Clinical trial results:
A Randomized, Double-Blind, Parallel-Group Study Assessing the Efficacy And Safety of Sarilumab Monotherapy Versus Adalimumab Monotherapy in Patients With Rheumatoid Arthritis

Summary

EudraCT number	2014-002541-22
Trial protocol	DE CZ HU ES GB
Global end of trial date	29 December 2020

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

Trial information

Trial identification

Sponsor protocol code	EFC14092

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02332590
WHO universal trial number (UTN)	U1111-1160-6154
Other trial identifiers	Study name: SARIL-RA-MONARCH

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	28 January 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that sarilumab monotherapy is superior to adalimumab monotherapy with respect to signs and symptoms as assessed by disease activity score 28 (DAS28)-erythrocyte sedimentation rate (ESR) in subjects with active rheumatoid arthritis (RA) who are either intolerant of or considered inappropriate candidates for continued treatment with methotrexate (MTX), or after at least 12 weeks of continuous treatment with MTX, are determined to be inadequate responders.

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: -

Evidence for comparator: -

Actual start date of recruitment	28 January 2015
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: 75
Country: Number of subjects enrolled	Romania: 4
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Czechia: 25
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Hungary: 22
Country: Number of subjects enrolled	Chile: 53
Country: Number of subjects enrolled	Israel: 16
Country: Number of subjects enrolled	Korea, Republic of: 9
Country: Number of subjects enrolled	Peru: 18
Country: Number of subjects enrolled	Russian Federation: 44
Country: Number of subjects enrolled	South Africa: 4
Country: Number of subjects enrolled	Ukraine: 39
Country: Number of subjects enrolled	United States: 36

Worldwide total number of subjects	369
EEA total number of subjects	150

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)	303
From 65 to 84 years	66
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 86 centres in 15 countries. A total of 540 subjects were involved in the study from 28 January 2015 to 29-December-2020, of whom 369 subjects were randomised and 171 were screen failures. Screen failures were mainly due to exclusion criteria met and inclusion criteria not met.

Pre-assignment

Screening details:

Subjects were randomised in 1:1 ratio (Adalimumab 40 milligrams [mg] every 2 weeks [q2w]: Sarilumab 200 mg q2w) and treated for 24 weeks in double-blind (DB) period of the study. Out of 321 subjects who completed DB period, 320 subjects entered the open label extension (OLE) period of the study.

Period 1

Period 1 title	DB Period (Up to 24-weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Subject, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Adalimumab 40 mg/Sarilumab 200 mg

Arm description:

Adalimumab 40 mg subcutaneous (SC) injection in combination with placebo for sarilumab q2w for 24 weeks during the DB period. The dosing frequency of adalimumab was adjusted to 40 mg every week (qw) dosing in case of subjects with inadequate response (less than [<] 20% improvement from baseline in tender joint count [TJC] and swollen joint count [SJC] for 2 consecutive visits) at or after Week 16 until Week 23. Subjects who completed 24 weeks in the DB period had the option to continue OLE period and received sarilumab 200 mg q2w until commercial availability of sarilumab in their country or up to a maximum of an additional 276 weeks (i.e. up to Week 300).

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

Dosage and administration details:

One SC injection of adalimumab 40 mg in combination with matching placebo was administered q2w for 24 weeks.

Arm title	Sarilumab 200 mg/Sarilumab 200 mg

Arm description:

Sarilumab 200 mg SC injection in combination with placebo for adalimumab q2w for 24 weeks during the DB period. The dosing frequency of placebo for adalimumab was adjusted to 40 mg qw dosing in case of subjects with inadequate response (<20% improvement from baseline in TJC and SJC for 2 consecutive visits) at or after Week 16 until Week 23. Subjects who completed 24 weeks in the DB period had the option to continue in OLE period and received sarilumab 200 mg q2w until commercial availability of sarilumab in their country or up to a maximum of an additional 276 weeks (i.e. up to Week 300).

Arm type	Experimental

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

Dosage and administration details:

One SC injection of sarilumab 200 mg in combination with matching placebo was administered q2w for 24 weeks.

Number of subjects in period 1	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg
Started	185	184
Treated	184	184
Completed	156	165
Not completed	29	19
Other than specified above	6	5
Adverse event	15	11
Randomised but not treated	1	-
Poor compliance to protocol	3	1
Lack of efficacy	4	2

Period 2

Period 2 title	OLE Period (Week 24 up to Week 300)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Adalimumab 40 mg/Sarilumab 200 mg

Arm description:

Adalimumab 40 mg subcutaneous (SC) injection in combination with placebo for sarilumab q2w for 24 weeks during the DB period. The dosing frequency of adalimumab was adjusted to 40 mg every week (qw) dosing in case of subjects with inadequate response (less than [<] 20% improvement from baseline in tender joint count [TJC] and swollen joint count [SJC] for 2 consecutive visits) at or after Week 16 until Week 23. Subjects who completed 24 weeks in the DB period had the option to continue OLE period and received sarilumab 200 mg q2w until commercial availability of sarilumab in their country or up to a maximum of an additional 276 weeks (i.e. up to Week 300).

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

Dosage and administration details:

Subjects who completed 24 weeks in the DB period and continued in OLE period: received sarilumab 200 mg q2w until commercial availability of sarilumab in their country or up to a maximum of an additional 276 weeks.

Arm title	Sarilumab 200 mg/Sarilumab 200 mg

Arm description:

Sarilumab 200 mg SC injection in combination with placebo for adalimumab q2w for 24 weeks during the DB period. The dosing frequency of placebo for adalimumab was adjusted to 40 mg qw dosing in case of subjects with inadequate response (<20% improvement from baseline in TJC and SJC for 2 consecutive visits) at or after Week 16 until Week 23. Subjects who completed 24 weeks in the DB period had the option to continue in OLE period and received sarilumab 200 mg q2w until commercial availability of sarilumab in their country or up to a maximum of an additional 276 weeks (i.e. up to Week 300).

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

Dosage and administration details:

Subjects who completed 24 weeks in the DB period and continued OLE period; received sarilumab 200 mg q2w until commercial availability of sarilumab in their country or up to a maximum of an additional 276 weeks (i.e. up to Week 300).

Number of subjects in period 2[1]	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg
Started	155	165
Completed	108	120
Not completed	47	45
Adverse event	20	23
Other- Unspecified	20	15
Poor compliance to protocol	5	1
Lack of efficacy	2	6

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: 155 subjects entered OLE period and 1 did not enroll.

Baseline characteristics

Reporting groups	
Reporting group title	Adalimumab 40 mg/Sarilumab 200 mg
Reporting group description:	
Adalimumab 40 mg subcutaneous (SC) injection in combination with placebo for sarilumab q2w for 24 weeks during the DB period. The dosing frequency of adalimumab was adjusted to 40 mg every week (qw) dosing in case of subjects with inadequate response (less than [<] 20% improvement from baseline in tender joint count [TJC] and swollen joint count [SJC] for 2 consecutive visits) at or after Week 16 until Week 23. Subjects who completed 24 weeks in the DB period had the option to continue OLE period and received sarilumab 200 mg q2w until commercial availability of sarilumab in their country or up to a maximum of an additional 276 weeks (i.e. up to Week 300).	
Reporting group title	Sarilumab 200 mg/Sarilumab 200 mg
Reporting group description:	
Sarilumab 200 mg SC injection in combination with placebo for adalimumab q2w for 24 weeks during the DB period. The dosing frequency of placebo for adalimumab was adjusted to 40 mg qw dosing in case of subjects with inadequate response (<20% improvement from baseline in TJC and SJC for 2 consecutive visits) at or after Week 16 until Week 23. Subjects who completed 24 weeks in the DB period had the option to continue in OLE period and received sarilumab 200 mg q2w until commercial availability of sarilumab in their country or up to a maximum of an additional 276 weeks (i.e. up to Week 300).	

Reporting group values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg	Total
Number of subjects	185	184	369
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	53.6	50.9	
standard deviation	± 11.9	± 12.6	-
Gender categorical Units: Subjects			
Female	150	157	307
Male	35	27	62
Race/Ethnicity Units: Subjects			
Caucasian/White	164	171	335
Black	3	1	4
Asian/Oriental	9	2	11
Other	9	10	19
Disease Activity Score 28 based on erythrocyte sedimentation rate (DAS28-ESR)			
DAS28-ESR is a composite score that includes 4 variables: TJC (based on 28 joints); SJC (based on 28 joints); General health (GH) assessment by the subject assessed from the American College of Rheumatology (ACR) rheumatoid arthritis (RA) core set questionnaire (subject global assessment) in 100 mm visual analog scale (VAS); Marker of inflammation assessed by ESR in mm/hr.			
Units: units on a scale			
arithmetic mean	6.76	6.83	
standard deviation	± 0.83	± 0.76	-

End points

End points reporting groups

Reporting group title	Adalimumab 40 mg/Sarilumab 200 mg

Reporting group description:

Adalimumab 40 mg subcutaneous (SC) injection in combination with placebo for sarilumab q2w for 24 weeks during the DB period. The dosing frequency of adalimumab was adjusted to 40 mg every week (qw) dosing in case of subjects with inadequate response (less than [<] 20% improvement from baseline in tender joint count [TJC] and swollen joint count [SJC] for 2 consecutive visits) at or after Week 16 until Week 23. Subjects who completed 24 weeks in the DB period had the option to continue OLE period and received sarilumab 200 mg q2w until commercial availability of sarilumab in their country or up to a maximum of an additional 276 weeks (i.e. up to Week 300).

Reporting group title	Sarilumab 200 mg/Sarilumab 200 mg

Reporting group description:

Sarilumab 200 mg SC injection in combination with placebo for adalimumab q2w for 24 weeks during the DB period. The dosing frequency of placebo for adalimumab was adjusted to 40 mg qw dosing in case of subjects with inadequate response (<20% improvement from baseline in TJC and SJC for 2 consecutive visits) at or after Week 16 until Week 23. Subjects who completed 24 weeks in the DB period had the option to continue in OLE period and received sarilumab 200 mg q2w until commercial availability of sarilumab in their country or up to a maximum of an additional 276 weeks (i.e. up to Week 300).

Reporting group title	Adalimumab 40 mg/Sarilumab 200 mg

Reporting group description:

Adalimumab 40 mg subcutaneous (SC) injection in combination with placebo for sarilumab q2w for 24 weeks during the DB period. The dosing frequency of adalimumab was adjusted to 40 mg every week (qw) dosing in case of subjects with inadequate response (less than [<] 20% improvement from baseline in tender joint count [TJC] and swollen joint count [SJC] for 2 consecutive visits) at or after Week 16 until Week 23. Subjects who completed 24 weeks in the DB period had the option to continue OLE period and received sarilumab 200 mg q2w until commercial availability of sarilumab in their country or up to a maximum of an additional 276 weeks (i.e. up to Week 300).

Reporting group title	Sarilumab 200 mg/Sarilumab 200 mg

Reporting group description:

Sarilumab 200 mg SC injection in combination with placebo for adalimumab q2w for 24 weeks during the DB period. The dosing frequency of placebo for adalimumab was adjusted to 40 mg qw dosing in case of subjects with inadequate response (<20% improvement from baseline in TJC and SJC for 2 consecutive visits) at or after Week 16 until Week 23. Subjects who completed 24 weeks in the DB period had the option to continue in OLE period and received sarilumab 200 mg q2w until commercial availability of sarilumab in their country or up to a maximum of an additional 276 weeks (i.e. up to Week 300).

Primary: DB Period: Change From Baseline in Disease Activity Score for 28 Joints - Erythrocyte Sedimentation Rate (DAS28-ESR) Score at Week 24

End point title	DB Period: Change From Baseline in Disease Activity Score for 28 Joints - Erythrocyte Sedimentation Rate (DAS28-ESR) Score at Week 24

End point description:

DAS28-ESR is a composite score that includes 4 variables: TJC (based on 28 joints); SJC (based on 28 joints); GH assessment by the subject assessed from the ACR and RA core set questionnaire (subject global assessment) in 100 mm VAS; marker of inflammation assessed by ESR in mm/hr. The DAS28-ESR score provides a number indicating the current disease activity of the RA. DAS28-ESR total score ranges from 2-10. A DAS28-ESR score above 5.1 means high disease activity, DAS28-ESR score below 3.2 indicates low disease activity and DAS28-ESR score below 2.6 means disease remission. Least square (LS) mean and standard error (SE) at Week 24 were obtained using Mixed-effect model with repeated measures (MMRM) approach. Intent-to-treat (ITT) population included all subjects. Here, number of subjects analysed = subjects with DAS28-ESR assessment at both baseline and Week 24.

End point type	Primary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	165		
Units: units on a scale				
least squares mean (standard error)	-2.20 (± 0.106)	-3.28 (± 0.105)		

Statistical analyses

Statistical analysis title	Adalimumab 40 mg/Sarilumab 200 mg, Sarilumab 200mg

Statistical analysis description:

Analysis was performed using MMRM approach with treatment, region, visits, and treatment-by-visit interaction as fixed effects and baseline DAS28-ESR score as a continuous covariate. Hierarchical testing procedure was used to control overall alpha error rate at 0.05 level and handle multiple endpoint analyses. Testing was then performed sequentially in order endpoints are reported. Hierarchical testing sequence continued only when previous endpoint was statistically significant at 0.05 level.

Comparison groups	Adalimumab 40 mg/Sarilumab 200 mg v Sarilumab 200 mg/Sarilumab 200 mg
Number of subjects included in analysis	328
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.077
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.361
upper limit	-0.793

Notes:

[1] - Threshold for significance at 0.05 level.

Secondary: DB Period: Percentage of Subjects Achieving Clinical Remission Score (DAS28-ESR <2.6) at Week 24

End point title	DB Period: Percentage of Subjects Achieving Clinical Remission Score (DAS28-ESR <2.6) at Week 24

End point description:

DAS28-ESR is a composite score that includes 4 variables: TJC (based on 28 joints); SJC (based on 28 joints); GH assessment by the subject assessed from the ACR RA core set questionnaire (subject global assessment) in 100 mm VAS; marker of inflammation assessed by ESR in mm/hr. The DAS28-ESR score provides a number indicating the current disease activity of the RA. DAS28-ESR total score ranges from 2-10. A DAS28-ESR score above 5.1 means high disease activity, DAS28-ESR score below 3.2 indicates low disease activity and DAS28-ESR score below 2.6 means disease remission. Subjects who discontinued treatment prior to Week 24 were analysed as non-responders. ITT population.

End point type	Secondary

End point timeframe:

Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	184		
Units: percentage of subjects				
number (not applicable)	7.0	26.6		

Statistical analyses

Statistical analysis title	Adalimumab 40 mg/Sarilumab 200 mg, Sarilumab 200mg

Statistical analysis description:

Testing according to the hierarchical testing procedure (only performed if the previous endpoint was statistically significant). Analysis was performed using Cochran-Mantel-Haenszel method stratified by region.

Comparison groups	Sarilumab 200 mg/Sarilumab 200 mg v Adalimumab 40 mg/Sarilumab 200 mg
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	4.879
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.536
upper limit	9.389

Notes:

[2] - Threshold for significance at 0.05 level.

Secondary: DB Period: Percentage of Subjects Achieving ACR50 Criteria at Week 24

End point title	DB Period: Percentage of Subjects Achieving ACR50 Criteria at Week 24

End point description:

ACR responses are assessed with a composite rating scale of the ACR that includes 7 variables: TJC (68 joints); SJC (66 joints); levels of an acute phase reactant (C-reactive protein [CRP] level); subject's assessment of pain (measured on 0 [no pain]-100 mm [worst pain] VAS); subject's global assessment of disease activity (measured on 0 [no arthritis activity]-100 mm [maximal arthritis activity] VAS); physician's global assessment of disease activity (measured on 0 [no arthritis activity]-100 mm [maximal arthritis activity] VAS); subject's assessment of physical function (measured by Health Assessment Questionnaire - Disability Index [HAQ-DI], with scoring range of 0 [better physical function] - 3 [worst physical function]). ACR50 is defined as achieving at least 50% improvement in both TJC and SJC, and at least 50% improvement in at least 3 of the 5 other assessments of the ACR. Subjects were analysed as non-responders from the time they discontinued treatment. ITT Population.

End point type	Secondary

End point timeframe:

Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	184		
Units: percentage of subjects				
number (not applicable)	29.7	45.7		

Statistical analyses

Statistical analysis title	Adalimumab 40 mg/Sarilumab 200 mg, Sarilumab 200mg

Statistical analysis description:

Testing according to the hierarchical testing procedure (only performed if the previous endpoint was statistically significant). Analysis was performed using Cochran-Mantel-Haenszel method stratified by region.

Comparison groups	Adalimumab 40 mg/Sarilumab 200 mg v Sarilumab 200 mg/Sarilumab 200 mg
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0017 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.976
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.289
upper limit	3.028

Notes:

[3] - Threshold for significance at 0.05 level.

Secondary: DB Period: Percentage of Subjects Achieving ACR70 Criteria at Week 24

End point title	DB Period: Percentage of Subjects Achieving ACR70 Criteria at Week 24

End point description:

ACR responses are assessed with a composite rating scale of the ACR that includes 7 variables: TJC (68 joints); SJC (66 joints); levels of an acute phase reactant (CRP level); subject's assessment of pain (measured on 0 [no pain]-100 mm [worst pain] VAS); subject's global assessment of disease activity (measured on 0 [no arthritis activity]-100 mm [maximal arthritis activity] VAS); physician's global assessment of disease activity (measured on 0 [no arthritis activity]-100 mm [maximal arthritis activity] VAS); subject's assessment of physical function (measured by HAQ-DI, with scoring range of 0 [better physical function] - 3 [worst physical function]). ACR70 was defined as achieving at least 70% improvement in both TJC and SJC, and at least 70% improvement in at least 3 of the 5 other assessments. Subjects were analysed as non-responders from the time they discontinued treatment. ITT Population.

End point type	Secondary

End point timeframe:

Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	184		
Units: percentage of subjects				
number (not applicable)	11.9	23.4		

Statistical analyses

Statistical analysis title	Adalimumab 40 mg/Sarilumab 200 mg, Sarilumab 200mg

Statistical analysis description:

Testing according to the hierarchical testing procedure (only performed if the previous endpoint was statistically significant). Analysis was performed using Cochran-Mantel- Haenszel method stratified by region.

Comparison groups	Adalimumab 40 mg/Sarilumab 200 mg v Sarilumab 200 mg/Sarilumab 200 mg
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0036 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.286
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	4.02

Notes:

[4] - Threshold for significance at 0.05 level.

Secondary: DB Period: Percentage of Subjects Achieving ACR20 Criteria at Week 24

End point title	DB Period: Percentage of Subjects Achieving ACR20 Criteria at Week 24

End point description:

ACR responses are assessed with a composite rating scale of the ACR that includes 7 variables: TJC (68 joints); SJC (66 joints); levels of an acute phase reactant (CRP level); subject's assessment of pain (measured on 0 [no pain]-100 mm [worst pain] VAS); subject's global assessment of disease activity (measured on 0 [no arthritis activity]-100 mm [maximal arthritis activity] VAS); physician's global assessment of disease activity (measured on 0 [no arthritis activity]-100 mm [maximal arthritis activity] VAS); subject's assessment of physical function (measured by HAQ-DI, with scoring range of 0 [better physical function] - 3 [worst physical function]). ACR20 was defined as achieving at least 20% improvement in both TJC and SJC, and at least 20% improvement in at least 3 of the 5 other assessments. Subjects were analysed as non-responders from the time they discontinued treatment. ITT population.

End point type	Secondary

End point timeframe:

Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	184		
Units: percentage of subjects				
number (not applicable)	58.4	71.7		

Statistical analyses

Statistical analysis title	Adalimumab 40 mg/Sarilumab 200 mg, Sarilumab 200mg

Statistical analysis description:

Testing according to the hierarchical testing procedure (only performed if the previous endpoint was statistically significant). Analysis was performed using Cochran-Mantel-Haenszel method stratified by region.

Comparison groups	Adalimumab 40 mg/Sarilumab 200 mg v Sarilumab 200 mg/Sarilumab 200 mg
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0074 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.168
upper limit	2.773

Notes:

[5] - Threshold for significance 0.05 level.

Secondary: DB Period: Change From Baseline in HAQ-DI at Week 24

End point title	DB Period: Change From Baseline in HAQ-DI at Week 24

End point description:

Physical function was assessed by HAQ-DI. It consisted of at least 2 or 3 questions per category, subject reported assessment of ability to perform tasks in 8 categories of daily living activities: dress/groom; arise; eat; walk; reach; grip; hygiene; and common activities over past week rated on a 4-point scale where 0 = no difficulty; 1 = some difficulty; 2 = much difficulty; 3 = unable to do. Overall score was computed as the sum of category scores and divided by the number of categories answered, ranging from 0 to 3, where 0 = no disability and 3 = unable to do, high-dependency disability. LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with HAQ-DI assessment at both baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	165		
Units: units on a scale				
least squares mean (standard error)	-0.43 (± 0.045)	-0.61 (± 0.045)		

Statistical analyses

Statistical analysis title	Adalimumab 40 mg/Sarilumab 200 mg, Sarilumab 200mg

Statistical analysis description:

Testing according to the hierarchical testing procedure (only performed if the previous endpoint was statistically significant). Analysis was performed using MMRM approach with treatment, region, visits, and treatment-by-visit interaction as fixed effects and baseline HAQ-DI score as a continuous covariate.

Comparison groups	Adalimumab 40 mg/Sarilumab 200 mg v Sarilumab 200 mg/Sarilumab 200 mg
Number of subjects included in analysis	323
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0037 [6]
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.182
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.305
upper limit	-0.059

Notes:

[6] - Threshold for significance at 0.05 level.

Secondary: DB Period: Change From Baseline in Short-Form-36 (SF-36) - Physical Component Summary (PCS) Score at Week 24

End point title	DB Period: Change From Baseline in Short-Form-36 (SF-36) - Physical Component Summary (PCS) Score at Week 24

End point description:

SF-36 is a generic 36-item questionnaire of 8 sub-scales, measures health-related quality of life (HRQL) in last 4 weeks covering 2 summary measures: PCS and mental component summary (MCS). PCS with 4 sub-scales: physical function, role limitations due to physical problems, pain, general health perception; and MCS with 4 subscales: vitality, social function, role limitations due to emotional problems, and mental health. Subjects self-report on items in a sub-scale that have between 2-6 choices per item using Likert-type responses (e.g. none of the time, some of the time, etc.). Summations of item scores of same sub-scale give the sub-scale scores, which are transformed into a range from 0-100; 0= worst HRQL, 100=best HRQL. Both PCS and MCS range from 0-100 with higher scores indicating better physical and mental health. LS mean and SE at Week 24 by MMRM approach. ITT population. Here, number of subjects analysed = subjects with SF-36 PCS score assessment at baseline and week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	159		
Units: units on a scale				
least squares mean (standard error)	6.09 (± 0.555)	8.74 (± 0.555)		

Statistical analyses

Statistical analysis title	Adalimumab 40 mg/Sarilumab 200 mg, Sarilumab 200mg

Statistical analysis description:

Testing according to the hierarchical testing procedure (only performed if the previous endpoint was statistically significant). Analysis was performed using MMRM approach with treatment, region, visits, and treatment-by-visit interaction as fixed effects and baseline SF-36 PCS score as a continuous covariate.

Comparison groups	Sarilumab 200 mg/Sarilumab 200 mg v Adalimumab 40 mg/Sarilumab 200 mg
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006 [7]
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	2.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.147
upper limit	4.153

Notes:

[7] - Threshold for significance at 0.05 level.

Secondary: DB Period: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score at Week 24

End point title	DB Period: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Score at Week 24

End point description:

The FACIT-F is a 13-item questionnaire assessing fatigue where subjects scored each item on a 5-point scale (0-4): 0=not at all, 1=a little bit, 2=somewhat, 3=quite a bit, 4=very much. A total score ranges from 0 to 52, where higher score corresponds to a lower level of fatigue. A positive change from baseline score indicates an improvement. LS mean and SE at Week 24 by MMRM approach. ITT population. Here, number of subjects analysed = subjects with FACIT-F score assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	165		
Units: units on a scale				
least squares mean (standard error)	8.41 (± 0.709)	10.18 (± 0.701)		

Statistical analyses

Statistical analysis title	Adalimumab 40 mg/Sarilumab 200 mg, Sarilumab 200mg

Statistical analysis description:

Testing according to the hierarchical testing procedure (only performed if the previous endpoint was statistically significant). Analysis was performed using MMRM approach with treatment, region, visits, and treatment-by-visit interaction as fixed effects and baseline FACIT-F score as a continuous covariate.

Comparison groups	Adalimumab 40 mg/Sarilumab 200 mg v Sarilumab 200 mg/Sarilumab 200 mg
Number of subjects included in analysis	323
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0689 [8]
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	1.768
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.137
upper limit	3.674

Notes:

[8] - Threshold for significance at 0.05 level.

Secondary: DB Period: Change From Baseline in SF-36 - Mental Health Component Summary Score at Week 24

End point title	DB Period: Change From Baseline in SF-36 - Mental Health Component Summary Score at Week 24

End point description:

SF-36 is a generic 36-item questionnaire consisting of 8 sub-scales, measures HRQL in the last 4 weeks covering 2 summary measures: PCS and MCS. PCS with 4 subscales: physical function, role limitations due to physical problems, pain, and general health perception; and MCS with 4 subscales: vitality, social function, role limitations due to emotional problems, and mental health. Subjects self-report on items in a subscale that have between 2-6 choices per item using Likert-type responses (e.g. none of the time, some of the time, etc.). Summations of item scores of the same subscale give the sub-scale scores, which are transformed into a range from 0 to 100; 0= worst HRQL, 100=best HRQL. Both PCS and MCS range from 0-100 with higher scores indicating better physical and mental health. LS mean and SE at Week 24 by MMRM approach. ITT population. Here, number of subjects analysed = subjects with SF-36 - mental health component summary score assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	159		
Units: units on a scale				
least squares mean (standard error)	6.83 (± 0.774)	7.86 (± 0.773)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in Disease Activity Score for 28 Joints Based on C-Reactive Protein (DAS28-CRP Score) at Week 24

End point title	DB Period: Change From Baseline in Disease Activity Score for 28 Joints Based on C-Reactive Protein (DAS28-CRP Score) at Week 24

End point description:

DAS28-CRP is a composite score that includes 4 variables: TJC (based on 28 joints); SJC (based on 28 joints); GH assessment by the subject assessed from the ACR RA core set questionnaire (subject global assessment) in 100 mm VAS; Marker of inflammation assessed by high sensitivity C-reactive protein (hs-CRP) in mg/L. The DAS28-CRP score provides a number indicating the current disease activity of the RA. DAS28-CRP total score ranges from 2-10. A DAS28-CRP score above 5.1 means high disease activity, whereas a DAS28-CRP score below 3.2 indicates low disease activity and a DAS28-CRP score below 2.6 means disease remission. LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with DAS28-CRP score assessment at both baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	163		
Units: units on a scale				
least squares mean (standard error)	-1.97 (± 0.094)	-2.86 (± 0.093)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

DAS28-CRP is a composite score that includes 4 variables: TJC (based on 28 joints); SJC (based on 28 joints); GH assessment by the subject assessed from the ACR RA core set questionnaire (subject global assessment) in 100 mm VAS; Marker of inflammation assessed by hs-CRP in mg/L. The DAS28-CRP score provides a number indicating the current disease activity of the RA. DAS28-CRP total score ranges from 2-10. A DAS28-CRP score above 5.1 means high disease activity, whereas a DAS28-CRP score below 3.2 indicates low disease activity and a DAS28-CRP score below 2.6 means disease remission. Subjects were analysed as non-responders from the time they discontinued treatment. ITT population.

End point type	Secondary

End point timeframe:

Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	184		
Units: percentage of subjects				
number (not applicable)	13.5	34.2		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Percentage of Subjects Achieving Low Disease Activity (DAS28-ESR < 3.2) at Week 24

End point title	DB Period: Percentage of Subjects Achieving Low Disease Activity (DAS28-ESR < 3.2) at Week 24

End point description:

DAS28-ESR is a composite score that includes 4 variables: TJC (based on 28 joints); SJC (based on 28 joints); GH assessment by the subject assessed from the ACR RA core set questionnaire (subject global assessment) in 100 mm VAS; Marker of inflammation assessed by ESR in mm/hr. The DAS28-ESR score provides a number indicating the current disease activity of the RA. DAS28-ESR total score ranges from 2-10. A DAS28-ESR score above 5.1 means high disease activity, DAS28-ESR score below 3.2 indicates low disease activity and DAS28-ESR score below 2.6 means disease remission. Subjects were analysed as non-responders from the time they discontinued treatment. ITT population.

End point type	Secondary

End point timeframe:

Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	184		
Units: percentage of subjects				
number (not applicable)	14.1	42.9		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Percentage of Subjects Achieving Clinical Disease Activity Index (CDAI) Remission (CDAI <=2.8) at Week 24

End point title	DB Period: Percentage of Subjects Achieving Clinical Disease Activity Index (CDAI) Remission (CDAI <=2.8) at Week 24

End point description:

CDAI is a composite index constructed to measure clinical remission in RA that does not include a laboratory test, and is a numerical summation of 4 components: SJC (28 joints), TJC (28 joints), subject's global assessment of disease activity (in cm), and physician's global assessment of disease activity (in cm). Total score ranges from 0 to 76 with a lower score indicating less disease activity. Subjects were analysed as non-responders from the time they discontinued treatment. ITT population.

End point type	Secondary

End point timeframe:

Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	184		
Units: percentage of subjects				
number (not applicable)	2.7	7.1		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in CDAI at Week 24

End point title	DB Period: Change From Baseline in CDAI at Week 24

End point description:

CDAI is a composite index constructed to measure clinical remission in RA that does not include a laboratory test, and is a numerical summation of 4 components: SJC (28 joints), TJC (28 joints), subject's global assessment of disease activity (in cm), and physician's global assessment of disease activity (VAS in cm). Total score ranges from 0 to 76 with a lower score indicating less disease activity. A negative change in CDAI score indicates an improvement in disease activity and a positive change in score indicates a worsening of disease activity. LS means and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with CDAI assessment both at

baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	165		
Units: units on a scale				
least squares mean (standard error)	-25.20 (± 0.842)	-28.94 (± 0.834)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in European Quality of Life-5 Dimension 3 Level (EQ-5D-3L) Scores at Week 24

End point title	DB Period: Change From Baseline in European Quality of Life-5 Dimension 3 Level (EQ-5D-3L) Scores at Week 24

End point description:

EQ-5D-3L is a standardised, generic measure of health outcome. EQ-5D was designed for self-completion by subjects. EQ-5D was specifically included to address concerns regarding health economic impact of RA. EQ-5D-3L comprises of 5 questions on mobility, self-care, pain/discomfort, usual activities, and psychological status with 3 possible answers for each item (1=no problem, 2=moderate problems, 3=severe problems). 5-dimensional 3-level systems are converted into a single index utility score between 0 to 1, where higher score indicates a better health state. EQ-5D-3L-VAS records the subject’s self-rated health on a vertical VAS that allows the subjects to indicate their health state ranging from 0 (worst imaginable) to 100 (best imaginable). LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, "number of subjects analysed" = subjects with EQ-5D-3L score assessment both at baseline and Week 24, and "n" = subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	164		
Units: units on a scale				
least squares mean (standard error)				
EQ-5D Single index utility score (n=156,160)	0.26 (± 0.019)	0.32 (± 0.019)		
EQ-5D VAS (n=156,164)	19.94 (± 1.720)	24.22 (± 1.686)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in Rheumatoid Arthritis Impact of Disease (RAID) at Week 24

End point title	DB Period: Change From Baseline in Rheumatoid Arthritis Impact of Disease (RAID) at Week 24

End point description:

