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	v1
This version publication date	17 February 2023
First version publication date	17 February 2023

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	980 Great West 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:

This was a multicenter study conducted across 14 countries. Participants were randomized to receive either GSK3196165 or Sarilumab or placebo. After week 12, the participants were switched to either GSK3196165 or Sarilumab.

Pre-assignment

Screening details:

Total of 550 participants were randomized and one participant from the randomized set withdrew from the study before receiving study intervention of GSK3196165 90 mg + csDMARD arm due to Protocol Deviation. Hence the participant was removed from intent-to-treat (ITT) 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 90 mg + 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 90 mg of GSK3196165 once every week

Arm title	GSK3196165 150 mg + 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 150 mg of GSK3196165 once every week

Arm title	Sarilumab 200 mg or placebo + 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 200 mg of Sarilumab once every alternate week.

Arm title	Pooled Placebo

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 administered by weekly subcutaneous injectionuntil Week

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

Number of subjects in period 1[1]	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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]	Pooled Placebo
Started	79
Completed	74
Not completed	5
Physician decision	-
Adverse event, non-fatal	-
Informed Consent Withdrawn	2
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: One participant from the randomized set withdrew from the study before receiving study intervention of GSK3196165 90 mg + csDMARD arm due to Protocol Deviation. Hence the participant was removed from intent-to-treat (ITT) and safety population.

Baseline characteristics

Reporting groups	
Reporting group title	GSK3196165 90 mg + 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 150 mg + 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 200 mg or placebo + 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	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 injectionuntil Week	

Reporting group values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD
Number of subjects	156	158	156
Age categorical			
Total of 550 participants were randomized and one participant from the randomized population withdrew from the study before receiving study intervention. Hence the participant was removed from intent-to-treat (ITT) and safety population (N=549).			
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
Age continuous			
Units: years			
arithmetic mean	56.7	56.0	57.5
standard deviation	± 10.59	± 10.52	± 10.69
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	Pooled Placebo	Total	
Number of subjects	79	549	
Age categorical			
Total of 550 participants were randomized and one participant from the randomized population withdrew from the study before receiving study intervention. Hence the participant was removed from intent-to-treat (ITT) and safety population (N=549).			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	63	418	
From 65-84 years	16	131	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	55.5		
standard deviation	± 10.64	-	
Sex: Female, Male			
Units: Participants			
Female	65	466	
Male	14	83	
Race/Ethnicity, Customized			
Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	0	1	
ASIAN	7	47	
BLACK OR AFRICAN AMERICAN	4	23	
MISSING	0	2	
MULTIPLE	1	1	
WHITE	67	475	
Age, Continuous			
Units: YEARS			
arithmetic mean	55.5		
standard deviation	± 10.64	-	

End points

End points reporting groups

Reporting group title	GSK3196165 90 mg + 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 150 mg + 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 200 mg or placebo + 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	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 injectionuntil Week

Subject analysis set title	Placebo + csDMARD and GSK3196165 90 mg + csDMARD
Subject analysis set type	Sub-group analysis

Subject analysis set description:

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

Subject analysis set title	Placebo + csDMARD and GSK3196165 150 mg + csDMARD
Subject analysis set type	Sub-group analysis

Subject analysis set description:

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

Subject analysis set title	Placebo + csDMARD and Sarilumab 200 mg + csDMARD
Subject analysis set type	Sub-group analysis

Subject analysis set 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.

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

End point description:

ACR20 is calculated as a 20% improvement from Baseline in both tender and swollen joint counts and a 20% improvement in 3 of the following 5 measures: patient global assessment of disease activity, physician global assessment of disease activity, pain visual analogue scale, (HAQ-DI) and an acute-phase reactant (hsCRP or ESR). For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm.

