costochondritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences (all)	0	1	
Pain In Extremity			
subjects affected / exposed	1 / 13 (7.69%)	2 / 322 (0.62%)	
occurrences (all)	1	2	

Osteoporotic Fracture			
subjects affected / exposed	1 / 13 (7.69%)	0 / 322 (0.00%)	
occurrences (all)	1	0	
Tenosynovitis Stenosans			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Body Tinea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 322 (0.00%)	
occurrences (all)	1	0	
Hordeolum			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences (all)	0	0	
Onychomycosis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 322 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	1 / 13 (7.69%)	3 / 322 (0.93%)	
occurrences (all)	1	3	
Pharyngitis Streptococcal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	1 / 13 (7.69%)	5 / 322 (1.55%)	
occurrences (all)	1	5	
Rash Pustular			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences (all)	0	0	
Tinea Versicolour			
subjects affected / exposed	0 / 13 (0.00%)	0 / 322 (0.00%)	
occurrences (all)	0	0	
Urinary Tract Infection			
subjects affected / exposed	0 / 13 (0.00%)	4 / 322 (1.24%)	
occurrences (all)	0	4	
Upper Respiratory Tract Infection			

subjects affected / exposed	1 / 13 (7.69%)	16 / 322 (4.97%)	
occurrences (all)	1	17	
Viral Pharyngitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 322 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 322 (0.31%)	
occurrences (all)	0	1	
Vitamin D Deficiency			
subjects affected / exposed	1 / 13 (7.69%)	1 / 322 (0.31%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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 study was prematurely terminated due to small number of subjects entering randomization.

Notes: