# 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)<br>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