End point type	Primary

End point timeframe:

Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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	Pooled Placebo v GSK3196165 90 mg + csDMARD
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
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 proportion of participants achieving ACR20 response at Week 12 versus the alternative hypothesis that the 150 mg dose of GSK3196165 differs from placebo in the proportion of participants with ACR20 response at Week 12

Comparison groups	GSK3196165 150 mg + csDMARD v Pooled Placebo
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	superiority
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 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 200 mg or placebo + csDMARD v Pooled Placebo
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
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

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 90 mg + csDMARD v Sarilumab 200 mg or placebo + csDMARD
Number of subjects included in analysis	312
Analysis specification	Pre-specified
Analysis type	superiority
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 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 150 mg + csDMARD v Sarilumab 200 mg or placebo + csDMARD
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
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

Secondary: Change from Baseline in HAQ-DI (verus Placebo) at Week 12

End point title	Change from Baseline in HAQ-DI (verus Placebo) at Week 12

End point description:

The HAQ-DI Score is calculated from 20-questions which assesses the degree of difficulty a participant has in accomplishing tasks in eight functional areas: dressing/grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	156	158	156	79
Units: Score on 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

End point description:

The CDAI total score is a composite score to determine disease severity using only clinical data. It is calculated by the simple sum of the 4 following parameters: Tender joint count 28 (TJC28), Swollen joint count 28 (SJC28), Patient's global assessment of arthritis and Physician's global assessment of arthritis both transformed to a 0-10 scale. Total score approximate range 0-76, higher total score indicating more severe disease. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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

End point title	Percentage of participants with CDAI total score <=10 (CDAI LDA) at Week 24[1]

End point description:

The CDAI total score is a composite score to determine disease severity using only clinical data. It is calculated by the simple sum of the 4 following parameters: TJC28, SJC28, Patient's global assessment of arthritis and Physician's global assessment of arthritis. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Week 24

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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: Change from Baseline in CDAI total score at Week 12

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

End point description:

The CDAI total score is a composite score to determine disease severity using only clinical data. It is calculated by the simple sum of the 4 following parameters: TJC28, SJC28, Patient's global assessment of arthritis and Physician's global assessment of arthritis. Total score approximate range 0-76, higher total score indicates more severe disease. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	156	158	156	79
Units: Score on 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

End point title	Change from Baseline in CDAI total score at Week 24[2]

End point description:

The CDAI total score is a composite score to determine disease severity using only clinical data. It is calculated by the simple sum of the 4 following parameters: TJC28, SJC28, Patient's global assessment of arthritis and Physician's global assessment of arthritis. Total score approximate range 0-76, higher total score indicates more severe disease. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and Week 24

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Score on 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 VAS at Week 12

End point title	Change from Baseline in Arthritis pain VAS at Week 12

End point description:

Participants assessment of the severity of their arthritis pain over the past week, using a 100 unit VAS, with anchors "0" (no pain) and "100" (most severe pain). For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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 Arthritis pain VAS at Week 24

End point title	Change from Baseline in Arthritis pain VAS at Week 24[3]

End point description:

Participants assessment of the severity of their arthritis pain over the past week, using a 100 unit VAS, with anchors "0" (no pain) and "100" (most severe pain). Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and Week 24

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Score on 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 12

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

End point description:

The CDAI total score is a composite score to determine disease severity using only clinical data. It is calculated by the simple sum of the 4 following parameters: TJC28, SJC28, Patient's global assessment of arthritis and Physician's global assessment of arthritis. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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 CDAI total score <=2.8 (CDAI Remission) at Week 24

End point title	Percentage of participants with CDAI total score <=2.8 (CDAI Remission) at Week 24[4]

End point description:

The CDAI total score is a composite score to determine disease severity using only clinical data. It is calculated by the simple sum of the 4 following parameters: TJC28, SJC28, Patient's global assessment of arthritis and Physician's global assessment of arthritis. Placebo was not administered beyond Week 12.

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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 ACR20 at Week 24

End point title	Percentage of participants with ACR20 at Week 24[5]

End point description:

ACR20 is calculated as a 20% improvement from Baseline in both tender and swollen joint counts and a 20% improvement in 3 of the following 5 measures: patient global assessment of disease activity, physician global assessment of disease activity, pain VAS, HAQ-DI and an acute-phase reactant (hsCRP or ESR). Placebo was not administered beyond Week 12.

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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 ACR50 at Week 12

End point title	Percentage of participants with ACR50 at Week 12

End point description:

ACR50 is calculated as a 50% improvement from Baseline in both tender and swollen joint counts and a 50% improvement in 3 of the following 5 measures: patient global assessment of disease activity, physician global assessment of disease activity, pain VAS, HAQ-DI and an acute-phase reactant (hsCRP or ESR). For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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

End point title	Percentage of participants with ACR50 at Week 24[6]

End point description:

ACR50 is calculated as a 50% improvement from Baseline in both tender and swollen joint counts and a 50% improvement in 3 of the following 5 measures: Patient global assessment of disease activity, physician global assessment of disease activity, pain VAS, HAQ-DI and an acute-phase reactant (hsCRP or ESR). Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Week 24

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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 ACR70 at Week 12

End point title	Percentage of participants with ACR70 at Week 12

End point description:

ACR70 is calculated as a 70% improvement from Baseline in both tender and swollen joint counts and a 70% improvement in 3 of the following 5 measures: patient global assessment of disease activity, physician global assessment of disease activity, pain VAS, HAQ-DI and an acute-phase reactant (hsCRP or ESR). For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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

End point title	Percentage of participants with ACR70 at Week 24[7]

End point description:

ACR70 is calculated as a 70% improvement from Baseline in both tender and swollen joint counts and a

70% improvement in 3 of the following 5 measures: patient global assessment of disease activity, physician global assessment of disease activity, pain VAS, HAQ-DI and an acute-phase reactant (hsCRP or ESR). Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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 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

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using the number of TJC28, SJC28, hsCRP (mg per liter [/L]) and patient's global assessment of disease activity (transformed to a 0-10 scale). Total score approximate range 0-9.4, higher score indicating more severe disease. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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

End point title	Percentage of participants with (DAS28-CRP) <=3.2 (DAS28-CRP LDA) at Week 24[8]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using the number of TJC28, SJC28, hsCRP (mg per liter [/L]) and patient's global assessment of disease activity (transformed to a 0-10 scale). Total score approximate range 0-9.4, higher score indicating more severe disease. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Week 24

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using the number of TJC28, SJC28, hsCRP (mg per liter [/L]) and patient's global assessment of disease activity (transformed to a 0-10 scale). Total score approximate range 0-9.4, higher score indicating more severe disease. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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

End point title	Percentage of participants with DAS28-ESR <=3.2 (DAS28-ESR LDA) at Week 24[9]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using the number of TJC28, SJC28, hsCRP (mg per liter [/L]) and patient's global assessment of disease activity (transformed to a 0-10 scale). Total score approximate range 0-9.4, higher score indicating more severe disease. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using the number of TJC28, SJC28, hsCRP (mg per liter [/L]) and patient's global assessment of disease activity (transformed to a 0-10 scale). Total score approximate range 0-9.4, higher score indicating more severe disease. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the

pooled placebo arm.

End point type	Secondary

End point timeframe:

Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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-CRP <2.6 (DAS28-CRP Remission) at Week 24

End point title	Percentage of participants with DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24[10]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using the number of TJC28, SJC28, hsCRP (mg per liter [/L]) and patient's global assessment of disease activity (transformed to a 0-10 scale). Total score approximate range 0-9.4, higher score indicating more severe disease. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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) at Week 12

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

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using the number of TJC28, SJC28, hsCRP (mg per liter [/L]) and patient's global assessment of disease activity (transformed to a 0-10 scale). Total score approximate range 0-9.4, higher score indicating more severe disease. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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

End point title	Percentage of participants with DAS28-ESR <2.6 (DAS28-ESR Remission) Week 24[11]

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using the number of TJC28, SJC28, hsCRP (mg per liter [/L]) and patient's global assessment of disease activity (transformed to a 0-10 scale). Total score approximate range 0-9.4, higher score indicating more severe disease. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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 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

End point description:

EULAR response criteria defined as Good response = DAS28 change >1.2 with DAS28 <=3.2; Moderate response = DAS28 change >0.6 with DAS28 >3.2-5.1; Non-response = DAS28 change <=0.6 and absolute DAS28 >5.1. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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 a good/moderate EULAR response at Week 24

End point title	Percentage of participants with a good/moderate EULAR response at Week 24[12]

End point description:

EULAR response criteria defined as Good response = DAS28 change >1.2 with DAS28 <=3.2; Moderate response = DAS28 change >0.6 with DAS28 >3.2-5.1; Non-response = DAS28 change <=0.6 and absolute DAS28 >5.1. Placebo was not administered beyond Week 12.

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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 ACR/EULAR remission at Week 12

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

End point description:

Percentage of participants achieving ACR/EULAR remission at Week 12 is summarized. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	156	158	156	79
Units: Percentage of participants				
number (not applicable)	2	4	9	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ACR/EULAR remission at Week 24

End point title	Percentage of participants with ACR/EULAR remission at Week 24[13]

End point description:

Percentage of participants with ACR/EULAR remission at Week 24 is summarized. Placebo was not administered beyond Week 12.

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

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

End point description:

DAS28 (CRP) and DAS28-ESR are measure of RA disease activity calculated using tender joint count and swollen joint count (28-joint count), hsCRP (mg/L)/ESR (mm/hour) and patient's global assessment of disease activity (PtGA) transformed to a 0-10 scale. Total score approximate range 0-9.4, higher score indicating more disease activity. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	156	158	156	79
Units: Score on 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

End point title	Change from Baseline in DAS28 (CRP) and DAS28-ESR at Week 24[14]

End point description:

DAS28 (CRP) and DAS28-ESR are measure of RA disease activity calculated using TJC28, SJC28, hsCRP (mg/L)/ESR (mm/hour) and PtGA transformed to a 0-10 scale. Total score approximate range 0-9.4, higher score indicating more disease activity. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and Week 24

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Score on 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 HAQ-DI at Week 24

End point title	Change from Baseline in HAQ-DI at Week 24[15]

End point description:

HAQ-DI: 20-questions which assesses the degree of difficulty a participant has in accomplishing tasks in eight functional areas: dressing/grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and 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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Score on 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 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

End point description:

FACIT-fatigue is a validated patient-reported measure developed originally to assess fatigue in individuals with cancer and has subsequently been used and validated in numerous chronic conditions, including RA. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	156	158	156	79
Units: Score on 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

End point title	Change from Baseline in FACIT-Fatigue at Week 24[16]

End point description:

FACIT-fatigue is a validated patient-reported measure developed originally to assess fatigue in individuals with cancer and has subsequently been used and validated in numerous chronic conditions, including RA. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and 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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Score on 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 Short form (36) (SF-36) physical component scores at Week 12

End point title	Change from Baseline in Short form (36) (SF-36) physical component scores at Week 12

End point description:

SF-36 is a generic health survey that contains 36 questions covering eight domains of health: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue and general health perceptions. SF-36 scores each item on a 0 to 100 range so that the lowest and highest possible scores are 0 and 100, respectively. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	156	158	156	79
Units: Score on 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 SF-36 physical component scores at Week 24

End point title	Change from Baseline in SF-36 physical component scores at Week 24[17]

End point description:

SF-36 is a generic health survey that contains 36 questions covering eight domains of health: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue and general health perceptions. SF-36 scores each item on a 0 to 100 range so that the lowest and highest possible scores are 0 and 100, respectively. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and Week 24

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Score on 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 SF-36 mental component scores at Week 12

End point title	Change from Baseline in SF-36 mental component scores at Week 12

End point description:

SF-36 is a generic health survey that contains 36 questions covering eight domains of health: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue and general health perceptions. SF-36 scores each item on a 0 to 100 range so that the lowest and highest possible scores are 0 and 100, respectively. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	156	158	156	79
Units: Score on 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 mental component scores at Week 24

End point title	Change from Baseline in SF-36 mental component scores at Week 24[18]

End point description:

SF-36 is a generic health survey that contains 36 questions covering eight domains of health: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue and general health perceptions. SF-36 scores each item on a 0 to 100 range so that the lowest and highest possible scores are 0 and 100, respectively. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and 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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Score on 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 domain scores at Week 12

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

End point description:

SF-36 is a generic health survey that contains 36 questions covering eight domains of health: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue and general health perceptions. SF-36 scores each item on a 0 to 100 range so that the lowest and highest possible scores are 0 and 100, respectively. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	156	158	156	79
Units: Percentage of participants				
arithmetic mean (standard deviation)				
Bodily Pain	17 (± 21.45)	16.8 (± 22.2)	19.8 (± 23.27)	10.7 (± 21.38)
General Health	6.3 (± 15.89)	6.7 (± 16.07)	6.7 (± 15.69)	4.2 (± 15.84)
Mental Health	4.3 (± 19.3)	7.6 (± 16.9)	8.2 (± 18.55)	4.8 (± 16.31)
Physical Function	9.69 (± 21.423)	14.22 (± 23.909)	13.15 (± 24.135)	6.55 (± 21.156)
Role Emotional	5.77 (± 22.405)	9.4 (± 25.128)	10.93 (± 23.908)	3.87 (± 22.219)
Role Physical	12.94 (± 22.371)	14.19 (± 25.155)	13.81 (± 23.488)	10.74 (± 19.456)
Social Function	6.99 (± 23.107)	10.73 (± 27.51)	11.59 (± 24.383)	6.87 (± 27.774)
Vitality	9.48 (± 18.03)	11.82 (± 19.94)	13 (± 19.895)	5.11 (± 18.61)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 domain scores at Week 24

End point title	Change from Baseline in SF-36 domain scores at Week 24[19]

End point description:

SF-36 is a generic health survey that contains 36 questions covering eight domains of health: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue and general health perceptions. SF-36 scores each item on a 0 to 100 range so that the lowest and highest possible scores are 0 and 100, respectively. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and 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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Percentage of participants				
arithmetic mean (standard deviation)				
Bodily Pain	20.7 (± 22.82)	18.5 (± 22.43)	23.9 (± 27.29)	
General Health	6.4 (± 15.25)	6.7 (± 16.3)	8.8 (± 17.3)	
Mental Health	6.1 (± 17.16)	8.4 (± 19.63)	10 (± 18.71)	
Physical Function	11.43 (± 23.714)	16.36 (± 25.64)	18.86 (± 24.472)	
Role Emotional	5.83 (± 23.522)	7.99 (± 28.03)	8.88 (± 26.589)	
Role Physical	13.97 (± 21.332)	15.22 (± 27.352)	17.37 (± 26.25)	
Social Function	9.46 (± 25.704)	10.37 (± 29.237)	12.04 (± 24.599)	
Vitality	11.29 (± 17.913)	13.22 (± 21.245)	16.31 (± 19.854)	

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)

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. Placebo was not administered beyond Week 12. The Pooled Placebo collected data during the timeframe Week 0 to Week 12; Subject Analysis Sets collected from Week 12 to Week 24 and the Reporting Groups collected from Week 0 to Week 24.

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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

End point values	Placebo + csDMARD and GSK3196165 90 mg + csDMARD	Placebo + csDMARD and GSK3196165 150 mg + csDMARD	Placebo + csDMARD and Sarilumab 200 mg + csDMARD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	24	25	26	
Units: Participants				
AE	9	10	12	
SAE	1	3	1	
AESI	2	3	5	

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

End point description:

Blood samples was collected for the assessment of hematology parameters. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	156	158	156	79
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)	0.009 (± 0.5354)

Neutrophils	-0.255 (± 1.5469)	-0.412 (± 2.0477)	-1.843 (± 2.1359)	-0.113 (± 1.4395)
Platelets	-10.9 (± 56.51)	-17.3 (± 60.17)	-76.5 (± 62.76)	-10.3 (± 62.82)

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

End point title	Change from Baseline in neutrophil, lymphocyte, platelet count (Giga cells per liter) at Week 24[20]

End point description:

Blood samples was collected for the assessment of hematology parameters. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and Week 24

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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)				
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 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

End point description:

Blood samples was collected for the assessment of hematology parameters. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the

pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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

End point title	Change from Baseline in WBC count (Giga cells per liter) at Week 24[21]

End point description:

Blood samples was collected for the assessment of hematology parameters. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and 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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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 hemoglobin level (Grams per liter) Week 12

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

End point description:

Blood samples was collected for the assessment of hematology parameters. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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

End point title	Change from Baseline in hemoglobin level (Grams per liter) Week 24[22]

End point description:

Blood samples was collected for the assessment of hematology parameters. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and 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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	156	158	156	79
Units: IU/L (International units per liter)				
arithmetic mean (standard deviation)				
AP	0.7 (± 14.42)	-3 (± 14.94)	-15.6 (± 20.63)	-1 (± 14.57)
ALT	0.8 (± 16.22)	-0.7 (± 12.95)	8.1 (± 21.3)	-1 (± 10.8)
AST	0.6 (± 10.29)	0.7 (± 8.52)	4.5 (± 11.43)	0.3 (± 9.82)
GGT	-0.8 (± 14.24)	-2.6 (± 15.23)	0.6 (± 12.37)	-1.8 (± 11.46)

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

End point title	Change from Baseline in AST, ALT, AP, GGT levels (International units per liter) at Week 24[23]

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and 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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: IU/L (International units per liter)				
arithmetic mean (standard deviation)				
AP	1.8 (± 16.48)	-1.7 (± 18.76)	-14.3 (± 19.23)	
ALT	1.6 (± 12.73)	1.9 (± 20.52)	6.2 (± 12.98)	
AST	1.7 (± 7.89)	2.1 (± 11.21)	3.0 (± 9.29)	
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 albumin level (Grams per liter) at Week 12

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

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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

End point title	Change from Baseline in albumin level (Grams per liter) at Week 24[24]

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and Week 24

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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 total bilirubin (Micromoles per liter) at Week 12

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

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
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

End point title	Change from Baseline in total bilirubin (Micromoles per liter) at Week 24[25]

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and 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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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 cholesterol (Millimoles per liter) at Week 12

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

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[26]	0[27]	0[28]	0[29]
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

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

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

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

[29] - 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

End point title	Change from Baseline in total cholesterol (Millimoles per liter) at Week 24[30]

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and 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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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 fasting lipid profile: LDL cholesterol, HDL cholesterol (Millimoles per liter) at Week 12

End point title	Change from Baseline in fasting lipid profile: LDL cholesterol, HDL cholesterol (Millimoles per liter) at Week 12

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[31]	0[32]	0[33]	0[34]
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

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

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

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

[34] - 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

End point title	Change from Baseline in fasting lipid profile: LDL cholesterol, HDL cholesterol (Millimoles per liter) at Week 24[35]

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and 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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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)				
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

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[36]	0[37]	0[38]	0[39]
Units: mmol/L (Millimoles per liter)				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

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

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

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

[39] - 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

End point title	Change from Baseline in fasting lipid profile triglycerides (Millimoles per liter) at Week 24[40]

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Baseline and 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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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: Number of participants with National Cancer Institute (NCI)-Common terminology criteria for adverse events (CTCAE) >=Grade 3 hematological/clinical chemistry abnormalities

End point title	Number of participants with National Cancer Institute (NCI)-Common terminology criteria for adverse events (CTCAE) >=Grade 3 hematological/clinical chemistry abnormalities[41]

End point description:

Number of participants who reported NCI-CTCAE Grade 3 or higher for hematological and clinical chemistry abnormalities were summarized. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Up to Week 34

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	158	156	
Units: Participants				
Alanine aminotransferase increased, Total, Grade 3	1	2	1	
Alanine aminotransferase increased, Total, Grade 4	0	0	0	

Aspartate aminotransferase increased,Total,Grade 3	1	1	0	
Aspartate aminotransferase increased,Total,Grade 4	0	0	0	
Blood bilirubin increased, Total, Grade 3	0	0	1	
Blood bilirubin increased, Total, Grade 4	0	0	0	
Lymphocyte count decreased, Total, Grade 3	6	1	2	
Lymphocyte count decreased, Total, Grade 4	0	0	1	
Lymphocyte count increased, Total, Grade 3	0	0	0	
Lymphocyte count increased, Total, Grade 4	0	0	0	
Neutrophil count decreased, Total, Grade 3	2	1	10	
Neutrophil count decreased, Total, Grade 4	1	1	4	
Platelet count decreased, Total, Grade 3	0	0	0	
Platelet count decreased, Total, Grade 4	0	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[42]

End point description:

Blood samples were collected for markers which may influence rheumatoid arthritis. Concentrations of GM-CSF autoantibodies was determined. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

At baseline

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Placebo + csDMARD and GSK3196165 90 mg + csDMARD
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	26
Units: ug/L (microgram per liter)				
arithmetic mean (standard deviation)	334.008 (± 823.7538)	417.378 (± 1632.7755)	250.015 (± 671.9296)	237.1 (± 357.4074)

End point values	Placebo + csDMARD and GSK3196165 150 mg + csDMARD	Placebo + csDMARD and Sarilumab 200 mg + csDMARD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	27		
Units: ug/L (microgram per liter)				
arithmetic mean (standard deviation)	330.527 (± 496.9961)	142.446 (± 169.6796)		

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[43]

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. Placebo was not administered beyond Week 12.

End point type	Secondary

End point timeframe:

Up to Week 34

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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Placebo + csDMARD and GSK3196165 90 mg + csDMARD
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	156	158	156	26
Units: Participants	4	2	0	1

End point values	Placebo + csDMARD and GSK3196165 150 mg + csDMARD	Placebo + csDMARD and Sarilumab 200 mg + csDMARD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	27		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

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

End point title	Change from Baseline 4-beta-hydroxyl cholesterol, cholesterol at (Millimoles per liter) Week 12

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. For the purpose of all analyses up to week 12, the placebo-sequence arms were pooled into a single placebo arm. All participants received the same (placebo) treatment during the study period (up to week 12) in the pooled placebo arm.

End point type	Other pre-specified

End point timeframe:

Baseline and Week 12

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	Pooled Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	139	141	134	71
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)	1.0913 (± 1.03027)
Cholesterol	58.5438 (± 13.25606)	59.1757 (± 14.83734)	64.3791 (± 15.12089)	58.6880 (± 14.62446)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline 4-beta-hydroxyl cholesterol, cholesterol at (Millimoles per liter) Week 24

End point title	Change from Baseline 4-beta-hydroxyl cholesterol, cholesterol at (Millimoles per liter) Week 24[44]

End point description:

Blood samples was collected for the assessment of clinical chemistry parameters. Placebo was not administered beyond Week 12.

End point type	Other pre-specified

End point timeframe:

Baseline 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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK3196165 90 mg + csDMARD	GSK3196165 150 mg + csDMARD	Sarilumab 200 mg or placebo + 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

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected from start of study intervention. The Pooled Placebo collected data during the timeframe Week 0 to Week 12; Subject Analysis Sets collected from Week 12 to Week 24 and the Reporting Groups collected from Week 0 to Week 24.

Adverse event reporting additional description:

The analysis was performed on Safety Set that include randomized participants who received at least one dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	GSK3196165 90 mg + 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 200 mg or placebo + 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	GSK3196165 150 mg + 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

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	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 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.

Serious adverse events	GSK3196165 90 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	GSK3196165 150 mg + csDMARD
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 156 (5.13%)	12 / 156 (7.69%)	1 / 158 (0.63%)

number of deaths (all causes) number of deaths resulting from adverse events	1	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (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
Rectal cancer			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	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
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (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
Post procedural hypotension			
subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (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
Congenital, familial and genetic disorders			
Gilbert's syndrome			

subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	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
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 156 (0.00%)	2 / 156 (1.28%)	0 / 158 (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 / 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
Nervous system disorders			
Optic neuritis			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (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			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	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
Cerebellar hemorrhage			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (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
Blood and lymphatic system disorders			
Neutropenia			

subjects affected / exposed	1 / 156 (0.64%)	2 / 156 (1.28%)	0 / 158 (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			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	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
Gastrointestinal disorders			
Obstructive pancreatitis			
subjects affected / exposed	0 / 156 (0.00%)	1 / 156 (0.64%)	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
Food poisoning			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (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 / 156 (0.00%)	0 / 156 (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			
subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (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
COVID-19 pneumonia			
subjects affected / exposed	1 / 156 (0.64%)	2 / 156 (1.28%)	0 / 158 (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
Liver abscess			

subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (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
Osteomyelitis bacterial			
subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (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			
subjects affected / exposed	1 / 156 (0.64%)	0 / 156 (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

Serious adverse events	Pooled Placebo	Placebo + csDMARD and GSK3196165 150 mg + csDMARD	Placebo + csDMARD and GSK3196165 90 mg + csDMARD
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 79 (2.53%)	3 / 25 (12.00%)	1 / 24 (4.17%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
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			

subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 79 (0.00%)	1 / 25 (4.00%)	0 / 24 (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			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
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			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
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			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
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 / 79 (0.00%)	1 / 25 (4.00%)	0 / 24 (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			

subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
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 / 79 (0.00%)	1 / 25 (4.00%)	0 / 24 (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			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
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			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
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			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
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	1 / 79 (1.27%)	0 / 25 (0.00%)	0 / 24 (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
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			

subjects affected / exposed	1 / 79 (1.27%)	0 / 25 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
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			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
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			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
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			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
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	Placebo + csDMARD and Sarilumab 200 mg + csDMARD		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 26 (3.85%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal cancer			
subjects affected / exposed	0 / 26 (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			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural hypotension			
subjects affected / exposed	0 / 26 (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			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Peripheral arterial occlusive disease			

subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Optic neuritis			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebellar hemorrhage			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 26 (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			

subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Obstructive pancreatitis			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Food poisoning			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Liver abscess			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis bacterial			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Sepsis			
subjects affected / exposed	0 / 26 (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 90 mg + csDMARD	Sarilumab 200 mg or placebo + csDMARD	GSK3196165 150 mg + csDMARD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 156 (16.03%)	41 / 156 (26.28%)	32 / 158 (20.25%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 156 (1.28%)	10 / 156 (6.41%)	6 / 158 (3.80%)
occurrences (all)	2	11	6
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	9 / 156 (5.77%)	17 / 156 (10.90%)	10 / 158 (6.33%)
occurrences (all)	17	35	11
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 156 (1.28%)	11 / 156 (7.05%)	1 / 158 (0.63%)
occurrences (all)	2	12	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 156 (3.21%)	1 / 156 (0.64%)	10 / 158 (6.33%)
occurrences (all)	6	1	10
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Urinary tract infection			
subjects affected / exposed	8 / 156 (5.13%)	6 / 156 (3.85%)	8 / 158 (5.06%)
occurrences (all)	10	6	9
Latent tuberculosis			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 156 (0.00%)	0 / 156 (0.00%)	0 / 158 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Pooled Placebo	Placebo + csDMARD and GSK3196165 150 mg + csDMARD	Placebo + csDMARD and GSK3196165 90 mg + csDMARD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 79 (6.33%)	4 / 25 (16.00%)	1 / 24 (4.17%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 79 (0.00%)	1 / 25 (4.00%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	5 / 79 (6.33%)	0 / 25 (0.00%)	0 / 24 (0.00%)
occurrences (all)	5	0	0
Back pain			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1

Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 79 (0.00%)	0 / 25 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Latent tuberculosis			
subjects affected / exposed	0 / 79 (0.00%)	1 / 25 (4.00%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	0 / 79 (0.00%)	2 / 25 (8.00%)	0 / 24 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	Placebo + csDMARD and Sarilumab 200 mg + csDMARD		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 26 (23.08%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 26 (7.69%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		
Back pain			

subjects affected / exposed	2 / 26 (7.69%)		
occurrences (all)	2		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 26 (0.00%)		
occurrences (all)	0		
Latent tuberculosis			
subjects affected / exposed	2 / 26 (7.69%)		
occurrences (all)	2		
COVID-19			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences (all)	1		

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