RAID is a composite measure of the impact of RA on subjects that takes into account 7 domains: pain, functional disability, fatigue, physical and emotional well-being, quality of sleep, and coping. The RAID is calculated based on 7 numerical rating scales (NRS) questions. Each NRS is assessed as a number between 0 and 10 that corresponds to the 7 domains. The values for each of these domains are weighed by subject assessment of relative importance and combined in a single score with a total score range of 0 (not affected, very good) to 10 (most affected). LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with RAID assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	161		
Units: units on a scale				
least squares mean (standard error)	-2.30 (± 0.168)	-3.08 (± 0.168)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in Work Productivity Survey - Rheumatoid Arthritis (WPS-RA) at Week 24: Work Days Missed Due to Arthritis

End point title	DB Period: Change From Baseline in Work Productivity Survey - Rheumatoid Arthritis (WPS-RA) at Week 24: Work Days Missed Due to Arthritis

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire is interviewer-administered and based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Number of work days missed in the last month by the subject was reported. LS mean and SE at Week 24 were obtained using MMRM

approach. ITT population. Here, number of subjects analysed = subjects with WPS-RA values available: Individual items assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	70		
Units: days				
least squares mean (standard error)	0.05 (± 0.611)	-0.28 (± 0.547)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in WPS-RA at Week 24: Days With Work Productivity Reduced by >= 50% Due to Arthritis

End point title	DB Period: Change From Baseline in WPS-RA at Week 24: Days With Work Productivity Reduced by >= 50% Due to Arthritis

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire is interviewer-administered and based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Number of work days with reduced productivity by >= 50% in the last month by the subjects was reported. LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with WPS-RA values available: Individual items assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	70		
Units: days				
least squares mean (standard error)	-3.50 (± 0.525)	-3.74 (± 0.456)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in WPS-RA at Week 24: Arthritis Interference With Work Productivity

End point title	DB Period: Change From Baseline in WPS-RA at Week 24: Arthritis Interference With Work Productivity

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire is interviewer-administered and based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Interference in the last month with work productivity was measured on a scale that ranges from 0 (no interference) to 10 (complete interference). LS mean and SE at Week 24 were obtained using MMRM approach. ITT Population. Here, number of subjects analysed = subjects with WPS-RA values available: Individual items assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	69		
Units: units on a scale				
least squares mean (standard error)	-2.510 (± 0.3470)	-2.919 (± 0.3073)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in WPS-RA at Week 24: House Work Days Missed Due to Arthritis

End point title	DB Period: Change From Baseline in WPS-RA at Week 24: House Work Days Missed Due to Arthritis

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire is interviewer-administered and based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Number of days with no household work in the last month by the subjects was reported. LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with WPS-RA values available: Individual items assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	169		
Units: days				
least squares mean (standard error)	-4.22 (± 0.405)	-5.49 (± 0.400)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in WPS-RA at Week 24: Days With Household Work Productivity Reduced by >= 50% Due to Arthritis

End point title	DB Period: Change From Baseline in WPS-RA at Week 24: Days With Household Work Productivity Reduced by >= 50% Due to Arthritis

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire is interviewer-administered and based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Number of days with reduced household work productivity by >= 50% in the last month by the subjects was reported. LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with WPS-RA values available: Individual items assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	169		
Units: days				
least squares mean (standard error)	-4.87 (± 0.451)	-6.70 (± 0.445)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in WPS-RA at Week 24: Days With Family/Social/Leisure Activities Missed Due to Arthritis

End point title	DB Period: Change From Baseline in WPS-RA at Week 24: Days With Family/Social/Leisure Activities Missed Due to Arthritis

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within

home associated with RA over the previous month. The questionnaire is interviewer-administered and based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Number of days missed of family/social/leisure activities in the last month by the subjects was reported. LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with WPS-RA values available: Individual items assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	169		
Units: days				
least squares mean (standard error)	-3.33 (± 0.376)	-4.14 (± 0.371)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in WPS-RA at Week 24: Days With Outside Help Hired Due to Arthritis

End point title	DB Period: Change From Baseline in WPS-RA at Week 24: Days With Outside Help Hired Due to Arthritis

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire is interviewer-administered and based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Number of days with outside help hired in the last month by the subject was reported. LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with WPS-RA values available: Individual items assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	168		
Units: days				
least squares mean (standard error)	-2.57 (± 0.401)	-3.43 (± 0.398)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in WPS-RA at Week 24: RA Interference With Household Work Productivity

End point title	DB Period: Change From Baseline in WPS-RA at Week 24: RA Interference With Household Work Productivity

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire is interviewer-administered and based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). The RA interference in the last month with household work productivity was measured on a scale that ranges from 0 (no interference) to 10 (complete interference). LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with WPS-RA values available: Individual items assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	168		
Units: units on a scale				
least squares mean (standard error)	-2.605 (± 0.2110)	-3.276 (± 0.2099)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in Morning Stiffness VAS at Week 24

End point title	DB Period: Change From Baseline in Morning Stiffness VAS at Week 24

End point description:

RA is associated with stiffness of joints, especially in the morning after prolonged stationery state. The degree of stiffness can be an indicator of disease severity. The severity of morning stiffness was assessed on a VAS scale from 0 mm (no problem) to 100 mm (major problem). LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with morning stiffness VAS assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	165		
Units: mm				
least squares mean (standard error)	-29.29 (± 1.970)	-35.08 (± 1.947)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in Individual ACR Component - TJC and SJC at Week 24

End point title	DB Period: Change From Baseline in Individual ACR Component - TJC and SJC at Week 24

End point description:

ACR components were: TJC, SJC, physician global VAS, subject global VAS, pain VAS, HAQ-DI & acute phase reactant (hs-CRP and ESR levels). 68 joints were assessed for tenderness (TJC scoring 0-68) and 66 joints for swelling (SJC scoring 0-66). The 66 SJC evaluated the following joints: temporomandibular, sternoclavicular, acromioclavicular, shoulder, elbow, wrist, metacarpophalangeal, interphalangeal of thumb, distal interphalangeal, proximal interphalangeal, knee, ankle mortise, ankle tarsus, metatarsophalangeal, interphalangeal of great toe, and proximal/distal interphalangeal of the toes. The TJC examined hip joints, in addition to the joints assessed for SJC. Increase in number of tender joints/swollen joints indicated severity. LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with TJC and SJC assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	166		
Units: joints				
least squares mean (standard error)				
TJC	-16.45 (± 0.781)	-18.23 (± 0.772)		
SJC	-12.20 (± 0.450)	-13.44 (± 0.444)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in Individual ACR Component - Physician Global VAS, Subject Global VAS and Pain VAS at Week 24

End point title	DB Period: Change From Baseline in Individual ACR Component - Physician Global VAS, Subject Global VAS and Pain VAS at Week 24

End point description:

ACR components were: TJC, SJC, physician global VAS, subject global VAS, pain VAS, HAQ-DI & acute phase reactant (hs-CRP and ESR levels). Physician global VAS & subject global VAS was done on 100 mm horizontal anchored VAS, ranging from 0 “no arthritis activity” to 100 “maximal arthritis activity” and Pain VAS on 100 mm VAS, ranging from 0 “no pain” to 100 “worst pain”. LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with individual ACR components assessment both at baseline and Week 24, and "n" = subjects with available data for specified category for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	166		
Units: mm				
least squares mean (standard error)				
Physician global VAS (n=158,166)	-37.80 (± 1.431)	-45.33 (± 1.414)		
Subject global VAS (n=158,165)	-24.82 (± 1.752)	-33.30 (± 1.731)		
Pain VAS (n=157,165)	-27.41 (± 1.802)	-36.19 (± 1.776)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in Individual ACR Component - CRP Level at Week 24

End point title	DB Period: Change From Baseline in Individual ACR Component - CRP Level at Week 24

End point description:

ACR components were: TJC, SJC, physician global VAS, subject global VAS, pain VAS, HAQ-DI and acute phase reactant (hs-CRP and ESR levels). An elevated CRP level is considered a non-specific "marker" for RA. A decrease indicates improvement. LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with CRP assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	164		
Units: mg/L				
least squares mean (standard error)	-2.91 (± 1.461)	-17.01 (± 1.431)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Change From Baseline in Individual ACR Component- ESR Level at Week 24

End point title	DB Period: Change From Baseline in Individual ACR Component- ESR Level at Week 24

End point description:

ACR components were: TJC, SJC, physician global VAS, subject global VAS, pain VAS, HAQ-DI & acute phase reactant (hs-CRP and ESR levels). The ESR is a blood test that can reveal inflammatory activity. Inflammation can cause the cells to clump together. The farther the red blood cells have descended, the greater the inflammatory response. LS mean and SE at Week 24 were obtained using MMRM approach. ITT population. Here, number of subjects analysed = subjects with ESR assessment both at baseline and Week 24.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	166		
Units: mm/hr				
least squares mean (standard error)	-12.74 (± 1.398)	-32.11 (± 1.388)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point title	DB Period: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point description:

Adverse event (AE) was defined as any untoward medical occurrence in subject who received investigational medicinal product (IMP) and did not necessarily had to have causal relationship with treatment. All reported AEs were TEAEs developed/worsened during 'on treatment period' (time from first dose of study drug up to day before first dose of open-label treatment for subjects who completed 24-week randomised//DB treatment). SAEs were AEs resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly or a medically important event. DB period safety population which consisted of all randomised subjects who received at least one dose of study medication analysed according to the treatment they have actually received.

End point type	Secondary

End point timeframe:

From Week 0 to Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	184		
Units: subjects				
TEAEs	117	118		
SAEs	13	9		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Subjects With Treatment-emergent Adverse Events and Serious Adverse Events

End point title	OLE Period: Number of Subjects With Treatment-emergent Adverse Events and Serious Adverse Events

End point description:

AE was defined as any untoward medical occurrence in subject who received IMP and did not necessarily had to have causal relationship with treatment. All reported AEs were TEAEs developed/worsened during 'on treatment period' (from end of week 24 [Baseline of OLE Period] up to last dose in OLE period + 6 weeks [follow-up], regardless of unplanned intermittent discontinuations). SAEs were AEs resulting in

any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly or a medically important event. OLE period safety population which included all randomised subjects who continued OLE period and received at least one dose of the study medication during OLE period, analysed according to the treatment they have actually received.

End point type	Secondary

End point timeframe:

From end of Week 24 (Baseline of OLE Period) up to last dose in OLE + 6 weeks of follow up (i.e. up to Week 306)

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	155	165		
Units: subjects				
TEAE	135	143		
SAE	31	25		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Number of Subjects With Potentially Clinically Significant Abnormalities (PCSA) - Hematological Parameters

End point title	DB Period: Number of Subjects With Potentially Clinically Significant Abnormalities (PCSA) - Hematological Parameters

End point description:

Criteria for PCSA included:
• Hemoglobin (Hb): less than or equal to (<=) 115 grammes per litre (g/L)(Male), <= 95 g/L (Female); greater than or equal to (>=) 185 g/L (18.5 g/dL) (Male), >= 165 g/L (16.5 g/dL) (Female); Decrease From Baseline (DFB) = 20 g/L (2g/dL).
• Hematocrit: <= 0.37 volume/volume (v/v) (Male); <= 0.32 v/v (Female); >= 0.55 v/v (Male); >= 0.5 v/v(Female).
• Red Blood Cells (RBCs): >=6 Tera/ litre (L).
• Platelets: < 50 Giga/L (G/L), 50 - 100 G/L, >= 700 G/L.
• White blood cells (WBC): < 3.0 G/L (Non-Black); < 2.0 G/L (Black), >= 16.0 G/L.
• Neutrophils: < 1.0 G/L, < 1.5 G/L (Non-Black); < 1.0 G/L (Black).
• Lymphocytes: < 0.5 G/L, >= 0.5 G/L - lower limit of normal (LLN), > 4.0 G/L.
• Monocytes: > 0.7 G/L.
• Basophils: > 0.1 G/L.
• Eosinophils: > 0.5 G/L or > upper limit of normal (ULN) (if ULN >= 0.5 G/L).
DB safety population. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

From Week 0 to Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	184		
Units: subjects				
Hb:<=115 g/L, <=95 g/L (n=184,184)	12	7		
Hb: >=185 g/L, >=165 g/L (n=184,184)	0	1		
Hb: DFB >=20 g/L (n=184,184)	5	5		
Hematocrit: <= 0.37 v/v; <=0.32 v/v (n=183,184)	21	10		
Hematocrit: >=0.55 v/v; >=0.5 v/v (n=183,184)	1	3		
RBCs: >=6 Tera/L (n=184,184)	0	1		
Platelets: < 50 G/L (n=183,184)	0	1		
Platelets: 50 - 100 G/L (n=183,184)	0	0		
Platelets: >= 700 G/L (n=183,184)	1	0		
WBC:<3.0G/L(Non-Black);<2.0 G/L(Black)(n=184,184)	1	32		
WBC: >= 16.0 G/L (n=184,184)	8	5		
Neutrophils: < 1.0 G/L (n=183,184)	2	19		
Neutrophils: <1.5 G/L; <1.0 G/L (n=183,184)	7	50		
Lymphocytes: < 0.5 G/L (n=183,184)	2	2		
Lymphocytes: >= 0.5G/L - LLN (n=183,184)	8	21		
Lymphocytes: > 4.0 G/L (n=183,184)	17	6		
Monocytes: > 0.7 G/L (n=183,184)	46	38		
Basophils: > 0.1 G/L (n=183,184)	53	37		
Eosinophils: > 0.5 G/L or > ULN (n=183,184)	4	9		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Hematological Parameters

End point title	OLE Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Hematological Parameters

End point description:

Criteria for PCSA included:
• Hb: <=115 g/L (Male), <= 95 g/L (Female); >=185 g/L (18.5 g/dL) (Male), >= 165 g/L (16.5 g/dL)(Female);DFB >= 20 g/L (2g/dL).
• Hematocrit: <= 0.37 v/v (Male); <= 0.32 v/v (Female); >= 0.55 v/v (Male); >= 0.5 v/v (Female).
• RBCs: >=6 Tera/ L.
• Platelets: < 50 G/L, 50 - 100 G/L, >= 700 G/L.
• WBC: < 3.0 G/L (Non-Black); < 2.0 G/L (Black), >= 16.0 G/L.
• Neutrophils: < 1.0 G/L, < 1.5 G/L (Non-Black); < 1.0 G/L (Black).
• Lymphocytes: < 0.5 G/L, >= 0.5 G/L - LLN, > 4.0 G/L.
• Monocytes: > 0.7 G/L.
• Basophils: > 0.1 G/L.
• Eosinophils: > 0.5 G/L or > ULN (if ULN >= 0.5 G/L).
OLE period safety population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From end of Week 24 (Baseline of OLE Period) up to Week 300

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	165		
Units: subjects				
Hb:<=115 g/L, <=95 g/L	8	5		
Hb: >=185 g/L, >=165 g/L	3	3		
Hb: DFB >=20 g/L	13	13		
Hematocrit: <= 0.37 v/v; <=0.32 v/v	12	14		
Hematocrit: >=0.55 v/v; >=0.5 v/v	5	8		
RBCs: >=6 Tera/L	3	2		
Platelets: < 50 G/L	0	0		
Platelets: 50 - 100 G/L	4	4		
Platelets: >= 700 G/L	2	1		
WBC: < 3.0 G/L(Non-Black); < 2.0 G/L(Black)	34	46		
WBC: >= 16.0 G/L	11	7		
Neutrophils: < 1.0 G/L	24	25		
Neutrophils: <1.5 G/L(Non-Black); <1.0 G/L(Black)	62	69		
Lymphocytes: < 0.5 G/L	2	3		
Lymphocytes: >= 0.5 G/L - LLN	28	42		
Lymphocytes: > 4.0 G/L	15	7		
Monocytes: > 0.7 G/L	48	43		
Basophils: > 0.1 G/L	78	70		
Eosinophils: > 0.5G/L or > ULN(if ULN >= 0.5G/L)	11	14		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Liver Function Tests

End point title	DB Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Liver Function Tests

End point description:

Criteria for PCSA:
• Alanine Aminotransferase (ALT): >1 ULN and <=1.5 ULN; >1.5 ULN and <=3 ULN; >3 ULN and <=5 ULN; >5 ULN and <=10 ULN; >10 ULN and <=20 ULN; >20 ULN.
• Aspartate aminotransferase (AST): >1 ULN and <=1.5 ULN; >1.5 ULN and <=3 ULN; >3 ULN and <=5 ULN; >5 ULN and <=10 ULN; >10 ULN and <=20 ULN; >20 ULN.
• Alkaline phosphatase: >1.5 ULN.
• Total bilirubin (TBILI): >1.5 ULN; >2 ULN.
• Conjugated bilirubin (CBILI): >1.5 ULN.
• Unconjugated bilirubin: >1.5 ULN, >2 ULN.
• ALT >3 ULN and TBILI >2 ULN.

• CBILI >35% TBILI and TBILI >1.5 ULN.
• Albumin: <=25 g/L.
DB Period safety population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary
End point timeframe: From Week 0 to Week 24	

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	183	184		
Units: subjects				
ALT >1 ULN and <=1.5 ULN	22	36		
ALT >1.5 ULN and <=3 ULN	17	26		
ALT >3 ULN and <=5 ULN	3	5		
ALT >5 ULN and <=10 ULN	1	1		
ALT >10 ULN and <=20 ULN	1	0		
ALT >20 ULN	0	0		
AST >1 ULN and <=1.5 ULN	16	22		
AST >1.5 ULN and <=3 ULN	7	13		
AST >3 ULN and <=5 ULN	3	2		
AST >5 ULN and <=10 ULN	0	0		
AST >10 ULN and <=20 ULN	1	0		
AST >20 ULN	0	0		
Alkaline Phosphatase >1.5 ULN	6	2		
TBILI >1.5 ULN	1	7		
TBILI >2 ULN	0	2		
CBILI >1.5 ULN	0	0		
Unconjugated Bilirubin >1.5 ULN	5	13		
Unconjugated Bilirubin >2 ULN	1	7		
ALT> 3 ULN and TBILI >2ULN	0	0		
CBILI >35% TBILI and TBILI >1.5 ULN	0	0		
Albumin <=25 g/L	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Liver Function Tests

End point title	OLE Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Liver Function Tests

End point description:

Criteria for PCSA:
• ALT: >1 ULN and <=1.5 ULN; >1.5 ULN and <=3 ULN; >3 ULN and <=5 ULN; >5 ULN and <=10 ULN; >10 ULN and <=20 ULN; >20 ULN.
• AST: >1 ULN and <=1.5 ULN; >1.5 ULN and <=3 ULN; >3 ULN and <=5 ULN; >5 ULN and <=10 ULN; >10 ULN and <=20 ULN; >20 ULN.

• Alkaline phosphatase: >1.5 ULN.
• TBILI: >1.5 ULN; >2 ULN.
• CBILI: >1.5 ULN.
• Unconjugated bilirubin: >1.5 ULN, >2 ULN.
• ALT >3 ULN and TBILI >2 ULN.
• CBILI >35% TBILI and TBILI >1.5 ULN.
• Albumin: <=25 g/L.
OLE period safety population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From end of Week 24 (Baseline of OLE Period) up to Week 300

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	165		
Units: subjects				
ALT >1 ULN and <=1.5 ULN	41	36		
ALT >1.5 ULN and <=3 ULN	31	34		
ALT >3 ULN and <=5 ULN	11	10		
ALT >5 ULN and <=10 ULN	1	6		
ALT >10 ULN and <=20 ULN	0	2		
ALT >20 ULN	1	1		
AST >1 ULN and <=1.5 ULN	25	39		
AST >1.5 ULN and <=3 ULN	23	17		
AST >3 ULN and <=5 ULN	2	7		
AST >5 ULN and <=10 ULN	2	2		
AST >10 ULN and <=20 ULN	0	0		
AST >20 ULN	0	1		
Alkaline Phosphatase >1.5 ULN	0	1		
TBILI >1.5 ULN	11	6		
TBILI >2 ULN	3	1		
CBILI >1.5 ULN	0	0		
Unconjugated Bilirubin >1.5 ULN	21	22		
Unconjugated Bilirubin >2 ULN	11	10		
ALT> 3 ULN and TBILI >2ULN	1	0		
CBILI >35% TBILI and TBILI >1.5 ULN	0	0		
Albumin <=25 g/L	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Metabolic Parameters

End point title	DB Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Metabolic Parameters

End point description:

Criteria for potentially clinically significant abnormalities:
• Glucose: <=3.9 millimole/litre (mmol/L) and <LLN; >=11.1 mmol/L (unfasted [UF]) or >=7 mmol/L (fasted [FA]).
• Hemoglobin A1c (HbA1c): >8%.
• Total cholesterol: >=6.2 mmol/L; >=7.74 mmol/L.
• LDL cholesterol: >=4.1 mmol/L; >=4.9 mmol/L.
• Triglycerides: >=4.6 mmol/L; >=5.6 mmol/L.
DB period safety population. Here "n" = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

From Week 0 to Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	184		
Units: subjects				
Glucose <=3.9 mmol/L and <LLN (n=181,184)	10	8		
Glucose >=11.1mmol/L(UF)or>=7mmol/L(FA)(n	17	12		
HbA1c >8% (n=178,179)	3	3		
Total Cholesterol >=6.2mmol/L (n=181,184)	52	88		
Total Cholesterol >=7.74 mmol/L (n=181,184)	15	14		
LDL Cholesterol >=4.1 mmol/L (n=180,184)	35	59		
LDL Cholesterol >=4.9 mmol/L (n=180,184)	18	20		
Triglycerides >=4.6 mmol/L (n=181,184)	4	8		
Triglycerides >=5.6 mmol/L (n=181,184)	3	6		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Metabolic Parameters

End point title	OLE Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Metabolic Parameters

End point description:

Criteria for potentially clinically significant abnormalities:
• Glucose: <=3.9 mmol/L and <LLN; >=11.1 mmol/L (UF) or >=7 mmol/L (FA).
• HbA1c: >8%.
• Total cholesterol: >=6.2 mmol/L; >=7.74 mmol/L.
• LDL cholesterol: >=4.1 mmol/L; >=4.9 mmol/L.
• Triglycerides: >=4.6 mmol/L; >=5.6 mmol/L.
OLE period safety population. Here, "n" = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

From end of Week 24 (Baseline of OLE Period) up to Week 300

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	155	165		
Units: subjects				
Glucose <=3.9 mmol/L and <LLN (n=153,165)	5	6		
Glucose >=11.1mmol/L(UF)or>=7mmol/L(FA)(n	20	14		
HbA1c >8% (n=147,161)	2	2		
Total Cholesterol >=6.2mmol/L (n=153,165)	77	69		
Total Cholesterol >=7.74 mmol/L (n=153,165)	22	19		
LDL Cholesterol >=4.1 mmol/L (n=151,164)	57	48		
LDL Cholesterol >=4.9 mmol/L (n=151,164)	25	16		
Triglycerides >=4.6 mmol/L (n=153,165)	13	6		
Triglycerides >=5.6 mmol/L (n=153,165)	4	6		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Number of Subjects With Different Post-baseline Categories of High-density Lipoprotein (HDL)

End point title	DB Period: Number of Subjects With Different Post-baseline Categories of High-density Lipoprotein (HDL)

End point description:

Number of subjects with different post-baseline status of HDL: < 40 mg/dL, 40 - < 60 mg/dL, >= 60 mg/dL, is reported here. DB period safety population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Week 0 to Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	184		
Units: subjects				
HDL: < 40 mg/dL	5	7		
HDL: 40 - < 60 mg/dL	57	45		
HDL: >=60 mg/dL	119	132		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Subjects With Different Post-baseline Categories of High-density Lipoprotein

End point title	OLE Period: Number of Subjects With Different Post-baseline Categories of High-density Lipoprotein

End point description:

Number of subjects with different post-baseline status of HDL: < 40 mg/dL, 40 - < 60 mg/dL, >=60 mg/dL, is reported here. OLE period safety population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From end of Week 24 (Baseline of OLE Period) up to Week 300

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	165		
Units: subjects				
HDL: < 40 mg/dL	7	5		
HDL: 40 - < 60 mg/dL	52	49		
HDL: >=60 mg/dL	94	111		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Renal Function

End point title	DB Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Renal Function

End point description:

Criteria for potentially clinically significant abnormalities:
• Creatinine: >=150 micromol/L (adults); >=30% change from baseline, >=100% change from

baseline.
• Creatinine clearance: <15 mL/min; >=15 to <30 mL/min; >=30 to <60 mL/min; >=60 to <90 mL/min.
• Blood urea nitrogen: >=17 mmol/L.
• Uric acid: <120 micromol/L; >408 micromol/L.
DB period safety population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Week 0 to Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	183	184		
Units: subjects				
Creatinine >=150 micromol/L (Adults)	0	3		
Creatinine >=30% change from baseline	19	23		
Creatinine >=100% change from baseline	0	1		
Creatinine Clearance <15 mL/min	0	0		
Creatinine clearance >=15 to <30 mL/min	0	1		
Creatinine clearance >=30 to <60 mL/min	21	22		
Creatinine clearance >=60 to <90 mL/min	74	65		
Blood Urea Nitrogen >=17 mmol/L	0	2		
Uric acid <120 micromol/L	4	3		
Uric acid >408 micromol/L	25	35		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Renal Function

End point title	OLE Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Renal Function

End point description:

Criteria for potentially clinically significant abnormalities:
• Creatinine: >=150 micromol/L (adults); >=30% change from baseline, >=100% change from baseline.
• Creatinine clearance: <15 mL/min; >=15 to <30 mL/min; >=30 to <60 mL/min; >=60 to <90 mL/min.
• Blood urea nitrogen: >=17 mmol/L.
• Uric acid: <120 micromol/L; >408 micromol/L.
OLE period safety population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From end of Week 24 (Baseline of OLE Period) up to Week 300

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	165		
Units: subjects				
Creatinine >=150 micromol/L (Adults)	2	2		
Creatinine >=30% change from baseline	63	62		
Creatinine >=100% change from baseline	5	1		
Creatinine Clearance <15 mL/min	0	0		
Creatinine clearance >=15 to <30 mL/min	1	0		
Creatinine clearance >=30 to <60 mL/min	34	24		
Creatinine clearance >=60 to <90 mL/min	66	81		
Blood Urea Nitrogen >=17 mmol/L	1	3		
Uric acid <120 micromol/L	2	3		
Uric acid >408 micromol/L	44	43		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Urinalysis

End point title	DB Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Urinalysis

End point description:

Criteria with potentially clinically significant urine abnormalities: pH: <= 4.6; pH: >= 8.0. DB period safety population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Week 0 to Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	85		
Units: subjects				
pH <= 4.6	0	0		
pH>= 8.0	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Urinalysis

End point title	OLE Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Urinalysis

End point description:

Criteria with potentially clinically significant urine abnormalities: pH: <= 4.6; pH: >= 8.0. OLE period safety population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From end of Week 24 (Baseline of OLE Period) up to Week 300

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	109		
Units: subjects				
pH <= 4.6	0	0		
pH >= 8.0	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Electrolytes

End point title	DB Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Electrolytes

End point description:

Criteria for potentially clinically significant abnormalities:
• Sodium: <=129 mmol/L; >=160 mmol/L.
• Potassium: <3 mmol/L; >=5.5 mmol/L.
• Chloride: <80 mmol/L; >115 mmol/L.
DB period safety population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Week 0 to Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	183	184		
Units: subjects				
Sodium <=129 mmol/L	1	1		
Sodium >=160 mmol/L	0	0		
Potassium <3 mmol/L	3	0		
Potassium >=5.5 mmol/L	0	0		
Chloride <80 mmol/L	0	0		
Chloride >115 mmol/L	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Electrolytes

End point title	OLE Period: Number of Subjects With Potentially Clinically Significant Abnormalities - Electrolytes

End point description:

Criteria for potentially clinically significant abnormalities:
• Sodium: <=129 mmol/L; >=160 mmol/L.
• Potassium: <3 mmol/L; >=5.5 mmol/L.
• Chloride: <80 mmol/L; >115 mmol/L.
OLE period safety population. Here, number of subjects analysed = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From end of Week 24 (Baseline of OLE Period) up to Week 300

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	165		
Units: subjects				
Sodium <=129 mmol/L	3	0		
Sodium >=160 mmol/L	0	0		
Potassium <3 mmol/L	2	2		
Potassium >=5.5 mmol/L	6	7		
Chloride <80 mmol/L	1	0		
Chloride >115 mmol/L	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Number of Subjects With Potentially Clinically Significant Electrocardiogram (ECG) Abnormalities

End point title	DB Period: Number of Subjects With Potentially Clinically Significant Electrocardiogram (ECG) Abnormalities

End point description:

Criteria for potentially clinically significant ECG abnormalities:
• Heart rate (HR): <50 beats per minute (bpm); <50 bpm and DFB >=20 bpm; <40 bpm; <40 bpm and DFB >=20
bpm; <30 bpm; <30 bpm and DFB >=20 bpm; >90 bpm; >=90 bpm and increase from baseline (IFB) >=20 bpm;
>100 bpm; >=100 bpm and IFB >=20 bpm; >120 bpm; >=120 bpm and IFB >=20 bpm.
• PR Interval: >200 millisecond (ms); >200 ms and IFB >=25%; >220 ms; >220 ms and IFB >=25%; >240 ms; >240
ms and IFB >=25%.
• QRS Interval: >110 ms; >110 ms and IFB >=25%; >120 ms; >120 ms and IFB >=25%.
• QT Interval: >500 ms.
• QTc Bazett (QTc B): >450 ms; >480 ms; >500 ms; IFB >30 and <=60 ms; IFB >60 ms.
• QTc Fridericia (QTc F): >450 ms; >480 ms; >500 ms; IFB >30 and <=60 ms; IFB >60 ms.
DB period safety population. Here, number of subjects analysed = subjects evaluable for this endpoint and "n" = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

From Week 0 to Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	162		
Units: subjects				
HR <50 bpm (n=162,161)	4	5		
HR <50 bpm and DFB >=20 bpm (n=158,158)	0	0		
HR <40 bpm (n= 162,161)	0	0		
HR <40 bpm and DFB >=20 bpm (n= 158,158)	0	0		
HR <30 bpm (n=162,161)	0	0		
HR <30 bpm and DFB >=20 bpm (n=158,158)	0	0		
HR >90 bpm (n= 162,161)	11	2		
HR <90 bpm and IFB >=20 bpm (n=158,158)	5	1		
HR >100 bpm (n=162,161)	2	1		
HR >=100 bpm and IFB >=20 bpm (n=158,158)	2	0		

HR >120 bpm (n=162,161)	0	0		
HR >=120 bpm and IFB >=20 bpm (n=158,158)	0	0		
PR Interval >200 ms (n=163,161)	11	5		
PR Interval >200 ms and IFB >=25% (n=159,158)	1	0		
PR Interval >220 ms (n=163,161)	4	1		
PR Interval >220 ms and IFB >=25% (n=159,158)	0	0		
PR Interval >240 ms (n=163,161)	1	1		
PR Interval >240 ms and IFB >=25% (n=159,158)	0	0		
QRS Interval >110 ms (n= 163,162)	3	9		
QRS Interval >110 ms and IFB >=25% (n=159,159)	0	0		
QRS Interval >120 ms (n=163,162)	1	2		
QRS Interval >120 ms and IFB >=25% (n=159,159)	0	0		
QT Interval >500 ms (n=163,162)	0	1		
QTc B >450 ms (n=163,162)	16	7		
QTc B >480 ms (n=163,162)	2	0		
QTc B >500 ms (n=163,162)	0	0		
QTc B IFB >30 and <=60 ms (n=159,159)	11	5		
QTc B IFB >60 ms (n=159,159)	0	0		
QTc F>450 ms (n=163,162)	7	5		
QTc F>480 ms (n=163,162)	0	0		
QTc F>500 ms (n=163,162)	0	0		
QTc F IFB >30 and <=60 ms (n=159,159)	9	3		
QTc F IFB >60 ms (n=159,159)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Subjects With Potentially Clinically Significant Electrocardiogram Abnormalities

End point title	OLE Period: Number of Subjects With Potentially Clinically Significant Electrocardiogram Abnormalities

End point description:

Criteria for potentially clinically significant ECG abnormalities:
• HR: <50 bpm; <50 bpm and DFB >=20 bpm; <40 bpm; <40 bpm and DFB >=20 bpm; <30 bpm; <30 bpm and DFB >=20 bpm; >90 bpm; >=90 bpm and IFB >=20 bpm; >100 bpm; >=100 bpm and IFB >=20 bpm; >120 bpm; >=120 bpm and IFB >=20 bpm.
• PR Interval: >200 ms; >200 ms and IFB >=25%; >220 ms; >220 ms and IFB >=25%; >240 ms; >240 ms and IFB >=25%.
• QRS Interval: >110 ms; >110 ms and IFB >=25%; >120 ms; >120 ms and IFB >=25%.
• QT Interval: >500 ms.
• QTc B: >450 ms; >480 ms; >500 ms; IFB >30 and <=60 ms; IFB >60 ms.
• QTc F: >450 ms; >480 ms; >500 ms; IFB >30 and <=60 ms; IFB >60 ms.
OLE period safety population. Here, number of subjects analysed = subjects evaluable for this endpoint and n = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:
From end of Week 24 (Baseline of OLE Period) up to Week 300

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	163		
Units: subjects				
HR <50 bpm (n=154,163)	10	19		
HR <50 bpm and DFB >=20 bpm (n=152,159)	0	3		
HR <40 bpm (n=154,163)	1	1		
HR <40 bpm and DFB >=20 bpm (n=152,159)	0	1		
HR <30 bpm (n=154,163)	0	0		
HR <30 bpm and DFB >=20 bpm (n=152,159)	0	0		
HR >90 bpm (n=154,163)	16	11		
HR >=90 bpm and IFB >=20 bpm (n=152,159)	7	6		
HR >100 bpm (n=154,163)	3	3		
HR >=100 bpm and IFB >=20 bpm (n=152,159)	2	1		
HR >120 bpm (n=154,163)	0	0		
HR >=120 bpm and IFB >=20 bpm (n=152,159)	0	0		
PR Interval >200 ms (n=154,163)	17	14		
PR Interval >200 ms and IFB >=25% (n=152,158)	6	3		
PR Interval >220 ms (n=154,163)	8	6		
PR Interval >220 ms and IFB >=25% (n=152,158)	4	3		
PR Interval >240 ms (n=154,163)	2	2		
PR Interval >240 ms and IFB >=25% (n=152,158)	2	1		
QRS Interval >110 ms (n=154,163)	8	18		
QRS Interval >110 ms and IFB >=25% (n=152,159)	2	1		
QRS Interval >120 ms (n=154,163)	3	7		
QRS Interval >120 ms and IFB >=25% (n=152,159)	1	0		
QT Interval >500 ms (n=154,163)	2	2		
QTc B >450 ms (n=154,163)	35	33		
QTc B >480 ms (n=154,163)	3	30		
QTc B >500 ms (n=154,163)	1	1		
QTc B IFB >30 and <=60ms (n=152,159)	18	23		
QTc B IFB >60 ms (n=152,159)	3	2		
QTc F>450 ms (n=154,163)	16	16		
QTc F>480 ms (n=154,163)	3	2		
QTc F>500 ms (n=154,163)	0	1		
QTc F IFB >30 and <=60 ms (n=152,159)	19	19		

QTc F IFB >60 ms (n=152,159)	4	3		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Number of Subjects With Potentially Clinically Significant Vital Signs Abnormalities

End point title	DB Period: Number of Subjects With Potentially Clinically Significant Vital Signs Abnormalities

End point description:

Criteria for potentially clinically significant vital sign abnormalities:
Systolic blood pressure (SBP) supine: <=95 mmHg and DFB>=20 mmHg; >=160 mmHg and IFB >=20 mmHg.
Diastolic blood pressure (DBP) supine: <=45 mmHg and DFB >=10 mmHg; >=110 mmHg and IFB >=10 mmHg.
SBP (Orthostatic): <=-20 mmHg. DBP (Orthostatic): <=-10 mmHg. HR supine: <=50 bpm and DFB >=20 bpm; >=120 bpm and IFB >=20 bpm. Weight: >=5% DFB; >=5% IFB.
DB period safety population. Here, "n" = subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

From Week 0 to Week 24

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	184	184		
Units: subjects				
SBP (supine) <=95 mmHg, DFB >=20mmHg (n=182,182)	4	3		
SBP (supine) >=160mmHg, IFB >=20mmHg (n=182,182)	4	5		
DBP (supine) <=45mmHg, DFB >=10mmHg (n=182,182)	1	1		
DBP (supine) >=110mmHg, IFB >=10mmHg (n=182,182)	1	1		
SBP (orthostatic) <=-20mmHg (n=150,161)	13	10		
DBP (orthostatic) <=-10mmHg (n=150,161)	20	27		
HR (supine) <=50 bpm, DFB >= 20 bpm (n=182,182)	2	1		
HR (supine) >=120 bpm, IFB >=20 bpm (n=182,182)	1	0		
Weight >=5% DFB (n=178,180)	12	6		
Weight >=5% IFB (n=178,180)	21	23		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Number of Subjects With Potentially Clinically Significant Vital Signs Abnormalities

End point title	OLE Period: Number of Subjects With Potentially Clinically Significant Vital Signs Abnormalities

End point description:

Criteria for potentially clinically significant vital sign abnormalities:
SBP supine: <=95 mmHg and DFB >=20 mmHg; >=160 mmHg and IFB >=20 mmHg. DBP supine: <=45 mmHg and
DFB >=10 mmHg; >=110 mmHg and IFB >=10 mmHg. SBP (Orthostatic): <=-20 mmHg. DBP (Orthostatic): <=-10
mmHg. HR supine: <=50 bpm and DFB >=20 bpm; >=120 bpm and IFB >=20 bpm. Weight: >=5% DFB; >=5% IFB.
OLE period safety population. Here, "n" = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

From end of Week 24 (Baseline of OLE Period) up to Week 300

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	155	165		
Units: subjects				
SBP (supine) <=95 mmHg, DFB >=20mmHg (n=154,164)	3	9		
SBP (supine) >=160 mmHg, IFB >=20mmHg (n=154,164)	10	11		
DBP (supine) <=45mmHg, DFB >=10mmHg (n=154,164)	0	0		
DBP (supine) >=110mmHg, IFB >=10mmHg (n=154,164)	1	2		
SBP (orthostatic) <=-20mmHg (n=150,162)	24	32		
DBP (orthostatic) <=-10mmHg (n=150,162)	41	46		
HR (supine) <=50 bpm, DFB >= 20 bpm (n=154,164)	3	0		
HR (supine) >=120 bpm, IFB >=20 bpm (n=154,164)	0	0		
Weight >=5% DFB (n=151,164)	44	51		
Weight >=5% IFB (n=151,164)	82	87		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Number of Subjects With Treatment-emergent and Treatment-boosted Anti-drug Antibody (ADA) Responses

End point title	DB Period: Number of Subjects With Treatment-emergent and Treatment-boosted Anti-drug Antibody (ADA) Responses[9]

End point description:

Anti-drug antibody response was categorised as: Treatment emergent and Treatment-boosted. Treatment emergent ADAs was defined as a subject with no positive assay response at baseline but with a positive assay response during the TEAE period. Treatment boosted ADAs: was defined as subjects with a positive ADA assay response at baseline and with at least a 4-fold increase in titer compared to baseline during the TEAE period. TEAE period: time from first dose of the study drug up to the day before first dose of open-label treatment for subjects who completed 24-week randomised/DB treatment. Analysis was performed on ADA population which consisted of all subjects who had signed informed consent and had been allocated to a randomised treatment; received at least 1 dose or part of a dose of IMP with at least 1 post-dose evaluable ADA sample. Data for this endpoint was not planned to be collected and analysed for Adalimumab 40 mg/Sarilumab 200 mg arm.

End point type	Secondary

End point timeframe:

From Week 0 to Week 24

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for applicable arms in the study.

End point values	Sarilumab 200 mg/Sarilumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	184			
Units: subjects				
Treatment-emergent ADA	13			
Treatment-boosted ADA	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent and Treatment-boosted Anti-drug Antibody Response During Entire Treatment-emergent Adverse Event Period

End point title	Number of Subjects With Treatment-emergent and Treatment-boosted Anti-drug Antibody Response During Entire Treatment-emergent Adverse Event Period

End point description:

Anti-drug antibody response was categorised as: Treatment emergent ADAs was defined as a subject with no positive assay response at baseline but with a positive assay response during the entire TEAE period. Treatment boosted ADAs was defined as a subjects with a positive ADA assay response at baseline and with at least a 4-fold increase in titer compared to baseline during the entire TEAE period. Entire TEAE period: last OLE dose - first DB dose date + 6 weeks (follow-up), regardless of unplanned intermittent discontinuations. Analysis was performed on immunogenicity population which consisted of all subjects who received at least 1 dose or part of a dose with at least 1 post-dose evaluable ADA sample.

End point type	Secondary

End point timeframe:

From Week 0 up to last dose in OLE + 6 weeks of follow up (i.e. up to Week 306)

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150	163		
Units: subjects				
Treatment-emergent ADAs	11	11		
Treatment-boosted ADAs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Period: Pharmacokinetics: Serum Trough (Pre-Dose) Concentrations of Functional Sarilumab

End point title	DB Period: Pharmacokinetics: Serum Trough (Pre-Dose) Concentrations of Functional Sarilumab[10]

End point description:

Data for this endpoint was not planned to be collected and analysed for "Adalimumab 40 mg/Sarilumab 200 mg” arm. Analysis was performed on Pharmacokinetic (PK) population which consisted of all randomised Sarilumab subjects who received at least 1 dose of IMP with at least one post-dose, non-missing concentration of functional Sarilumab in serum concentration value. Here, "n" = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Pre-dose at Week 0 (Baseline), 2, 4, 12, 16, 20, and 24

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for applicable arms in the study.

End point values	Sarilumab 200 mg/Sarilumab 200 mg			
Subject group type	Reporting group			
Number of subjects analysed	184			
Units: nanograms per millilitre (ng/mL)				
arithmetic mean (standard deviation)				
Baseline (n=177)	0.00 (± 0.00)			
Week 2 (n=176)	5566.03 (± 4843.57)			
Week 4 (n=167)	11209.64 (± 8202.70)			
Week 12 (n=152)	21355.19 (± 14805.63)			
Week 16 (n=155)	23143.39 (± 16508.71)			
Week 20 (n=152)	25252.43 (± 17319.04)			
Week 24 (n=148)	24233.10 (± 17581.72)			

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Pharmacokinetics: Serum Trough (Pre-Dose) Concentrations of Functional Sarilumab

End point title	OLE Period: Pharmacokinetics: Serum Trough (Pre-Dose) Concentrations of Functional Sarilumab

End point description:

Analysis was performed on PK population (OLE period) which consisted of all subjects from the randomised population who received at least 1 dose of IMP with at least one post-dose, non-missing serum sarilumab concentration. Here, "n" = subjects with available data for each specified category and '99999' is used as space filler which denotes that no subject was available for the assessment at the specified timepoint.

End point type	Secondary

End point timeframe:

Pre-dose at Week 24 (Baseline of OLE period), 36, 48, 60, 84, 108, 132, 156, 180, 204, 228, 252, 276, 300 and 306

End point values	Adalimumab 40 mg/Sarilumab 200 mg	Sarilumab 200 mg/Sarilumab 200 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150	163		
Units: ng/mL				
arithmetic mean (standard deviation)				
Week 24 (Baseline of OLE period) (n=128,146)	109.38 (± 1237.44)	24403.72 (± 17588.31)		
Week 36 (n=134,146)	18952.69 (± 15125.86)	26006.07 (± 19194.79)		

Week 48 (n=125,133)	21911.87 (± 17926.01)	25571.16 (± 18958.00)		
Week 60 (n=121,127)	21583.82 (± 17594.87)	24005.78 (± 18541.46)		
Week 84 (n=104,108)	23230.92 (± 18274.09)	23873.23 (± 19794.57)		
Week 108 (n=109,119)	20405.02 (± 15553.02)	21023.55 (± 17792.89)		
Week 132 (n=104,110)	20814.89 (± 17848.70)	20021.53 (± 18580.91)		
Week 156 (n=97,113)	23604.11 (± 19660.31)	22423.29 (± 18757.11)		
Week 180 (n=96,105)	18611.01 (± 16417.46)	21856.85 (± 18612.43)		
Week 204 (n=93,107)	17982.66 (± 16640.61)	18244.96 (± 16383.47)		
Week 228 (n=84,85)	19451.40 (± 17694.09)	18315.19 (± 17525.62)		
Week 252 (n=55,61)	19663.10 (± 16020.11)	19224.47 (± 16964.41)		
Week 276 (n=52,63)	19071.00 (± 18425.13)	17014.75 (± 16207.18)		
Week 300 (n=0,2)	99999 (± 99999)	9260.00 (± 8683.27)		
Week 306 (Follow-up) (n=72,86)	1237.01 (± 2856.88)	2280.98 (± 7909.71)		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AEs) were collected from up to Week 24 in DB period and from end of Week 24 (Baseline of OLE Period) up to Week 306 in OLE Period regardless of seriousness or relationship to study drug.

Adverse event reporting additional description:

Reported AEs are TEAEs developed/worsened during 'on treatment period'(DB:time from first dose up to day before first dose of open-label treatment; OLE:from end of Week 24 [Baseline of OLE Period] up to the last dose in OLE + 6 weeks [follow-up]). Safety population. For OLE, data was reported for pooled population (all subjects received Sarilumab).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	DB Period - Adalimumab 40 mg

Reporting group description:

Adalimumab 40 mg SC injection in combination with placebo for sarilumab q2w for 24 weeks during DB period. The dosing frequency of adalimumab was adjusted to 40 mg qw dosing in case of subjects with inadequate response (<20% improvement from baseline in TJC and SJC for 2 consecutive visits) at or after Week 16 until Week 23.

Reporting group title	DB Period - Sarilumab 200mg

Reporting group description:

Sarilumab 200 mg SC injection in combination with placebo for adalimumab q2w for 24 weeks during DB period. The dosing frequency of placebo for adalimumab was adjusted to 40 mg qw dosing in case of subjects with inadequate response (<20% improvement from baseline in TJC and SJC for 2 consecutive visits) at or after Week 16 until Week 23.

Reporting group title	OLE Period - Sarilumab 200mg

Reporting group description:

All subjects who completed 24 weeks DB period had the option to continue in OLE period and received sarilumab 200 mg q2w until commercial availability of sarilumab in their country or up to maximum of additional 276 weeks (i.e. up to Week 300).

Serious adverse events	DB Period - Adalimumab 40 mg	DB Period - Sarilumab 200mg	OLE Period - Sarilumab 200mg
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 184 (7.07%)	9 / 184 (4.89%)	56 / 320 (17.50%)
number of deaths (all causes)	0	1	8
number of deaths resulting from adverse events	0	1	8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	1 / 184 (0.54%)	0 / 184 (0.00%)	0 / 320 (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
Chronic Lymphocytic Leukaemia			

subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Adenocarcinoma Stage Iv			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung Squamous Cell Carcinoma Stage Ii			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant Melanoma			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant Mesenteric Neoplasm			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Metastases To Peritoneum			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Ureteric Cancer Metastatic			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Yolk Sac Tumour Site Unspecified			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vascular disorders			
Aortic Dissection			

subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Haematoma			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iliac Artery Occlusion			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iliac Artery Stenosis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Ischaemia			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Serum Sickness			
subjects affected / exposed	1 / 184 (0.54%)	0 / 184 (0.00%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Reproductive system and breast disorders			
Cervical Dysplasia			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterovaginal Prolapse			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal Prolapse			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary Alveolar Haemorrhage			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Embolism			
subjects affected / exposed	1 / 184 (0.54%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device Defective			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Dislocation			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine Aminotransferase Increased			

subjects affected / exposed	1 / 184 (0.54%)	0 / 184 (0.00%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic Enzyme Increased			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (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
Ankle Fracture			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head Injury			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Vertebral Fracture			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital Haematoma			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib Fracture			

subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute Myocardial Infarction			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial Fibrillation			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial Flutter			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Failure Acute			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary Artery Disease			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary Muscle Rupture			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sinus Node Dysfunction			

subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral Ischaemia			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular Accident			
subjects affected / exposed	1 / 184 (0.54%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Demyelinating Polyneuropathy			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial Aneurysm			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple Sclerosis			
subjects affected / exposed	1 / 184 (0.54%)	0 / 184 (0.00%)	0 / 320 (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
Subarachnoid Haemorrhage			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Syncope			

subjects affected / exposed	1 / 184 (0.54%)	0 / 184 (0.00%)	1 / 320 (0.31%)
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			
Anaemia			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	2 / 320 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood Loss Anaemia			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	2 / 320 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uveitis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Duodenal Ulcer Haemorrhage			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal Hernia			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Intestinal Obstruction			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large Intestine Polyp			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic Necrosis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pancreatitis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis Acute			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	2 / 320 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small Intestinal Obstruction			
subjects affected / exposed	1 / 184 (0.54%)	0 / 184 (0.00%)	0 / 320 (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
Hepatobiliary disorders			
Biliary Obstruction			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Cholelithiasis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	4 / 320 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			

subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic Haematoma			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Panniculitis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stevens-Johnson Syndrome			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Thyroid Mass			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			

subjects affected / exposed	1 / 184 (0.54%)	0 / 184 (0.00%)	0 / 320 (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
Back Pain			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Spinal Stenosis			
subjects affected / exposed	1 / 184 (0.54%)	0 / 184 (0.00%)	1 / 320 (0.31%)
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	1 / 184 (0.54%)	0 / 184 (0.00%)	5 / 320 (1.56%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid Arthritis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	3 / 320 (0.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Stenosis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Arthritis Bacterial			

subjects affected / exposed	1 / 184 (0.54%)	0 / 184 (0.00%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone Abscess			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bullous Erysipelas			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis Infective			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (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
Epididymitis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastitis			
subjects affected / exposed	0 / 184 (0.00%)	1 / 184 (0.54%)	0 / 320 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			

subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pharyngotonsillitis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	5 / 320 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 184 (0.54%)	0 / 184 (0.00%)	0 / 320 (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 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular Neuronitis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 184 (0.00%)	1 / 320 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	DB Period - Adalimumab 40 mg	DB Period - Sarilumab 200mg	OLE Period - Sarilumab 200mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	62 / 184 (33.70%)	79 / 184 (42.93%)	220 / 320 (68.75%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	6 / 184 (3.26%)	7 / 184 (3.80%)	23 / 320 (7.19%)
occurrences (all)	6	7	30
Injury, poisoning and procedural			

complications			
Accidental Overdose			
subjects affected / exposed	11 / 184 (5.98%)	5 / 184 (2.72%)	39 / 320 (12.19%)
occurrences (all)	12	5	54
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 184 (1.63%)	4 / 184 (2.17%)	28 / 320 (8.75%)
occurrences (all)	3	4	34
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 184 (6.52%)	7 / 184 (3.80%)	17 / 320 (5.31%)
occurrences (all)	13	9	34
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 184 (0.54%)	25 / 184 (13.59%)	59 / 320 (18.44%)
occurrences (all)	2	45	150
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	7 / 184 (3.80%)	14 / 184 (7.61%)	26 / 320 (8.13%)
occurrences (all)	8	72	220
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 184 (3.26%)	5 / 184 (2.72%)	20 / 320 (6.25%)
occurrences (all)	7	5	31
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	3 / 184 (1.63%)	3 / 184 (1.63%)	21 / 320 (6.56%)
occurrences (all)	3	3	23
Rheumatoid Arthritis			
subjects affected / exposed	7 / 184 (3.80%)	3 / 184 (1.63%)	21 / 320 (6.56%)
occurrences (all)	7	3	34
Infections and infestations			
Bronchitis			
subjects affected / exposed	7 / 184 (3.80%)	12 / 184 (6.52%)	41 / 320 (12.81%)
occurrences (all)	7	15	63
Nasopharyngitis			

subjects affected / exposed	14 / 184 (7.61%)	11 / 184 (5.98%)	60 / 320 (18.75%)
occurrences (all)	15	11	107
Upper Respiratory Tract Infection			
subjects affected / exposed	7 / 184 (3.80%)	3 / 184 (1.63%)	36 / 320 (11.25%)
occurrences (all)	9	3	52
Urinary Tract Infection			
subjects affected / exposed	4 / 184 (2.17%)	5 / 184 (2.72%)	30 / 320 (9.38%)
occurrences (all)	5	7	43

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 June 2015	Following changes were made: i) added the assessment of potential opportunistic infections and study treatment continuation. ii) correct errors or inconsistencies in the protocol schedule of events and footnotes. iii) correct inconsistencies in criteria for dose escalation. iv) detail the requirement for an independent joint assessor.
20 November 2015	Following changes were made: modified the study duration in order to provide long-term open-label treatment with sarilumab 200 mg q2w beyond Week 48, until anticipated commercial availability of sarilumab or until 2020, and collect long-term data for sarilumab in the monotherapy setting.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported