Clinical trial results:
A 24-week, phase 3, multicentre, randomised, double-blind, efficacy and safety study, comparing GSK3196165 with placebo and with sarilumab, in combination with conventional synthetic DMARDs, in participants with moderately to severely active rheumatoid arthritis who have an inadequate response to biological DMARDs and/or Janus Kinase inhibitors.

Summary

EudraCT number	2019-000868-18
Trial protocol	GB DE PL LT ES BE CZ HU IT
Global end of trial date	01 February 2022

Results information

Result version number	v3 (current)
This version publication date	03 August 2023
First version publication date	17 February 2023
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	202018

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	GreatWest Road, Brentford,Middlesex, United Kingdom, TW8 9GS
Public contact	GSK Response Center, GlaxoSmithKline, +1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, +1 8664357343, GSKClinicalSupportHD@gsk.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	15 March 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare efficacy and safety of GSK3196165 (Otilimab) versus placebo and sarilumab in participants with moderately to severely active rheumatoid arthritis.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 104
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Czechia: 46
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Hungary: 6
Country: Number of subjects enrolled	Japan: 38
Country: Number of subjects enrolled	Lithuania: 6
Country: Number of subjects enrolled	Poland: 108
Country: Number of subjects enrolled	South Africa: 11
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 5
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 199
Worldwide total number of subjects	550
EEA total number of subjects	187

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)	419
From 65 to 84 years	131
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were randomized in a ratio of 6:6:6:1:1:1 to 3 experimental and 3 Placebo arms. At Week 12, participants randomized to one of the three placebo arms switched to experimental arms, receiving the active intervention for 12 weeks. Participants randomized to experimental arms from study start received the active intervention for 24 weeks.

Pre-assignment

Screening details:

Analysis was reported for experimental, and all placebo arms are pooled till Week 12 to serve as reference for comparison. Total 550 participants were randomized; one participant withdrew from 90mg GSK3196165 before receiving intervention due to Protocol Deviation. The participant was removed from intent-to-treat and safety population (N=549).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK3196165 90mg + csDMARD

Arm description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received GSK3196165 90 mg + csDMARD administered by weekly subcutaneous injection.

Arm type	Experimental
Investigational medicinal product name	GSK3196165
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 90mg of GSK3196165 once every week

Arm title	GSK3196165 150mg + csDMARD

Arm description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received GSK3196165 150 mg + csDMARD administered by weekly subcutaneous

Arm type	Experimental
Investigational medicinal product name	GSK3196165
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 150mg of GSK3196165 once every week

Arm title	Sarilumab 200mg + csDMARD

Arm description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received Sarilumab 200 mg + csDMARD administered by subcutaneous injection of sarilumab every other week plus with placebo injection in the intervening weeks to maintain the blind.

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

Dosage and administration details:

Participants received 200mg of Sarilumab once every alternate week.

Arm title	Placebo + csDMARD and GSK3196165 90mg + csDMARD

Arm description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to(<=)84 years received Placebo +csDMARD until Week 12 later switched toGSK3196165 90 mg +csDMARD administered by weekly subcutaneous injection.

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

Dosage and administration details:

Participants received placebo once every week until Week 12

Investigational medicinal product name	GSK3196165
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 90mg of GSK3196165once every week from Week 12 to Week 24.

Arm title	Placebo + csDMARD and GSK3196165 150mg + csDMARD

Arm description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received Placebo + csDMARD until Week 12 later switched to GSK3196165 150 mg + csDMARD administered by weekly subcutaneous injection.

Arm type	Placebo
Investigational medicinal product name	GSK3196165
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 150mg of GSK3196165once every week from Week 12 to Week 24.

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

Dosage and administration details:

Participants received placebo once every week until Week 12

Arm title	Placebo + csDMARD and Sarilumab 200mg + csDMARD

Arm description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received Placebo + csDMARD until Week 12 later switched to Sarilumab 200mg + csDMARD

administered by subcutaneous injection of sarilumab every other week plus with placebo injection in the intervening weeks to maintain the blind.

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

Dosage and administration details:

Participants received 200mg of Sarilumab once every alternate week between Week 12 to Week24

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

Dosage and administration details:

Participants received placebo once every week until Week 12

Number of subjects in period 1[1]	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD
Started	156	158	156
Completed	143	144	133
Not completed	13	14	23
Physician decision	2	-	-
Adverse event, non-fatal	3	2	9
Informed Consent Withdrawn	3	6	8
Protocol Deviation	-	-	1
Investigator Site Closed	-	1	1
Protocol-Specified Withdrawal Criterion Met	1	-	2
Lost to follow-up	1	2	1
Lack of efficacy	3	3	1

Number of subjects in period 1[1]	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD
Started	26	26	27
Completed	23	25	26
Not completed	3	1	1
Physician decision	-	-	-
Adverse event, non-fatal	-	-	-
Informed Consent Withdrawn	1	1	-
Protocol Deviation	-	-	-
Investigator Site Closed	-	-	-
Protocol-Specified Withdrawal Criterion Met	-	-	-

Lost to follow-up	-	-	1
Lack of efficacy	2	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Total 550 participants were randomized; one participant withdrew from 90mg GSK3196165 before receiving intervention due to Protocol Deviation. The participant was removed from intent-to-treat and safety population (N=549)

Baseline characteristics

Reporting groups	
Reporting group title	GSK3196165 90mg + csDMARD
Reporting group description:	
Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received GSK3196165 90 mg + csDMARD administered by weekly subcutaneous injection.	
Reporting group title	GSK3196165 150mg + csDMARD
Reporting group description:	
Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received GSK3196165 150 mg + csDMARD administered by weekly subcutaneous	
Reporting group title	Sarilumab 200mg + csDMARD
Reporting group description:	
Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received Sarilumab 200 mg + csDMARD administered by subcutaneous injection of sarilumab every other week plus with placebo injection in the intervening weeks to maintain the blind.	
Reporting group title	Placebo + csDMARD and GSK3196165 90mg + csDMARD
Reporting group description:	
Participants between the ages of greater than or equal to (>=)18 years and less than or equal to(<=)84 years received Placebo +csDMARD until Week 12 later switched toGSK3196165 90 mg +csDMARD administered by weekly subcutaneous injection.	
Reporting group title	Placebo + csDMARD and GSK3196165 150mg + csDMARD
Reporting group description:	
Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received Placebo + csDMARD until Week 12 later switched to GSK3196165 150 mg + csDMARD administered by weekly subcutaneous injection.	
Reporting group title	Placebo + csDMARD and Sarilumab 200mg + csDMARD
Reporting group description:	
Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received Placebo + csDMARD until Week 12 later switched to Sarilumab 200mg + csDMARD administered by subcutaneous injection of sarilumab every other week plus with placebo injection in the intervening weeks to maintain the blind.	

Reporting group values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD
Number of subjects	156	158	156
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	119	121	115
From 65-84 years	37	37	41
85 years and over	0	0	0
Sex: Female, Male Units: Participants			
Female	134	135	132
Male	22	23	24

Race/Ethnicity, Customized Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	1	0	0
ASIAN	13	15	12
BLACK OR AFRICAN AMERICAN	5	8	6
MISSING	0	2	0
MULTIPLE	0	0	0
WHITE	137	133	138
Age, Continuous Units: YEARS			
arithmetic mean	56.7	56.0	57.5
standard deviation	± 10.59	± 10.52	± 10.69

Reporting group values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD
Number of subjects	26	26	27
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	23	21	19
From 65-84 years	3	5	8
85 years and over	0	0	0
Sex: Female, Male Units: Participants			
Female	22	18	25
Male	4	8	2
Race/Ethnicity, Customized Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	0	0	0
ASIAN	3	2	2
BLACK OR AFRICAN AMERICAN	2	0	2
MISSING	0	0	0
MULTIPLE	1	0	0
WHITE	20	24	23
Age, Continuous Units: YEARS			
arithmetic mean	51.6	57.3	57.6
standard deviation	± 11.19	± 8.99	± 10.89

Reporting group values	Total		
Number of subjects	549		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	418		
From 65-84 years	131		
85 years and over	0		
Sex: Female, Male Units: Participants			
Female	466		
Male	83		
Race/Ethnicity, Customized Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	1		
ASIAN	47		
BLACK OR AFRICAN AMERICAN	23		
MISSING	2		
MULTIPLE	1		
WHITE	475		
Age, Continuous Units: YEARS			
arithmetic mean			
standard deviation	-		

Subject analysis sets

Subject analysis set title	Pooled Placebo
Subject analysis set type	Per protocol

Subject analysis set description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received Placebo + csDMARD administered by weekly subcutaneous injection until Week 12. The placebo arms are pooled into a single placebo arm.

Reporting group values	Pooled Placebo		
Number of subjects	79		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			

From 65-84 years 85 years and over			

Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE ASIAN BLACK OR AFRICAN AMERICAN MISSING MULTIPLE WHITE			
Age, Continuous Units: YEARS			
arithmetic mean	37.7		
standard deviation	± 5.74		

End points

End points reporting groups

Reporting group title	GSK3196165 90mg + csDMARD

Reporting group description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received GSK3196165 90 mg + csDMARD administered by weekly subcutaneous injection.

Reporting group title	GSK3196165 150mg + csDMARD

Reporting group description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received GSK3196165 150 mg + csDMARD administered by weekly subcutaneous

Reporting group title	Sarilumab 200mg + csDMARD

Reporting group description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received Sarilumab 200 mg + csDMARD administered by subcutaneous injection of sarilumab every other week plus with placebo injection in the intervening weeks to maintain the blind.

Reporting group title	Placebo + csDMARD and GSK3196165 90mg + csDMARD

Reporting group description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to(<=)84 years received Placebo +csDMARD until Week 12 later switched toGSK3196165 90 mg +csDMARD administered by weekly subcutaneous injection.

Reporting group title	Placebo + csDMARD and GSK3196165 150mg + csDMARD

Reporting group description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received Placebo + csDMARD until Week 12 later switched to GSK3196165 150 mg + csDMARD administered by weekly subcutaneous injection.

Reporting group title	Placebo + csDMARD and Sarilumab 200mg + csDMARD

Reporting group description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received Placebo + csDMARD until Week 12 later switched to Sarilumab 200mg + csDMARD administered by subcutaneous injection of sarilumab every other week plus with placebo injection in the intervening weeks to maintain the blind.

Subject analysis set title	Pooled Placebo
Subject analysis set type	Per protocol

Subject analysis set description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received Placebo + csDMARD administered by weekly subcutaneous injection until Week 12. The placebo arms are pooled into a single placebo arm.

Primary: Percentage of participants with 20% improvement in American College of Rheumatology criteria (ACR20) at Week 12 superiority comparison with placebo

End point title	Percentage of participants with 20% improvement in American College of Rheumatology criteria (ACR20) at Week 12 superiority comparison with placebo[1]

End point description:

ACR20 is calculated as a 20% improvement from Baseline in Tender Joint Count 68 (TJC68) and Swollen Joint Count 66 (SJC66) and a 20% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale (VAS) with values from 0=best to 100=worst), Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty) and an acute-phase reactant (high sensitivity C-reactive Protein mg/L (hsCRP)). For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Primary

End point timeframe:

Week 12

Notes:

[1] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Percentage of participants				
number (not applicable)	44.8	50.7	57.5	37.7

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The null hypothesis is that there is no difference between 90 mg dose of GSK3196165 and placebo in the proportion of participants achieving ACR20 response at Week 12 versus the alternative hypothesis that the 90 mg dose of GSK3196165 differs from placebo in the proportion of participants with ACR20 response at Week 12

Comparison groups	GSK3196165 90mg + csDMARD v Pooled Placebo
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2868
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	0.76
upper limit	2.48

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The null hypothesis is that there is no difference between 150 mg dose of GSK3196165 and placebo in the percentage of participants achieving ACR20 response at Week 12 versus the alternative hypothesis that the 150 mg dose of GSK3196165 differs from placebo in the percentage of participants with ACR20 response at Week 12

Comparison groups	GSK3196165 150mg + csDMARD v Pooled Placebo

Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0596
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.75
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	0.98
upper limit	3.15

Statistical analysis title	Statistical Analysis 5

Statistical analysis description:

The null hypothesis is that there is no difference between 150 mg dose of GSK3196165 and 200 mg dose of sarilumab alternating with placebo every week in the proportion of participants achieving ACR20 response at Week 12 versus the alternative hypothesis that the 150 mg dose of GSK3196165 differs from 200 mg dose of sarilumab alternating with placebo every week in the proportion of participants with ACR20 response at Week 12

Comparison groups	GSK3196165 150mg + csDMARD v Sarilumab 200mg + csDMARD
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2308
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.75
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	0.47
upper limit	1.2

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The null hypothesis is that there is no difference between 90 mg dose of GSK3196165 and 200 mg dose of sarilumab alternating with placebo every week in the proportion of participants achieving ACR20 response at Week 12 versus the alternative hypothesis that the 90 mg dose of GSK3196165 differs from 200 mg dose of sarilumab alternating with placebo every week in the proportion of participants with ACR20 response at Week 12

Comparison groups	GSK3196165 90mg + csDMARD v Sarilumab 200mg + csDMARD

Number of subjects included in analysis	312
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0293
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.59
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	0.36
upper limit	0.95

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The null hypothesis is that there is no difference between 200 mg dose of Sarilumab alternating with placebo every week and placebo in the proportion of participants achieving ACR20 response at Week 12 versus the alternative hypothesis that the 200 mg dose of Sarilumab alternating with placebo every week differs from placebo in the proportion of participants with ACR20 response at Week 12

Comparison groups	Sarilumab 200mg + csDMARD v Pooled Placebo
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0049
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.34
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	1.29
upper limit	4.23

Secondary: Change from Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) (versus Placebo) at Week 12

End point title	Change from Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) (versus Placebo) at Week 12[2]

End point description:

Health Assessment Questionnaire-Disability Index (HAQ-DI) is a 20-question instrument that assesses the difficulty of a participant in eight domains of daily living activities: Dressing & grooming, Arising, Eating, Walking, Hygiene, Reach, Grip, Common daily activities. Overall HAQ-DI score was computed as the sum of the domain scores divided by the number of domains answered. The total possible score ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty. Higher overall score indicates greater disability. A negative change from baseline indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Scores on a scale				
least squares mean (standard error)	-0.33 (± 0.044)	-0.41 (± 0.043)	-0.46 (± 0.044)	-0.23 (± 0.061)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Clinical disease activity index (CDAI) total score <=10 (CDAI Low disease activity [LDA]) at Week 12

End point title	Percentage of participants with Clinical disease activity index (CDAI) total score <=10 (CDAI Low disease activity [LDA]) at Week 12[3]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (TJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[3] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Percentage of participants				
number (not applicable)	20.7	18.2	28.1	14.2

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with CDAI total score <=10 (CDAI LDA) at Week 24 for treatment arms that started study intervention from Day 1

End point title	Percentage of participants with CDAI total score <=10 (CDAI LDA) at Week 24 for treatment arms that started study intervention from Day 1[4]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (TJC28),Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. LDA is achieved when CDAI total score <=10.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Percentage of participants				
number (not applicable)	31.2	30.1	42.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with CDAI total score <=10 (CDAI LDA) at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Percentage of participants with CDAI total score <=10 (CDAI LDA) at Week 24 for placebo switched arms that started study intervention from Week 12[5]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (TJC28),Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. LDA is achieved when CDAI total score <=10.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[5] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Percentage of participants				
number (not applicable)	24.0	42.0	36.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI total score at Week 12

End point title	Change from Baseline in CDAI total score at Week 12[6]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (TJC28),Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. A negative CDAI total score change from baseline indicates an improvement in disease activity. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Scores on a scale				
least squares mean (standard error)	-16.87 (± 1.03)	-17.23 (± 1.018)	-20.22 (± 1.027)	-14.86 (± 1.438)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI total score at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in CDAI total score at Week 24 for treatment arms that started study intervention from Day 1[7]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (TJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). CDAI total score ranges from 0 to 76 with higher values representing higher disease activity.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[7] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Scores on a scale				
least squares mean (standard error)	-20.93 (± 1.04)	-20.75 (± 1.022)	-23.22 (± 1.048)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Arthritis pain Visual Analogue Scale (VAS) at Week 12

End point title	Change from Baseline in Arthritis pain Visual Analogue Scale (VAS) at Week 12[8]

End point description:

For the Arthritis Pain VAS, participants assess the severity of their current arthritis pain using a continuous visual analogue scale (VAS) with anchors at "0" (no pain) and "100" (most severe pain). A negative change from baseline indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Score on scale				
least squares mean (standard error)	-19.35 (± 2.127)	-21.17 (± 2.088)	-25.93 (± 2.12)	-16.73 (± 2.939)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI total score at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in CDAI total score at Week 24 for placebo switched arms that started study intervention from Week 12[9]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (TJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). CDAI total score ranges from 0 to 76 with higher values representing higher disease activity.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Scores on a scale				
least squares mean (standard error)	-16.84 (± 2.476)	-22.91 (± 2.439)	-20.38 (± 2.380)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Arthritis pain VAS at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in Arthritis pain VAS at Week 24 for placebo switched arms that started study intervention from Week 12[10]

End point description:

For the Arthritis Pain VAS, participants assess the severity of their current arthritis pain using a continuous visual analogue scale (VAS) with anchors at "0" (no pain) and "100" (most severe pain). A negative change from baseline indicates an improvement.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Scores on a scale				
least squares mean (standard error)	-16.98 (± 5.169)	-32.74 (± 5.029)	-18.60 (± 4.964)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Arthritis pain VAS at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in Arthritis pain VAS at Week 24 for treatment arms that started study intervention from Day 1[11]

End point description:

For the Arthritis Pain VAS, participants assess the severity of their current arthritis pain using a continuous visual analogue scale (VAS) with anchors at "0" (no pain) and "100" (most severe pain). A negative change from baseline indicates an improvement.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[11] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Scores on a scale				
least squares mean (standard error)	-25.06 (± 2.153)	-24.31 (± 2.115)	-30.62 (± 2.141)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with CDAI total score <=2.8 (CDAI Remission) at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Percentage of participants with CDAI total score <=2.8 (CDAI Remission) at Week 24 for placebo switched arms that started study intervention from Week 12[12]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (TJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). CDAI total score ranges from 0 to 76 with higher values representing higher disease activity.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Percentage of participants				
number (not applicable)	5.1	13.2	8.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with CDAI total score <=2.8 (CDAI Remission) at Week 24 for treatment arms that started study intervention from Day

1

End point title	Percentage of participants with CDAI total score <=2.8 (CDAI Remission) at Week 24 for treatment arms that started study intervention from Day 1[13]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (TJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). CDAI total score ranges from 0 to 76 with higher values representing higher disease activity.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[13] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Percentage of participants				
number (not applicable)	7.9	8.4	8.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with CDAI total score <=2.8 (CDAI Remission) at Week 12

End point title	Percentage of participants with CDAI total score <=2.8 (CDAI Remission) at Week 12[14]

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (TJC28),Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Percentage of participants				
number (not applicable)	2.2	4.3	8.7	0.6

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ACR20 at Week 24 for treatment arms that started study intervention from Day 1

End point title	Percentage of participants with ACR20 at Week 24 for treatment arms that started study intervention from Day 1[15]

End point description:

ACR20 is calculated as a 20% improvement from Baseline in TJC68 and SJC66 and a 20% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA), Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS values from 0=no pain to 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (0=least difficulty to 3=extreme difficulty) and an acute-phase reactant (high sensitivity C-reactive Protein mg/L (hsCRP).

End point type	Secondary

End point timeframe:

Week 24

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Percentage of participants				
number (not applicable)	58.1	60.5	65.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ACR20 at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Percentage of participants with ACR20 at Week 24 for placebo switched arms that started study intervention from Week 12[16]

End point description:

ACR20 is calculated as a 20% improvement from Baseline in TJC68 and SJC66 and a 20% improvement

in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA), Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS values from 0=no pain to 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (0=least difficulty to 3=extreme difficulty) and an acute-phase reactant (high sensitivity C-reactive Protein mg/L (hsCRP).

End point type	Secondary

End point timeframe:

Week 24

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Percentage of participants				
number (not applicable)	61.2	70.7	55.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with 50% improvement in American College of Rheumatology criteria (ACR50) at Week 12

End point title	Percentage of participants with 50% improvement in American College of Rheumatology criteria (ACR50) at Week 12[17]

End point description:

ACR50 is calculated as a 50% improvement from Baseline in Tender Joint Count 68 (TJC68) and Swollen Joint Count 66 (SJC66) and a 50% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale (VAS) with values from 0=best to 100=worst), Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty) and an acute-phase reactant (high sensitivity C-reactive Protein mg/L (hsCRP)). For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Percentage of participants				
number (not applicable)	18.2	22.5	25.9	11.5

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ACR50 at Week 24 for treatment arms that started study intervention from Day 1

End point title	Percentage of participants with ACR50 at Week 24 for treatment arms that started study intervention from Day 1[18]

End point description:

ACR50 is calculated as a 50% improvement from Baseline in TJC68 and SJC66 and a 50% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA), Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS values from 0=no pain to 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (0=least difficulty to 3=extreme difficulty) and an acute-phase reactant (high sensitivity C-reactive Protein mg/L (hsCRP).

End point type	Secondary

End point timeframe:

Week 24

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Percentage of participants				
number (not applicable)	23.6	30.1	42.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ACR50 at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Percentage of participants with ACR50 at Week 24 for placebo switched arms that started study intervention from Week 12[19]

End point description:

ACR50 is calculated as a 50% improvement from Baseline in TJC68 and SJC66 and a 50% improvement

in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA), Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS values from 0=no pain to 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (0=least difficulty to 3=extreme difficulty) and an acute-phase reactant (high sensitivity C-reactive Protein mg/L (hsCRP).

End point type	Secondary

End point timeframe:

Week 24

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Percentage of participants				
number (not applicable)	13.1	41.8	24.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with 70% improvement in American College of Rheumatology criteria (ACR70) at Week 12

End point title	Percentage of participants with 70% improvement in American College of Rheumatology criteria (ACR70) at Week 12[20]

End point description:

ACR70 is calculated as a 70% improvement from Baseline in Tender Joint Count 68 (TJC68) and Swollen Joint Count 66 (SJC66) and a 70% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale (VAS) with values from 0=best to 100=worst), Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty) and an acute-phase reactant (high sensitivity C-reactive Protein mg/L (hsCRP)). For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Percentage of participants				
number (not applicable)	5.9	10.8	13.3	6.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ACR70 at Week 24 for treatment arms that started study intervention from Day 1

End point title	Percentage of participants with ACR70 at Week 24 for treatment arms that started study intervention from Day 1[21]

End point description:

ACR70 is calculated as a 70% improvement from Baseline in TJC68 and SJC66 and a 70% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA), Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS values from 0=no pain to 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (0=least difficulty to 3=extreme difficulty) and an acute-phase reactant (high sensitivity C-reactive Protein mg/L (hsCRP).

End point type	Secondary

End point timeframe:

Week 24

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Percentage of participants				
number (not applicable)	12.3	13.2	22.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ACR70 at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Percentage of participants with ACR70 at Week 24 for placebo switched arms that started study intervention from Week 12[22]

End point description:

ACR70 is calculated as a 70% improvement from Baseline in TJC68 and SJC66 and a 70% improvement

in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA), Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS values from 0=no pain to 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (0=least difficulty to 3=extreme difficulty) and an acute-phase reactant (high sensitivity C-reactive Protein mg/L (hsCRP).

End point type	Secondary

End point timeframe:

Week 24

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Percentage of participants				
number (not applicable)	4.9	21.4	12.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with DAS28-CRP <=3.2 (DAS28-CRP LDA) at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Percentage of participants with DAS28-CRP <=3.2 (DAS28-CRP LDA) at Week 24 for placebo switched arms that started study intervention from Week 12[23]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicates less disease activity. Low disease activity (LDA) is achieved when DAS28-CRP<=3.2 . A negative change from baseline in DAS28-CRP indicates an improvement.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Percentage of participants				
number (not applicable)	12.5	43.1	55.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Disease Activity Score using 28 joint count and C-Reactive Protein (DAS28-CRP) <=3.2 (DAS28-CRP LDA) at Week 12

End point title	Percentage of participants with Disease Activity Score using 28 joint count and C-Reactive Protein (DAS28-CRP) <=3.2 (DAS28-CRP LDA) at Week 12[24]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicates less disease activity. Low disease activity (LDA) is achieved when DAS28-CRP<=3.2. A negative change from baseline in DAS28-CRP indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[24] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Percentage of participants				
number (not applicable)	17	17	40.1	13.2

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with DAS28-CRP <=3.2 (DAS28-CRP LDA) at Week 24 for treatment arms that started study intervention from Day 1

End point title	Percentage of participants with DAS28-CRP <=3.2 (DAS28-CRP LDA) at Week 24 for treatment arms that started study intervention from Day 1[25]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicates less disease activity. Low disease activity (LDA) is achieved when DAS28-CRP<=3.2 . A negative change from baseline in DAS28-CRP indicates an improvement.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[25] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Percentage of participants				
number (not applicable)	26.8	24.8	46.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with DAS28 Erythrocyte Sedimentation Rate (ESR) <=3.2 (DAS28-ESR LDA) at Week 12

End point title	Percentage of participants with DAS28 Erythrocyte Sedimentation Rate (ESR) <=3.2 (DAS28-ESR LDA) at Week 12[26]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-ESR<=3.2. A negative change from baseline in DAS28-ESR indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[26] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Percentage of participants				
number (not applicable)	13.3	8.5	36.2	1.9

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with DAS28-ESR <=3.2 (DAS28-ESR LDA) at Week 24 for treatment arms that started study intervention from Day 1

End point title	Percentage of participants with DAS28-ESR <=3.2 (DAS28-ESR LDA) at Week 24 for treatment arms that started study intervention from Day 1[27]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-ESR<=3.2. A negative change from baseline in DAS28-ESR indicates an improvement.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[27] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Percentage of participants				
number (not applicable)	17.4	17.2	45.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 12

End point title	Percentage of participants with DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 12[28]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicates less disease activity. Remission is achieved when DAS28-CRP <2.6. A negative change from baseline in DAS28-CRP indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[28] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Percentage of participants				
number (not applicable)	10.2	7.2	22.2	1.8

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with DAS28-ESR <=3.2 (DAS28-ESR LDA) at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Percentage of participants with DAS28-ESR <=3.2 (DAS28-ESR LDA) at Week 24 for placebo switched arms that started study intervention from Week 12[29]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-ESR<=3.2. A negative change from baseline in DAS28-ESR indicates an improvement.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[29] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Percentage of participants				
number (not applicable)	5.7	33.4	40.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Percentage of participants with DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 for placebo switched arms that started study intervention from Week 12[30]

End point description:

The DAS28-CRP arthritis is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicates less disease activity. Remission is achieved when DAS28-CRP <2.6. A negative change from baseline in DAS28-CRP indicates an improvement.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[30] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Percentage of participants				
number (not applicable)	6.8	26.6	32.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with DAS28-CRP <2.6 (DAS28-CRP

Remission) at Week 24 for treatment arms that started study intervention from Day 1

End point title	Percentage of participants with DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 for treatment arms that started study intervention from Day 1[31]

End point description:

The DAS28-CRP arthritis is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicates less disease activity. Remission is achieved when DAS28-CRP <2.6. A negative change from baseline in DAS28-CRP indicates an improvement.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[31] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Percentage of participants				
number (not applicable)	16.2	13.9	32.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with DAS28-ESR <2.6 (DAS28-ESR Remission) Week 24 for treatment arms that started study intervention from Day 1

End point title	Percentage of participants with DAS28-ESR <2.6 (DAS28-ESR Remission) Week 24 for treatment arms that started study intervention from Day 1[32]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicates less disease activity. Remission is achieved when DAS28-ESR <2.6. A negative change from baseline in DAS28-ESR indicates an improvement.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[32] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Percentage of participants				
number (not applicable)	10.8	8.9	29.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with DAS28-ESR <2.6 (DAS28-ESR Remission) at Week 12

End point title	Percentage of participants with DAS28-ESR <2.6 (DAS28-ESR Remission) at Week 12[33]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicates less disease activity. Remission is achieved when DAS28-ESR <2.6. A negative change from baseline in DAS28-ESR indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[33] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Percentage of participants				
number (not applicable)	3.1	5.7	23	0.7

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with DAS28-ESR <2.6 (DAS28-ESR Remission) Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Percentage of participants with DAS28-ESR <2.6 (DAS28-ESR Remission) Week 24 for placebo switched arms that started study intervention from Week 12[34]

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicates less disease activity. Remission is achieved when DAS28-ESR <2.6. A negative change from baseline in DAS28-ESR indicates an improvement.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[34] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Percentage of participants				
number (not applicable)	1.1	10.0	24.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a good/moderate EULAR response at Week 24 for treatment arms that started study intervention from Day 1

End point title	Percentage of participants with a good/moderate EULAR response at Week 24 for treatment arms that started study intervention from Day 1[35]

End point description:

DAS28-CRP and DAS28-ESR scores categorised using EULAR response criteria. Response based on the combination of current DAS28 score and the improvement in the current DAS28 score relative to baseline (Good response = DAS28 change >1.2 with current DAS28 ≤3.2; Moderate response = DAS28 change >0.6 with current DAS28 >3.2-5.1; Non-response = DAS28 change ≤0.6 and current DAS28 >5.1).

End point type	Secondary

End point timeframe:

Week 24

Notes:

[35] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Percentage of participants				
number (not applicable)	76.3	71.3	86.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a good/moderate European League against Rheumatism (EULAR) response at Week 12

End point title	Percentage of participants with a good/moderate European League against Rheumatism (EULAR) response at Week 12[36]

End point description:

DAS28-CRP and DAS28-ESR scores categorized using EULAR response criteria. Response based on the combination of current DAS28 score and the improvement in the current DAS28 score relative to baseline (Good response = DAS28 change >1.2 with current DAS28 ≤3.2; Moderate response = DAS28 change >0.6 with current DAS28 >3.2-5.1; Non-response = DAS28 change ≤0.6 and current DAS28 >5.1). For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[36] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Percentage of participants				
number (not applicable)	66.3	68.4	84.1	62.9

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ACR/EULAR remission at Week 12

End point title	Percentage of participants with ACR/EULAR remission at Week 12[37]

End point description:

Boolean-based ACR/EULAR remission is achieved if all of the following requirements are met at the same timepoint: Tender Joint Count 68 (TJC68) ≤ 1, Swollen Joint Count 66 (SJC66) ≤ 1, high sensitivity C-reactive Protein (hsCRP) ≤ 1mg/dl and patient's global assessment of disease activity (PtGA) ≤ 10. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Week 12

Notes:

[37] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Percentage of participants	2	4	9	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a good/moderate EULAR response at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Percentage of participants with a good/moderate EULAR response at Week 24 for placebo switched arms that started study intervention from Week 12[38]

End point description:

DAS28-CRP and DAS28-ESR scores categorised using EULAR response criteria. Response based on the combination of current DAS28 score and the improvement in the current DAS28 score relative to baseline (Good response = DAS28 change >1.2 with current DAS28 ≤3.2; Moderate response = DAS28 change >0.6 with current DAS28 >3.2-5.1; Non-response = DAS28 change ≤0.6 and current DAS28 >5.1).

End point type	Secondary

End point timeframe:

Week 24

Notes:

[38] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Percentage of participants				
number (not applicable)	73.3	76.7	83.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ACR/EULAR remission at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Percentage of participants with ACR/EULAR remission at Week 24 for placebo switched arms that started study intervention from Week 12[39]

End point description:

Boolean-based ACR/EULAR remission is achieved if all of the following requirements are met at the same timepoint: Tender Joint Count 68 (TJC68) ≤ 1, Swollen Joint Count 66 (SJC66) ≤ 1, high sensitivity C-reactive Protein (CRP) ≤ 1mg/dl and patient's global assessment of disease activity (PtGA) ≤ 10.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[39] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Percentage of participants	1	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ACR/EULAR remission at Week 24 for treatment arms that started study intervention from Day 1

End point title	Percentage of participants with ACR/EULAR remission at Week 24 for treatment arms that started study intervention from Day 1[40]

End point description:

Boolean-based ACR/EULAR remission is achieved if all of the following requirements are met at the same timepoint: Tender Joint Count 68 (TJC68) ≤ 1, Swollen Joint Count 66 (SJC66) ≤ 1, high sensitivity C-reactive Protein (CRP) ≤ 1mg/dl and patient's global assessment of disease activity (PtGA) ≤ 10.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[40] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Percentage of participants	6	4	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DAS28-CRP and DAS28-ESR at Week 12

End point title	Change from Baseline in DAS28-CRP and DAS28-ESR at Week 12[41]

End point description:

DAS28-CRP and DAS28-ESR are measure of RA disease activity calculated using Swollen Joint Count 28 (TJC28), Tender Joint Count 28 (TJC28), high sensitivity C-reactive Protein (hsCRP in mg/L)/Erythrocyte sedimentation rate (ESR in mm/hr (mm/hour) and patient's global assessment of disease activity (PtGA) transformed to a 0-10 scale. Total score approximate range 0-9.4, with higher scores indicating more disease activity. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[41] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Scores on a scale				
least squares mean (standard error)				
DAS28-CRP	-1.34 (± 0.1)	-1.42 (± 0.098)	-2.15 (± 0.1)	-1.08 (± 0.139)

DAS28-ESR	-1.41 (± 0.109)	-1.46 (± 0.106)	-2.57 (± 0.108)	-1.06 (± 0.152)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DAS28-CRP and DAS28-ESR at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in DAS28-CRP and DAS28-ESR at Week 24 for treatment arms that started study intervention from Day 1[42]

End point description:

DAS28-CRP and DAS28-ESR are measure of RA disease activity calculated using Swollen Joint Count 28 (TJC28), Tender Joint Count 28 (TJC28), high sensitivity C-reactive Protein (hsCRP in mg/L)/Erythrocyte sedimentation rate (ESR in mm/hr (mm/hour) and patient's global assessment of disease activity (PtGA) transformed to a 0-10 scale. Total score approximate range 0-9.4, with higher scores indicating more disease activity.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[42] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Scores on a scale				
least squares mean (standard error)				
DAS28-CRP	-1.67 (± 0.108)	-1.67 (± 0.106)	-2.38 (± 0.109)	
DAS28-ESR	-1.7 (± 0.121)	-1.68 (± 0.117)	-2.85 (± 0.121)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DAS28-CRP and DAS28-ESR at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in DAS28-CRP and DAS28-ESR at Week 24 for placebo switched arms that started study intervention from Week 12[43]

End point description:

DAS28-CRP and DAS28-ESR are measure of RA disease activity calculated using Swollen Joint Count 28 (TJC28), Tender Joint Count 28 (TJC28), high sensitivity C-reactive Protein (hsCRP in mg/L)/Erythrocyte sedimentation rate (ESR in mm/hr (mm/hour) and patient's global assessment of disease activity (PtGA) transformed to a 0-10 scale. Total score approximate range 0-9.4, with higher scores indicating more disease activity.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[43] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Scores on a scale				
least squares mean (standard error)				
DAS28-CRP	-1.25 (± 0.264)	-2.08 (± 0.258)	-2.15 (± 0.248)	
DAS28-ESR	-1.28 (± 0.282)	-1.94 (± 0.294)	-2.47 (± 0.266)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HAQ-DI at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in HAQ-DI at Week 24 for treatment arms that started study intervention from Day 1[44]

End point description:

Health Assessment Questionnaire-Disability Index (HAQ-DI) is a 20-question instrument that assesses the difficulty of a participant in eight domains of daily activities: Dressing & grooming, Arising, Eating, Walking, Hygiene, Reach, Grip, Common daily activities. HAQ-DI score was computed as sum of the domain scores divided by the number of domains answered. The total possible score ranges from 0=least difficulty to 3=extreme difficulty. Higher overall score indicates greater disability. A negative change from baseline indicates an improvement.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[44] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Scores on a scale				
least squares mean (standard error)	-0.39 (± 0.05)	-0.45 (± 0.049)	-0.48 (± 0.05)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HAQ-DI at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in HAQ-DI at Week 24 for placebo switched arms that started study intervention from Week 12[45]

End point description:

Health Assessment Questionnaire-Disability Index (HAQ-DI) is a 20-question instrument that assesses the difficulty of a participant in eight domains of daily activities: Dressing & grooming, Arising, Eating, Walking, Hygiene, Reach, Grip, Common daily activities. HAQ-DI score was computed as sum of the domain scores divided by the number of domains answered. The total possible score ranges from 0=least difficulty to 3=extreme difficulty. Higher overall score indicates greater disability. A negative change from baseline indicates an improvement.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[45] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Scores on a scale				
least squares mean (standard error)	-0.27 (± 0.121)	-0.62 (± 0.119)	-0.32 (± 0.116)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Functional assessment of chronic illness therapy (FACIT)-Fatigue at Week 12

End point title	Change from Baseline in Functional assessment of chronic illness therapy (FACIT)-Fatigue at Week 12[46]

End point description:

The Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue is a validated patient-reported measure of 13 statements regarding the feeling of fatigue. The total score ranges from 0 to 52 with higher values representing a lower fatigue and a better quality of life. A positive change from baseline in FACIT-fatigue indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[46] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Scores on a scale				
least squares mean (standard error)	5.5 (± 0.735)	6.8 (± 0.724)	7.3 (± 0.749)	5.45 (± 1.023)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in FACIT-Fatigue at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in FACIT-Fatigue at Week 24 for treatment arms that started study intervention from Day 1[47]

End point description:

The Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue is a validated patient-reported measure of 13 statements regarding the feeling of fatigue. The total score ranges from 0 to 52 with higher values representing a lower fatigue and a better quality of life. A positive change from baseline in FACIT-fatigue indicates an improvement.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[47] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Scores on a scale				
least squares mean (standard error)	6.55 (± 0.795)	7.21 (± 0.777)	7.99 (± 0.806)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 PCS at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in SF-36 PCS at Week 24 for treatment arms that started study intervention from Day 1[48]

End point description:

The Short-Form 36 (SF-36) is a health-related survey that assesses quality of life covering 8 domains: physical functioning, bodily pain, role limitations due to physical and emotional problems, general health, mental health, social functioning, vitality. The score for a domain was an average of the individual question scores, which were scaled 0-100; higher score represents better health. The PCS is an aggregated score derived from 4 domains (physical functioning, role-physical, bodily pain and general health) representing overall physical health. T-score scale was used for PCS with mean of 50 and SD of 10; higher score represents better health. A positive change from baseline indicates an improvement in overall physical health. Quality Metrics software was used for scoring for SF-36.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[48] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Scores on a scale				
least squares mean (standard error)	5.67 (± 0.707)	5.5 (± 0.694)	7.18 (± 0.71)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Subject-completed Medical Outcomes Study Short-Form 36 (SF-36) Physical Component Scores (PCS) at Week 12

End point title	Change from Baseline in Subject-completed Medical Outcomes Study Short-Form 36 (SF-36) Physical Component Scores

	(PCS) at Week 12[49]

End point description:

The Short-Form 36 (SF-36) is a health-related survey that assesses quality of life covering 8 domains: physical functioning, bodily pain, role limitations due to physical and emotional problems, general health, mental health, social functioning, vitality. The score for a domain was an average of the individual question scores, which were scaled 0-100; higher score represents better health. The PCS is an aggregated score derived from 4 domains (physical functioning, role-physical, bodily pain and general health) representing overall physical health. T-score scale was used for PCS with mean of 50 and SD of 10; higher score represents better health. A positive change from baseline indicates an improvement in overall physical health. Quality Metrics software was used for scoring for SF-36. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[49] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Scores on a scale				
least squares mean (standard error)	5.08 (± 0.619)	5.03 (± 0.61)	5.61 (± 0.627)	3.72 (± 0.866)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in FACIT-Fatigue at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in FACIT-Fatigue at Week 24 for placebo switched arms that started study intervention from Week 12[50]

End point description:

The Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue is a validated patient-reported measure of 13 statements regarding the feeling of fatigue. The total score ranges from 0 to 52 with higher values representing a lower fatigue and a better quality of life. A positive change from baseline in FACIT-fatigue indicates an improvement.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[50] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Scores on a scale				
least squares mean (standard error)	5.48 (± 1.927)	8.56 (± 1.852)	7.21 (± 1.824)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 Mental Component Scores (MCS) at Week 12

End point title	Change from Baseline in SF-36 Mental Component Scores (MCS) at Week 12[51]

End point description:

The Short-Form 36 (SF-36) is a health-related survey that assesses quality of life covering 8 domains: physical functioning, bodily pain, role limitations due to physical and emotional problems, general health, mental health, social functioning, vitality. The score for a domain was an average of the individual question scores, which were scaled 0-100; higher score represents better health. The MCS is an aggregated score derived from 4 domains (social functioning, vitality, mental health, and role-emotional domains) representing overall mental health. T-score scale was used for MCS with mean of 50 and SD of 10; higher score represents better health. A positive change from baseline indicates an improvement in overall mental health. Quality Metrics software was used for scoring for SF-36. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[51] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Scores on a scale				
least squares mean (standard error)	1.64 (± 0.731)	3.45 (± 0.72)	4.15 (± 0.744)	1.61 (± 1.024)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 PCS at Week 24 for placebo switched

arms that started study intervention from Week 12

End point title	Change from Baseline in SF-36 PCS at Week 24 for placebo switched arms that started study intervention from Week 12[52]

End point description:

The Short-Form 36 (SF-36) is a health-related survey that assesses quality of life covering 8 domains: physical functioning, bodily pain, role limitations due to physical and emotional problems, general health, mental health, social functioning, vitality. The score for a domain was an average of the individual question scores, which were scaled 0-100; higher score represents better health. The PCS is an aggregated score derived from 4 domains (physical functioning, role-physical, bodily pain and general health) representing overall physical health. T-score scale was used for PCS with mean of 50 and SD of 10; higher score represents better health. A positive change from baseline indicates an improvement in overall physical health. Quality Metrics software was used for scoring for SF-36.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[52] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Scores on a scale				
least squares mean (standard error)	3.76 (± 1.687)	8.63 (± 1.672)	4.16 (± 1.611)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 MCS at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in SF-36 MCS at Week 24 for treatment arms that started study intervention from Day 1[53]

End point description:

The Short-Form 36 (SF-36) is a health-related survey that assesses quality of life covering 8 domains: physical functioning, bodily pain, role limitations due to physical and emotional problems, general health, mental health, social functioning, vitality. The score for a domain was an average of the individual question scores, which were scaled 0-100; higher score represents better health. The MCS is an aggregated score derived from 4 domains (social functioning, vitality, mental health, and role-emotional domains) representing overall mental health. T-score scale was used for MCS with mean of 50 and SD of 10; higher score represents better health. A positive change from baseline indicates an improvement in overall mental health. Quality Metrics software was used for scoring for SF-36.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[53] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Scores on a scale				
least squares mean (standard error)	2.22 (± 0.772)	3.05 (± 0.756)	3.61 (± 0.78)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 MCS at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in SF-36 MCS at Week 24 for placebo switched arms that started study intervention from Week 12[54]

End point description:

The Short-Form 36 (SF-36) is a health-related survey that assesses quality of life covering 8 domains: physical functioning, bodily pain, role limitations due to physical and emotional problems, general health, mental health, social functioning, vitality. The score for a domain was an average of the individual question scores, which were scaled 0-100; higher score represents better health. The MCS is an aggregated score derived from 4 domains (social functioning, vitality, mental health, and role-emotional domains) representing overall mental health. T-score scale was used for MCS with mean of 50 and SD of 10; higher score represents better health. A positive change from baseline indicates an improvement in overall mental health. Quality Metrics software was used for scoring for SF-36.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[54] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	26	27	
Units: Scores on a scale				
least squares mean (standard error)	1.44 (± 1.891)	1.10 (± 1.855)	2.76 (± 1.800)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 domain scores at Week 12

End point title	Change from Baseline in SF-36 domain scores at Week 12[55]

End point description:

The Short-Form 36 (SF-36) is a health-related survey that assesses quality of life covering 8 domains: physical functioning, bodily pain, role limitations due to physical and emotional problems, general health, mental health, social functioning, vitality. The MCS consists of 4 domains (social functioning, vitality, mental health, and role-emotional domains) and PCS consists of 4 domains (physical functioning, role-physical, bodily pain and general health). The individual question items are first summed for each item under the various sections. Then, those domain scores are scaled between 0 to 100, where higher score represents better health. A positive change from baseline indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[55] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	143	148	138	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Bodily Pain - PCS	17 (± 21.45)	16.8 (± 22.2)	19.8 (± 23.27)	
General Health - PCS	6.3 (± 15.89)	6.7 (± 16.07)	6.7 (± 15.69)	
Role Physical - PCS	12.94 (± 22.371)	14.19 (± 25.155)	13.81 (± 23.488)	
Physical Function - PCS	9.69 (± 21.423)	14.22 (± 23.909)	13.15 (± 24.135)	
Mental Health - MCS	4.3 (± 19.3)	7.6 (± 16.9)	8.2 (± 18.55)	
Role Emotional - MCS	5.77 (± 22.405)	9.4 (± 25.128)	10.93 (± 23.908)	
Social Function - MCS	6.99 (± 23.107)	10.73 (± 27.51)	11.59 (± 24.383)	
Vitality - MCS	9.48 (± 18.03)	11.82 (± 19.94)	13 (± 19.895)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 domain scores at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in SF-36 domain scores at Week 24 for treatment arms that started study intervention from Day 1[56]

End point description:

The Short-Form 36 (SF-36) is a health-related survey that assesses quality of life covering 8 domains: physical functioning, bodily pain, role limitations due to physical and emotional problems, general health, mental health, social functioning, vitality. The MCS consists of 4 domains (social functioning, vitality, mental health, and role-emotional domains) and PCS consists of 4 domains (physical functioning, role-physical, bodily pain and general health). The individual question items are first summed for each item under the various sections. Then, those domain scores are scaled between 0 to 100, where higher score represents better health. A positive change from baseline indicates an improvement.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[56] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	147	136	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Bodily Pain - PCS	20.7 (± 22.82)	18.5 (± 22.43)	23.9 (± 27.29)	
General Health - PCS	6.4 (± 15.25)	6.7 (± 16.3)	8.8 (± 17.3)	
Role Physical - PCS	13.97 (± 21.332)	15.22 (± 27.352)	17.37 (± 26.25)	
Physical Function - PCS	11.43 (± 23.714)	16.36 (± 25.64)	18.86 (± 24.472)	
Mental Health - MCS	6.1 (± 17.16)	8.4 (± 19.63)	10 (± 18.71)	
Role Emotional - MCS	5.83 (± 23.522)	7.99 (± 28.03)	8.88 (± 26.589)	
Social Function - MCS	9.46 (± 25.704)	10.37 (± 29.237)	12.04 (± 24.599)	
Vitality - MCS	11.29 (± 17.913)	13.22 (± 21.245)	16.31 (± 19.854)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 domain scores at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in SF-36 domain scores at Week 24 for

	placebo switched arms that started study intervention from Week 12[57]

End point description:

The Short-Form 36 (SF-36) is a health-related survey that assesses quality of life covering 8 domains: physical functioning, bodily pain, role limitations due to physical and emotional problems, general health, mental health, social functioning, vitality. The MCS consists of 4 domains (social functioning, vitality, mental health, and role-emotional domains) and PCS consists of 4 domains (physical functioning, role-physical, bodily pain and general health). The individual question items are first summed for each item under the various sections. Then, those domain scores are scaled between 0 to 100, where higher score represents better health. A positive change from baseline indicates an improvement.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[57] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	24	25	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Bodily Pain - PCS	15.7 (± 21.91)	20.4 (± 26.91)	16.9 (± 23.99)	
General Health - PCS	5.6 (± 14.98)	3.4 (± 17.47)	4.4 (± 17.20)	
Role Physical - PCS	10.33 (± 21.204)	17.19 (± 19.352)	12.25 (± 20.530)	
Physical Function - PCS	7.39 (± 19.121)	18.75 (± 23.417)	6.20 (± 20.630)	
Mental Health - MCS	5.9 (± 14.11)	5.2 (± 23.29)	5.4 (± 18.54)	
Role Emotional - MCS	7.97 (± 21.242)	4.17 (± 28.019)	6.67 (± 28.667)	
Social Function - MCS	13.04 (± 23.681)	6.25 (± 37.771)	5.50 (± 36.279)	
Vitality - MCS	8.42 (± 13.926)	10.16 (± 27.263)	11.75 (± 20.832)	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Adverse events (AEs), Serious adverse event (SAEs), Adverse events of special interest (AESI)

End point title	Incidence of Adverse events (AEs), Serious adverse event (SAEs), Adverse events of special interest (AESI)[58]

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. A SAE is any untoward medical occurrence that, is life-threatening, requires inpatient hospitalization or prolongation

of existing hospitalization, results in persistent disability/incapacity and/or can result in death.

End point type	Secondary

End point timeframe:

Up to Week 24

Notes:

[58] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: Participants				
AE	92	99	98	37
SAE	8	1	12	2
AESI	16	15	33	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in neutrophil, lymphocyte, platelet count (Giga cells per liter) at Week 12

End point title	Change from Baseline in neutrophil, lymphocyte, platelet count (Giga cells per liter) at Week 12[59]

End point description:

Blood samples was collected for the assessment of change from baseline in hematology parameters including neutrophil, lymphocyte, platelet count. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[59] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	141	143	138	
Units: 10^9/L (Giga cells per liter)				
arithmetic mean (standard deviation)				
Lymphocytes	-0.039 (± 0.5089)	-0.01 (± 0.508)	-0.057 (± 0.4989)	

Neutrophils	-0.255 (± 1.5469)	-0.412 (± 2.0477)	-1.843 (± 2.1359)	
Platelets	-10.9 (± 56.51)	-17.3 (± 60.17)	-76.5 (± 62.76)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in neutrophil, lymphocyte, platelet count (Giga cells per liter) at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in neutrophil, lymphocyte, platelet count (Giga cells per liter) at Week 24 for treatment arms that started study intervention from Day 1[60]

End point description:

Blood samples was collected for the assessment of change from baseline in hematology parameters including neutrophil, lymphocyte, platelet count.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[60] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	138	141	127	
Units: 10^9/L (Giga cells per liter)				
arithmetic mean (standard deviation)				
Lymphocytes	-0.079 (± 0.5135)	0.012 (± 0.5939)	-0.108 (± 0.52)	
Neutrophils	-0.388 (± 1.692)	-0.422 (± 1.7963)	-1.99 (± 2.3395)	
Platelets	-9.3 (± 50.96)	-9 (± 64.92)	-79.2 (± 71.13)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in neutrophil, lymphocyte, platelet count (Giga cells per liter) at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in neutrophil, lymphocyte, platelet count (Giga cells per liter) at Week 24 for placebo switched arms that

	started study intervention from Week 12[61]

End point description:

Blood samples was collected for the assessment of change from baseline in hematology parameters including neutrophil, lymphocyte, platelet count.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[61] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	24	26	
Units: 10^9/L (Giga cells per liter)				
arithmetic mean (standard deviation)				
Lymphocytes	-0.030 (± 0.4192)	0.083 (± 0.3298)	-0.094 (± 0.4478)	
Neutrophils	-0.611 (± 1.7602)	-0.643 (± 1.3489)	-2.016 (± 2.1132)	
Platelets	-43.6 (± 53.10)	-12.7 (± 74.80)	-70.8 (± 82.58)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in white blood cell (WBC) count (Giga cells per liter) at Week 12

End point title	Change from Baseline in white blood cell (WBC) count (Giga cells per liter) at Week 12[62]

End point description:

Blood samples was collected for the assessment of change from baseline in hematology parameter WBC count. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[62] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: 10^9/L (Giga cells per liter)				
arithmetic mean (standard deviation)	-0.29 (± 1.753)	-0.42 (± 2.072)	-1.95 (± 2.325)	-0.09 (± 1.558)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in WBC count (Giga cells per liter) at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in WBC count (Giga cells per liter) at Week 24 for treatment arms that started study intervention from Day 1[63]

End point description:

Blood samples was collected for the assessment of change from baseline in hematology parameter WBC count.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[63] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: 10^9/L (Giga cells per liter)				
arithmetic mean (standard deviation)	-0.45 (± 1.851)	-0.43 (± 1.787)	-2.15 (± 2.51)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in WBC count (Giga cells per liter) at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in WBC count (Giga cells per liter) at Week 24 for placebo switched arms that started study intervention from Week 12[64]

End point description:

Blood samples was collected for the assessment of change from baseline in hematology parameter WBC

count.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[64] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	24	26	
Units: 10^9/L (Giga cells per liter)				
arithmetic mean (standard deviation)	-0.66 (± 1.824)	-0.60 (± 1.452)	-2.05 (± 2.271)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hemoglobin level (Grams per liter) Week 12

End point title	Change from Baseline in hemoglobin level (Grams per liter) Week 12[65]

End point description:

Blood samples was collected for the assessment of change from baseline in hematology parameter hemoglobin level. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[65] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: g/L (Grams per liter)				
arithmetic mean (standard deviation)	-0.9 (± 8.06)	0.3 (± 8.54)	5.5 (± 9.19)	-2 (± 7.98)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hemoglobin level (Grams per liter) Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in hemoglobin level (Grams per liter) Week 24 for placebo switched arms that started study intervention from Week 12[66]

End point description:

Blood samples was collected for the assessment of change from baseline in in hematology parameter hemoglobin level.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[66] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	24	26	
Units: g/L (Grams per liter)				
arithmetic mean (standard deviation)	3.5 (± 7.44)	0.2 (± 10.85)	7.0 (± 11.51)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hemoglobin level (Grams per liter) Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in hemoglobin level (Grams per liter) Week 24 for treatment arms that started study intervention from Day 1[67]

End point description:

Blood samples was collected for the assessment of change from baseline in in hematology parameter hemoglobin level.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[67] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: g/L (Grams per liter)				
arithmetic mean (standard deviation)	-1.9 (± 9.05)	-1 (± 8.63)	5.8 (± 11.07)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP) gamma-glutamyl transferase(GGT) levels (International units per liter) at Week 12

End point title	Change from Baseline in aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP) gamma-glutamyl transferase(GGT) levels (International units per liter) at Week 12[68]

End point description:

Blood samples was collected for the assessment of change from baseline in laboratory parameters including aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP) gamma-glutamyl transferase (GGT) levels. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[68] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	146	146	139	
Units: IU/L (International units per liter)				
arithmetic mean (standard deviation)				
AST	0.6 (± 10.29)	0.7 (± 8.52)	4.5 (± 11.43)	
ALT	0.8 (± 16.22)	-0.7 (± 12.95)	8.1 (± 21.3)	

AP	0.7 (± 14.42)	-3 (± 14.94)	-15.6 (± 20.63)	
GGT	-0.8 (± 14.24)	-2.6 (± 15.23)	0.6 (± 12.37)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in AST, ALT, AP, GGT levels (International units per liter) at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in AST, ALT, AP, GGT levels (International units per liter) at Week 24 for treatment arms that started study intervention from Day 1[69]

End point description:

Blood samples was collected for the assessment of change from baseline in laboratory parameters including AST, ALT, AP, GGT levels.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[69] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	141	145	129	
Units: IU/L (International units per liter)				
arithmetic mean (standard deviation)				
AST	1.7 (± 7.89)	2.1 (± 11.21)	3.0 (± 9.29)	
ALT	1.6 (± 12.73)	1.9 (± 20.52)	6.2 (± 12.98)	
AP	1.8 (± 16.48)	-1.7 (± 18.76)	-14.3 (± 19.23)	
GGT	-0.3 (± 13.07)	-0.3 (± 25.67)	0.9 (± 15.73)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in AST, ALT, AP, GGT levels (International units per liter) at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in AST, ALT, AP, GGT levels (International units per liter) at Week 24 for placebo switched arms that started study intervention from Week 12[70]

End point description:

Blood samples was collected for the assessment of change from baseline in laboratory parameters including AST, ALT, AP, GGT levels.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[70] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	25	26	
Units: IU/L (International units per liter)				
arithmetic mean (standard deviation)				
AST	2.5 (± 6.12)	3.0 (± 9.46)	0.9 (± 17.04)	
ALT	3.3 (± 9.51)	4.2 (± 13.08)	3.5 (± 15.12)	
AP	2.0 (± 12.25)	1.4 (± 13.68)	-15.6 (± 18.77)	
GGT	4.4 (± 13.92)	-0.8 (± 7.11)	-1.4 (± 13.04)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in albumin level (Grams per liter) at Week 12

End point title	Change from Baseline in albumin level (Grams per liter) at Week 12[71]

End point description:

Blood samples was collected for the assessment of change from baseline in laboratory parameter albumin level. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[71] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: g/L (Grams per liter)				
arithmetic mean (standard deviation)	0 (± 2.5)	0.3 (± 2.38)	1.6 (± 2.64)	-0.4 (± 2.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in albumin level (Grams per liter) at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in albumin level (Grams per liter) at Week 24 for treatment arms that started study intervention from Day 1[72]

End point description:

Blood samples was collected for the assessment of change from baseline in laboratory parameter albumin level.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[72] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: g/L (Grams per liter)				
arithmetic mean (standard deviation)	0.2 (± 2.55)	0.2 (± 2.50)	2.0 (± 3.16)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in albumin level (Grams per liter) at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in albumin level (Grams per liter) at Week 24 for placebo switched arms that started study intervention from Week 12[73]

End point description:

Blood samples was collected for the assessment of change from baseline in laboratory parameter albumin level.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[73] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	24	26	
Units: g/L (Grams per liter)				
arithmetic mean (standard deviation)	1.6 (± 3.75)	0.5 (± 2.43)	1.7 (± 2.76)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total bilirubin (Micromoles per liter) at Week 12

End point title	Change from Baseline in total bilirubin (Micromoles per liter) at Week 12[74]

End point description:

Blood samples was collected for the assessment of change from baseline in laboratory parameter total bilirubin level. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[74] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	79
Units: umol/L (Micromoles per liter)				
arithmetic mean (standard deviation)	0.1 (± 2.35)	0.4 (± 3.07)	2.3 (± 4.5)	0.3 (± 2.64)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total bilirubin (Micromoles per liter) at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in total bilirubin (Micromoles per liter) at Week 24 for treatment arms that started study intervention from Day 1[75]

End point description:

Blood samples was collected for the assessment of change from baseline in laboratory parameter bilirubin level.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[75] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: umol/L (Micromoles per liter)				
arithmetic mean (standard deviation)	0.1 (± 2.06)	0.2 (± 2.70)	2.5 (± 4.11)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total bilirubin (Micromoles per liter) at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in total bilirubin (Micromoles per liter) at Week 24 for placebo switched arms that started study intervention from Week 12[76]

End point description:

Blood samples was collected for the assessment of change from baseline in laboratory parameter bilirubin level.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[76] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	25	26	
Units: umol/L (Micromoles per liter)				
arithmetic mean (standard deviation)	0.8 (± 1.97)	-0.2 (± 3.17)	1.1 (± 3.39)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total cholesterol (Millimoles per liter) at Week 12

End point title	Change from Baseline in total cholesterol (Millimoles per liter) at Week 12[77]

End point description:

Blood samples was collected for the assessment of change from baseline in lipid profile of total cholesterol levels. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[77] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[78]	0[79]	0[80]	
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[78] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[79] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[80] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total cholesterol (Millimoles per liter) at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in total cholesterol (Millimoles per liter) at Week 24 for treatment arms that started study intervention from Day 1[81]

End point description:

Blood samples was collected for the assessment of change from baseline in lipid profile of total cholesterol levels.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[81] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)	0.053 (± 1.0158)	0.061 (± 0.7881)	0.445 (± 0.8863)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total cholesterol (Millimoles per liter) at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in total cholesterol (Millimoles per liter) at Week 24 for placebo switched arms that started study intervention from Week 12[82]

End point description:

Blood samples was collected for the assessment of change from baseline in lipid profile of total cholesterol levels.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[82] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	23	25	
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)	0.126 (± 0.8456)	-0.006 (± 0.7593)	0.731 (± 0.8654)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in fasting lipid profile: low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol (Millimoles per liter) at Week 12

End point title	Change from Baseline in fasting lipid profile: low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol (Millimoles per liter) at Week 12[83]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile including LDL cholesterol, HDL cholesterol levels. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[83] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[84]	0[85]	0[86]	
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[84] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[85] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[86] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in fasting lipid profile: LDL cholesterol, HDL cholesterol (Millimoles per liter) at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in fasting lipid profile: LDL cholesterol, HDL cholesterol (Millimoles per liter) at Week 24 for placebo switched arms that started study intervention from Week 12[87]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile including

LDL cholesterol, HDL cholesterol levels.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[87] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	23	25	
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)				
HDL Cholesterol, Direct	0.049 (± 0.2578)	0.000 (± 0.2511)	0.107 (± 0.3202)	
LDL Cholesterol	0.041 (± 0.7034)	0.006 (± 0.6861)	0.513 (± 0.6822)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in fasting lipid profile: LDL cholesterol, HDL cholesterol (Millimoles per liter) at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in fasting lipid profile: LDL cholesterol, HDL cholesterol (Millimoles per liter) at Week 24 for treatment arms that started study intervention from Day 1[88]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile including LDL cholesterol, HDL cholesterol levels.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[88] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	142	125	
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)				
HDL Cholesterol, Direct	0.044 (± 0.2523)	0.051 (± 0.2931)	0.063 (± 0.2784)	
LDL Cholesterol	-0.026 (± 0.8577)	0.021 (± 0.6769)	0.334 (± 0.7472)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in fasting lipid profile triglycerides (Millimoles per liter) at Week 12

End point title	Change from Baseline in fasting lipid profile triglycerides (Millimoles per liter) at Week 12[89]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile triglycerides levels. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 12

Notes:

[89] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[90]	0[91]	0[92]	
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[90] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[91] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

[92] - Data was not collected as there is no corresponding time point in schedule of activity of Protocol.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in fasting lipid profile triglycerides (Millimoles per liter) at Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline in fasting lipid profile triglycerides

	(Millimoles per liter) at Week 24 for treatment arms that started study intervention from Day 1[93]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile triglycerides levels.

End point type	Secondary

End point timeframe:

Baseline (Day 01) and Week 24

Notes:

[93] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)	0.075 (± 0.5799)	-0.038 (± 0.5519)	0.103 (± 0.7552)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in fasting lipid profile triglycerides (Millimoles per liter) at Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline in fasting lipid profile triglycerides (Millimoles per liter) at Week 24 for placebo switched arms that started study intervention from Week 12[94]

End point description:

Blood samples was collected for the assessment of change from baseline in fasting lipid profile triglycerides levels.

End point type	Secondary

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[94] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	23	25	
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)	0.072 (± 0.4498)	-0.024 (± 0.5497)	0.243 (± 0.8130)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with National Cancer Institute (NCI)-Common terminology criteria for adverse events (CTCAE) >=Grade 3 hematological/clinical chemistry abnormalities for treatment arms that started study intervention from Day 1

End point title	Number of participants with National Cancer Institute (NCI)-Common terminology criteria for adverse events (CTCAE) >=Grade 3 hematological/clinical chemistry abnormalities for treatment arms that started study intervention from Day 1

End point description:

Number of participants who reported NCI-CTCAE Grade 3 or higher for hematological and clinical chemistry abnormalities were summarized.

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	Placebo + csDMARD and GSK3196165 90mg + csDMARD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	155	156	153	24
Units: Participants				
Alanine aminotransferase increased, Total,Grade 3	1	2	1	0
Alanine aminotransferase increased, Total,Grade 4	0	0	0	0
Aspartate aminotransferase increased,Total,Grade 3	1	1	0	0
Aspartate aminotransferase increased,Total,Grade 4	0	0	0	0
Blood bilirubin increased, Total, Grade 3	0	0	1	0
Blood bilirubin increased, Total, Grade 4	0	0	0	0
Lymphocyte count decreased, Total, Grade 3	6	1	2	0
Lymphocyte count decreased, Total, Grade 4	0	0	1	0

Lymphocyte count increased, Total, Grade 3	0	0	0	0
Lymphocyte count increased, Total, Grade 4	0	0	0	0
Neutrophil count decreased, Total, Grade 3	2	1	10	1
Neutrophil count decreased, Total, Grade 4	1	1	4	0
Platelet count decreased, Total, Grade 3	0	0	0	0
Platelet count decreased, Total, Grade 4	0	0	0	0

End point values	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: Participants				
Alanine aminotransferase increased, Total,Grade 3	0	0		
Alanine aminotransferase increased, Total,Grade 4	0	0		
Aspartate aminotransferase increased,Total,Grade 3	0	0		
Aspartate aminotransferase increased,Total,Grade 4	0	0		
Blood bilirubin increased, Total, Grade 3	0	0		
Blood bilirubin increased, Total, Grade 4	0	0		
Lymphocyte count decreased, Total, Grade 3	0	0		
Lymphocyte count decreased, Total, Grade 4	0	0		
Lymphocyte count increased, Total, Grade 3	0	0		
Lymphocyte count increased, Total, Grade 4	0	0		
Neutrophil count decreased, Total, Grade 3	1	2		
Neutrophil count decreased, Total, Grade 4	0	0		
Platelet count decreased, Total, Grade 3	0	0		
Platelet count decreased, Total, Grade 4	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Granulocyte-macrophage colony stimulating factor (GM-CSF) autoantibody

End point title	Concentrations of Granulocyte-macrophage colony stimulating factor (GM-CSF) autoantibody[95]

End point description:

Blood samples were collected for markers which may influence rheumatoid arthritis. Concentrations of GM-CSF autoantibodies was determined.

End point type	Secondary

End point timeframe:

At baseline

Notes:

[95] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: ug/L (microgram per liter)				
arithmetic mean (standard deviation)	334.008 (± 823.7538)	417.378 (± 1632.7755)	250.015 (± 671.9296)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with anti-GSK3196165 antibodies

End point title	Number of participants with anti-GSK3196165 antibodies[96]

End point description:

Blood samples were collected for anti-GSK3196165 antibodies detection assay using tiered testing schema: screening, confirmation and titration steps was used for immunogenicity analysis.

End point type	Secondary

End point timeframe:

Up to Week 24

Notes:

[96] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Participants	4	2	0	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline 4-beta-hydroxy cholesterol, cholesterol at (Millimoles per liter) Week 12

End point title	Change from Baseline 4-beta-hydroxy cholesterol, cholesterol at (Millimoles per liter) Week 12[97]

End point description:

Blood samples was collected for the assessment of change from baseline in lipid profile parameter including 4-beta-hydroxycholesterol, cholesterol levels. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms.

End point type	Other pre-specified

End point timeframe:

Baseline and Week 12

Notes:

[97] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	139	141	134	
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)				
4-Beta-Hydroxycholesterol	0.9897 (± 0.81483)	1.0156 (± 0.57323)	1.1148 (± 0.56873)	
Cholesterol	58.5438 (± 13.25606)	59.1757 (± 14.83734)	64.3791 (± 15.12089)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline 4-beta-hydroxy cholesterol, cholesterol at (Millimoles per liter) Week 24 for treatment arms that started study intervention from Day 1

End point title	Change from Baseline 4-beta-hydroxy cholesterol, cholesterol at (Millimoles per liter) Week 24 for treatment arms that started study intervention from Day 1[98]

End point description:

Blood samples was collected for the assessment of change from baseline in lipid profile parameter including 4-beta-hydroxycholesterol, cholesterol levels.

End point type	Other pre-specified

End point timeframe:

Baseline and Week 24

Notes:

[98] - 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: The endpoints are different for the different parts of the study.

End point values	GSK3196165 90mg + csDMARD	GSK3196165 150mg + csDMARD	Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	136	139	123	
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)				
4-Beta-Hydroxycholesterol	0.9766 (± 0.45665)	1.0064 (± 0.58945)	1.1925 (± 0.57339)	
Cholesterol	59.1937 (± 14.12055)	58.9174 (± 15.00108)	65.2270 (± 14.70946)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline 4-beta-hydroxy cholesterol, cholesterol at (Millimoles per liter) Week 24 for placebo switched arms that started study intervention from Week 12

End point title	Change from Baseline 4-beta-hydroxy cholesterol, cholesterol at (Millimoles per liter) Week 24 for placebo switched arms that started study intervention from Week 12[99]

End point description:

Blood samples was collected for the assessment of change from baseline in lipid profile parameter including 4-beta-hydroxycholesterol, cholesterol levels.

End point type	Other pre-specified

End point timeframe:

Baseline (Week 12) and Week 24

Notes:

[99] - 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: The endpoints are different for the different parts of the study.

End point values	Placebo + csDMARD and GSK3196165 90mg + csDMARD	Placebo + csDMARD and GSK3196165 150mg + csDMARD	Placebo + csDMARD and Sarilumab 200mg + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	23	24	
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)				
4-Beta-Hydroxycholesterol	1.0180 (± 0.42435)	0.9467 (± 0.29136)	1.3897 (± 1.31589)	
Cholesterol	56.7570 (± 13.92076)	62.4284 (± 13.72140)	68.7768 (± 17.39453)	

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

The Pooled Placebo arm collected during the timeframe Week 0 to Week 12. Placebo arms collected during the timeframe Week 12 to Week 24. Experimental arms collected during from Week 0 to Week 24.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	GSK3196165 90mg + csDMARD

Reporting group description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received GSK3196165 90 mg + csDMARD administered by weekly subcutaneous injection.

Reporting group title	Sarilumab 200mg + csDMARD

Reporting group description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received Sarilumab 200 mg + csDMARD administered by subcutaneous injection of sarilumab every other week plus with placebo injection in the intervening weeks to maintain the blind.

Reporting group title	Placebo + csDMARD and Sarilumab 200 mg + csDMARD

Reporting group description:

Participants received Placebo + csDMARD until Week 12 later switched to Sarilumab 200 mg + csDMARD administered by subcutaneous injection of sarilumab every other week plus with placebo injection in the intervening weeks to maintain the blind.

Reporting group title	Placebo + csDMARD and GSK3196165 90 mg + csDMARD

Reporting group description:

Participants received Placebo + csDMARD until Week 12 later switched to GSK3196165 90 mg + csDMARD administered by weekly subcutaneous injection.

Reporting group title	Placebo + csDMARD and GSK3196165 150 mg + csDMARD

Reporting group description:

Participants received Placebo + csDMARD until Week 12 later switched to GSK3196165 150 mg + csDMARD administered by weekly subcutaneous injection.

Reporting group title	GSK3196165 150mg + csDMARD

Reporting group description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received GSK3196165 150 mg + csDMARD administered by weekly subcutaneous

Reporting group title	Pooled Placebo

Reporting group description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)84 years received Placebo + csDMARD administered by weekly subcutaneous injection until Week 12. The placebo arms are pooled into a single placebo arm.

Serious adverse events	GSK3196165 90mg + csDMARD	Sarilumab 200mg + csDMARD	Placebo + csDMARD and Sarilumab 200 mg + csDMARD
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 156 (5.13%)	12 / 156 (7.69%)	1 / 26 (3.85%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (0.00%)	0 / 26 (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
Rectal cancer			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	0 / 26 (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
Investigations			
Aspartate aminotransferase increased			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	0 / 26 (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
Alanine aminotransferase increased			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Humerus fracture			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (0.00%)	0 / 26 (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
Post procedural hypotension			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (0.00%)	0 / 26 (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

Congenital, familial and genetic disorders			
Gilbert's syndrome			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral arterial occlusive disease			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	0 / 26 (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
Cardiac disorders			
Atrial fibrillation			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 156 (0.00%)	2 / 156 (1.28%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Optic neuritis			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	0 / 26 (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
Cerebellar hemorrhage			

subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	1 / 156 (0.64%)	2 / 156 (1.28%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Drowning			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	0 / 26 (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
Gastrointestinal disorders			
Obstructive pancreatitis			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	0 / 26 (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
Food poisoning			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
alternative dictionary used: v25.0 25.0			

subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (0.00%)	0 / 26 (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
COVID-19 pneumonia			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	1 / 156 (0.64%)	2 / 156 (1.28%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (0.00%)	0 / 26 (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
Osteomyelitis bacterial			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (0.00%)	0 / 26 (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
Sepsis			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo + csDMARD and GSK3196165 90 mg + csDMARD	Placebo + csDMARD and GSK3196165 150 mg + csDMARD	GSK3196165 150mg + csDMARD
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	3 / 25 (12.00%)	1 / 158 (0.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
alternative dictionary used: v25.0 25.0			

subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspartate aminotransferase increased			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Humerus fracture			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 25 (4.00%)	0 / 158 (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
Post procedural hypotension			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Gilbert's syndrome			
alternative dictionary used: v25.0			

25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral arterial occlusive disease			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 24 (0.00%)	1 / 25 (4.00%)	0 / 158 (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
Nervous system disorders			
Optic neuritis			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar hemorrhage			

subjects affected / exposed	0 / 24 (0.00%)	1 / 25 (4.00%)	0 / 158 (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
Blood and lymphatic system disorders			
Neutropenia			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Drowning			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Obstructive pancreatitis			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
alternative dictionary used: v25.0 25.0			

subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis bacterial			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	1 / 24 (4.17%)	0 / 25 (0.00%)	0 / 158 (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
Sepsis			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Pooled Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 79 (2.53%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
alternative dictionary used: v25.0 25.0			

subjects affected / exposed	0 / 79 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal cancer				
alternative dictionary used: v25.0 25.0				
subjects affected / exposed	0 / 79 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Aspartate aminotransferase increased				
alternative dictionary used: v25.0 25.0				
subjects affected / exposed	0 / 79 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alanine aminotransferase increased				
alternative dictionary used: v25.0 25.0				
subjects affected / exposed	0 / 79 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Humerus fracture				
alternative dictionary used: v25.0 25.0				
subjects affected / exposed	0 / 79 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural hypotension				
alternative dictionary used: v25.0 25.0				
subjects affected / exposed	0 / 79 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Gilbert's syndrome				
alternative dictionary used: v25.0				

25.0				
subjects affected / exposed	0 / 79 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Peripheral arterial occlusive disease				
alternative dictionary used: v25.0 25.0				
subjects affected / exposed	0 / 79 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
alternative dictionary used: v25.0 25.0				
subjects affected / exposed	0 / 79 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 79 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Optic neuritis				
alternative dictionary used: v25.0 25.0				
subjects affected / exposed	0 / 79 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sciatica				
alternative dictionary used: v25.0 25.0				
subjects affected / exposed	0 / 79 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebellar hemorrhage				

subjects affected / exposed	0 / 79 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Drowning			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Obstructive pancreatitis			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Food poisoning			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	1 / 79 (1.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
alternative dictionary used: v25.0 25.0			

subjects affected / exposed	0 / 79 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver abscess			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis bacterial			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	GSK3196165 90mg + csDMARD	Sarilumab 200mg + csDMARD	Placebo + csDMARD and Sarilumab 200 mg + csDMARD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 156 (16.03%)	41 / 156 (26.28%)	6 / 26 (23.08%)
Investigations			
Alanine aminotransferase increased			
alternative dictionary used: v25.0 25.0			

subjects affected / exposed	2 / 156 (1.28%)	10 / 156 (6.41%)	0 / 26 (0.00%)
occurrences (all)	2	11	0
Blood and lymphatic system disorders			
Neutropenia			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	2 / 156 (1.28%)	11 / 156 (7.05%)	2 / 26 (7.69%)
occurrences (all)	2	12	2
General disorders and administration site conditions			
Injection site reaction			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	9 / 156 (5.77%)	17 / 156 (10.90%)	0 / 26 (0.00%)
occurrences (all)	17	35	0
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	5 / 156 (3.21%)	1 / 156 (0.64%)	0 / 26 (0.00%)
occurrences (all)	6	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
Rheumatoid arthritis			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Latent tuberculosis			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
COVID-19			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Urinary tract infection			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	8 / 156 (5.13%)	6 / 156 (3.85%)	0 / 26 (0.00%)
occurrences (all)	10	6	0

Non-serious adverse events	Placebo + csDMARD and GSK3196165 90 mg + csDMARD	Placebo + csDMARD and GSK3196165 150 mg + csDMARD	GSK3196165 150mg + csDMARD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	4 / 25 (16.00%)	32 / 158 (20.25%)
Investigations			
Alanine aminotransferase increased			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	6 / 158 (3.80%)
occurrences (all)	0	0	6
Blood and lymphatic system disorders			
Neutropenia			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	1 / 25 (4.00%)	1 / 158 (0.63%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Injection site reaction			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	10 / 158 (6.33%)
occurrences (all)	0	0	11
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	10 / 158 (6.33%)
occurrences (all)	0	0	10
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 24 (4.17%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences (all)	1	0	0
Rheumatoid arthritis			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Latent tuberculosis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 25 (4.00%)	0 / 158 (0.00%)
occurrences (all)	0	1	0
COVID-19			

subjects affected / exposed	0 / 24 (0.00%)	2 / 25 (8.00%)	0 / 158 (0.00%)
occurrences (all)	0	2	0
Urinary tract infection			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 24 (0.00%)	0 / 25 (0.00%)	8 / 158 (5.06%)
occurrences (all)	0	0	9

Non-serious adverse events	Pooled Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 79 (6.33%)		
Investigations			
Alanine aminotransferase increased			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Neutropenia			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Injection site reaction			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences (all)	0		
Rheumatoid arthritis			

subjects affected / exposed	5 / 79 (6.33%)		
occurrences (all)	5		
Infections and infestations			
Latent tuberculosis			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
alternative dictionary used: v25.0 25.0			
subjects affected / exposed	0 / 79 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 May 2019	Correction of contraceptive requirements for Women of Child Bearing Potential (WOCBP) and additional clarifications.
21 January 2020	To introduce new medical device safety reporting wording, required in advance of roll out of pre-filled syringes to this study. Other minor corrections and clarifications added throughout the protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported