



Clinical trial results:

A 52-week, phase 3, multicentre, randomised, double blind, efficacy and safety study comparing GSK3196165 with placebo and with tofacitinib, in combination with methotrexate in participants with moderately to severely active rheumatoid arthritis who have an inadequate response to methotrexate

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2019-000797-39 |
| Trial protocol | GB LV ES PL LT CZ HU IT |
| Global end of trial date | 16 August 2022 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v2 (current) |
| This version publication date | 15 October 2023 |
| First version publication date | 27 August 2023 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 201790 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03980483 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | GlaxoSmithKline |
| Sponsor organisation address | 980 GreatWest Road, Brentford, Middlesex, United Kingdom, TW8 9GS |
| Public contact | GSK Response Center, GlaxoSmithKline, +1 8664357343, GSKClinicalSupportHD@gsk.com |
| Scientific contact | GSK Response Center, GlaxoSmithKline, +1 8664357343, GSKClinicalSupportHD@gsk.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 04 October 2022 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 August 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of GSK3196165 at doses of 90 mg and 150 mg weekly versus placebo for the treatment of participants with moderately to severely active RA who are on a stable background of MTX and who have had an inadequate response to MTX.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 16 May 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: 163 |
| Country: Number of subjects enrolled | Canada: 3 |
| Country: Number of subjects enrolled | China: 13 |
| Country: Number of subjects enrolled | Czechia: 48 |
| Country: Number of subjects enrolled | Hungary: 35 |
| Country: Number of subjects enrolled | India: 103 |
| Country: Number of subjects enrolled | Italy: 1 |
| Country: Number of subjects enrolled | Latvia: 11 |
| Country: Number of subjects enrolled | Lithuania: 40 |
| Country: Number of subjects enrolled | Malaysia: 6 |
| Country: Number of subjects enrolled | Mexico: 49 |
| Country: Number of subjects enrolled | Poland: 451 |
| Country: Number of subjects enrolled | Russian Federation: 100 |
| Country: Number of subjects enrolled | Serbia: 20 |
| Country: Number of subjects enrolled | South Africa: 116 |
| Country: Number of subjects enrolled | Spain: 5 |
| Country: Number of subjects enrolled | Ukraine: 247 |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Country: Number of subjects enrolled | United States: 123 |
| Worldwide total number of subjects | 1537 |
| EEA total number of subjects | 591 |

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) | 1267 |
| From 65 to 84 years | 269 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

Participants were randomized in a ratio of 6:6:3:1:1:1 to 3 experimental and 3 Placebo arms. At Week 12, participants randomized to one of the three placebo arms switched to experimental arms, receiving the active intervention for 40 weeks. Participants randomized to experimental arms from study day 1, received the active intervention for 52 weeks.

Pre-assignment

Screening details:

Analysis of this study were reported for GSK3196165 90mg, GSK3196165 150mg, Tofacitinib 5 mg and all placebo arms are pooled to a single group to serve as reference for comparison of active treatment arms versus Placebo for primary efficacy endpoint analysis at Week 12.

Period 1

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

Arms

| | |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | GSK3196165 90mg + MTX |

Arm description:

Participants received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with methotrexate (MTX).

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

Dosage and administration details:

Participants received 90mg of GSK3196165 once every week.

| | |
|------------------|------------------------|
| Arm title | GSK3196165 150mg + MTX |
|------------------|------------------------|

Arm description:

Participants received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with MTX.

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

Dosage and administration details:

Participants received 150mg of GSK3196165 once every week.

| | |
|------------------|-----------------------|
| Arm title | Tofacitinib 5mg + MTX |
|------------------|-----------------------|

Arm description:

Participants received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with MTX plus placebo injection weekly to maintain the blind for 52 weeks.

| | |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

| | |
|--|-------------|
| Investigational medicinal product name | Tofacitinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received 5mg of Tofacitinib once every alternate week.

| | |
|------------------|---|
| Arm title | Placebo + MTX and GSK3196165 90mg + MTX |
|------------------|---|

Arm description:

Participants received Placebo weekly SC injection in combination with MTX for 12 weeks. At Week 12, participants were switched from placebo to GSK3196165 90 mg, SC injection, once weekly in combination with MTX until Week 52.

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

Dosage and administration details:

Participants received 90mg of GSK3196165 once every week from week 12 to week 52.

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

Dosage and administration details:

Participants received placebo once every week until Week 12

| | |
|------------------|--|
| Arm title | Placebo + MTX and GSK3196165 150mg + MTX |
|------------------|--|

Arm description:

Participants received Placebo weekly SC injection in combination with MTX for 12 weeks. At Week 12, participants were switched from placebo to GSK3196165 150 mg, SC injection, once weekly in combination with MTX until Week 52.

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

Dosage and administration details:

Participants received 150mg of GSK3196165 once every week from week 12 to week 52.

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

Dosage and administration details:

Participants received placebo once every week until Week 12.

| | |
|------------------|---|
| Arm title | Placebo + MTX and Tofacitinib 5mg + MTX |
|------------------|---|

Arm description:

Participants received Placebo tablet weekly in combination with MTX for 12 weeks. At Week 12, participants were switched from placebo tablet to Tofacitinib 5mg, capsule, orally, BID in combination with MTX plus placebo injection to maintain the blind for 52 weeks.

| | |
|--|-------------|
| Arm type | Placebo |
| Investigational medicinal product name | Tofacitinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received 5mg of Tofacitinib once every alternate week from week 12 to week 52.

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

Dosage and administration details:

Participants received placebo once every week until Week 12.

| Number of subjects in period 1 | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX |
|---|------------------------------|-------------------------------|------------------------------|
| Started | 513 | 510 | 258 |
| Completed | 431 | 436 | 221 |
| Not completed | 82 | 74 | 37 |
| Physician decision | 14 | 10 | 7 |
| Consent withdrawn by subject | 38 | 21 | 15 |
| Adverse event, non-fatal | 13 | 29 | 11 |
| UNKNOWN | - | 1 | - |
| PROTOCOL-SPECIFIED WITHDRAWAL CRITERION MET | 4 | - | 1 |
| INVESTIGATOR SITE CLOSED | - | 1 | - |
| Lost to follow-up | 2 | 4 | 2 |
| Lack of efficacy | 7 | 6 | - |
| Protocol deviation | 4 | 2 | 1 |

| Number of subjects in period 1 | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX |
|---|--|---|--|
| Started | 85 | 86 | 85 |
| Completed | 69 | 73 | 75 |
| Not completed | 16 | 13 | 10 |
| Physician decision | 4 | 4 | 2 |
| Consent withdrawn by subject | 5 | 3 | 4 |
| Adverse event, non-fatal | 2 | 2 | 2 |
| UNKNOWN | - | - | - |
| PROTOCOL-SPECIFIED WITHDRAWAL CRITERION MET | - | 1 | 1 |
| INVESTIGATOR SITE CLOSED | - | - | - |
| Lost to follow-up | 1 | 2 | - |

| | | | |
|--------------------|---|---|---|
| Lack of efficacy | 3 | 1 | 1 |
| Protocol deviation | 1 | - | - |

Baseline characteristics

Reporting groups

| | |
|--|--|
| Reporting group title | GSK3196165 90mg + MTX |
| Reporting group description: | |
| Participants received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with methotrexate (MTX). | |
| Reporting group title | GSK3196165 150mg + MTX |
| Reporting group description: | |
| Participants received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with MTX. | |
| Reporting group title | Tofacitinib 5mg + MTX |
| Reporting group description: | |
| Participants received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with MTX plus placebo injection weekly to maintain the blind for 52 weeks. | |
| Reporting group title | Placebo + MTX and GSK3196165 90mg + MTX |
| Reporting group description: | |
| Participants received Placebo weekly SC injection in combination with MTX for 12 weeks. At Week 12, participants were switched from placebo to GSK3196165 90 mg, SC injection, once weekly in combination with MTX until Week 52. | |
| Reporting group title | Placebo + MTX and GSK3196165 150mg + MTX |
| Reporting group description: | |
| Participants received Placebo weekly SC injection in combination with MTX for 12 weeks. At Week 12, participants were switched from placebo to GSK3196165 150 mg, SC injection, once weekly in combination with MTX until Week 52. | |
| Reporting group title | Placebo + MTX and Tofacitinib 5mg + MTX |
| Reporting group description: | |
| Participants received Placebo tablet weekly in combination with MTX for 12 weeks. At Week 12, participants were switched from placebo tablet to Tofacitinib 5mg, capsule, orally, BID in combination with MTX plus placebo injection to maintain the blind for 52 weeks. | |

| Reporting group values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX |
|----------------------------------|-----------------------|------------------------|-----------------------|
| Number of subjects | 513 | 510 | 258 |
| Age categorical | | | |
| Units: Subjects | | | |
| <=18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 417 | 426 | 205 |
| >=65 years | 96 | 84 | 53 |
| Age Continuous | | | |
| Units: YEARS | | | |
| arithmetic mean | 53.7 | 54.2 | 54.3 |
| standard deviation | ± 12.14 | ± 10.77 | ± 11.66 |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 401 | 399 | 209 |
| Male | 112 | 111 | 49 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| AMERICAN INDIAN OR ALASKA NATIVE | 11 | 11 | 9 |
| ASIAN | 48 | 39 | 29 |
| BLACK OR AFRICAN AMERICAN | 11 | 11 | 12 |

| | | | |
|----------|-----|-----|-----|
| MISSING | 1 | 0 | 0 |
| MULTIPLE | 10 | 15 | 7 |
| WHITE | 432 | 434 | 201 |

| Reporting group values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX |
|---|---|--|---|
| Number of subjects | 85 | 86 | 85 |
| Age categorical Units: Subjects | | | |
| <=18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 72 | 71 | 76 |
| >=65 years | 13 | 15 | 9 |
| Age Continuous Units: YEARS | | | |
| arithmetic mean | 51.3 | 52.7 | 53.2 |
| standard deviation | ± 13.12 | ± 12.41 | ± 10.24 |
| Sex: Female, Male Units: Participants | | | |
| Female | 62 | 72 | 68 |
| Male | 23 | 14 | 17 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| AMERICAN INDIAN OR ALASKA NATIVE | 2 | 3 | 2 |
| ASIAN | 5 | 7 | 4 |
| BLACK OR AFRICAN AMERICAN | 3 | 2 | 2 |
| MISSING | 1 | 1 | 1 |
| MULTIPLE | 2 | 2 | 1 |
| WHITE | 72 | 71 | 75 |

| Reporting group values | Total | | |
|---|-------|--|--|
| Number of subjects | 1537 | | |
| Age categorical Units: Subjects | | | |
| <=18 years | 0 | | |
| Between 18 and 65 years | 1267 | | |
| >=65 years | 270 | | |
| Age Continuous Units: YEARS | | | |
| arithmetic mean | - | | |
| standard deviation | - | | |
| Sex: Female, Male Units: Participants | | | |
| Female | 1211 | | |
| Male | 326 | | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| AMERICAN INDIAN OR ALASKA NATIVE | 38 | | |
| ASIAN | 132 | | |
| BLACK OR AFRICAN AMERICAN | 41 | | |
| MISSING | 4 | | |

| | | | |
|----------|------|--|--|
| MULTIPLE | 37 | | |
| WHITE | 1285 | | |

Subject analysis sets

| | |
|----------------------------|--------------------|
| Subject analysis set title | Pooled Placebo |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants received Placebo weekly SC injection in combination with MTX until Week 12. The placebo arms are pooled into a single placebo arm.

| | |
|----------------------------|-----------------------|
| Subject analysis set title | Tofacitinib 5mg + MTX |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with MTX plus placebo injection weekly to maintain the blind for 52 weeks.

| | |
|----------------------------|-----------------|
| Subject analysis set title | Pooled Placebo |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants received Placebo weekly SC injection in combination with MTX until Week 12. The placebo arms are pooled into a single placebo arm.

| Reporting group values | Pooled Placebo | Tofacitinib 5mg + MTX | Pooled Placebo |
|---|----------------|-----------------------|----------------|
| Number of subjects | 256 | 273 | 241 |
| Age categorical Units: Subjects | | | |
| <=18 years | | | |
| Between 18 and 65 years | | | |
| >=65 years | | | |
| Age Continuous Units: YEARS | | | |
| arithmetic mean | 42.7 | | |
| standard deviation | ± | ± | ± |
| Sex: Female, Male Units: Participants | | | |
| Female | | | |
| Male | | | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| AMERICAN INDIAN OR ALASKA NATIVE | | | |
| ASIAN | | | |
| BLACK OR AFRICAN AMERICAN | | | |
| MISSING | | | |
| MULTIPLE | | | |
| WHITE | | | |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | GSK3196165 90mg + MTX |
| Reporting group description: Participants received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with methotrexate (MTX). | |
| Reporting group title | GSK3196165 150mg + MTX |
| Reporting group description: Participants received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with MTX. | |
| Reporting group title | Tofacitinib 5mg + MTX |
| Reporting group description: Participants received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with MTX plus placebo injection weekly to maintain the blind for 52 weeks. | |
| Reporting group title | Placebo + MTX and GSK3196165 90mg + MTX |
| Reporting group description: Participants received Placebo weekly SC injection in combination with MTX for 12 weeks. At Week 12, participants were switched from placebo to GSK3196165 90 mg, SC injection, once weekly in combination with MTX until Week 52. | |
| Reporting group title | Placebo + MTX and GSK3196165 150mg + MTX |
| Reporting group description: Participants received Placebo weekly SC injection in combination with MTX for 12 weeks. At Week 12, participants were switched from placebo to GSK3196165 150 mg, SC injection, once weekly in combination with MTX until Week 52. | |
| Reporting group title | Placebo + MTX and Tofacitinib 5mg + MTX |
| Reporting group description: Participants received Placebo tablet weekly in combination with MTX for 12 weeks. At Week 12, participants were switched from placebo tablet to Tofacitinib 5mg, capsule, orally, BID in combination with MTX plus placebo injection to maintain the blind for 52 weeks. | |
| Subject analysis set title | Pooled Placebo |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Participants received Placebo weekly SC injection in combination with MTX until Week 12. The placebo arms are pooled into a single placebo arm. | |
| Subject analysis set title | Tofacitinib 5mg + MTX |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with MTX plus placebo injection weekly to maintain the blind for 52 weeks. | |
| Subject analysis set title | Pooled Placebo |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Participants received Placebo weekly SC injection in combination with MTX until Week 12. The placebo arms are pooled into a single placebo arm. | |

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

| | |
|-----------------|---|
| End point title | Percentage of participants achieving 20 percentage (%) improvement in American College of Rheumatology Criteria (ACR20) at Week 12 superiority comparison with placebo ^[1] |
|-----------------|---|

End point description:
ACR20 is calculated as 20% improvement from Baseline in Tender Joint Count 68 (TJC68), Swollen Joint Count 66 (SJC66) and 20% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA), Physician Global Assessment of Arthritis Disease Activity (PhGA)

(visual analogue scale [VAS] with values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (ranges from 0=least difficulty to 3=extreme difficulty) and an acute-phase reactant [high sensitivity C-reactive Protein milligram per liter (mg/L) (hsCRP)]. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as reference for the comparison of active treatment arms. The analysis was performed on Intent-to-Treat (ITT) set. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Week 12 | |

Notes:

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

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-----------------------------------|-----------------------|------------------------|-----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 54.7 | 50.9 | 63.6 | 42.7 |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

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

| | |
|---|--|
| Comparison groups | GSK3196165 90mg + MTX v Pooled Placebo |
| Number of subjects included in analysis | 769 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0023 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.62 |
| Confidence interval | |
| level | Other: 0.95 % |
| sides | 2-sided |
| lower limit | 1.19 |
| upper limit | 2.21 |

| Statistical analysis title | Statistical Analysis 2 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

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

| | |
|-------------------|---|
| Comparison groups | GSK3196165 150mg + MTX v Pooled Placebo |
|-------------------|---|

| | |
|---|----------------------|
| Number of subjects included in analysis | 766 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0362 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.39 |
| Confidence interval | |
| level | Other: 0.95 % |
| sides | 2-sided |
| lower limit | 1.02 |
| upper limit | 1.89 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 5 |
|-----------------------------------|------------------------|

Statistical analysis description:

The null hypothesis is defined as there is no difference between the 150mg dose of GSK3196165 and 05mg dose of Tofacitinib in the proportion of participants achieving ACR20 response at Week 12, versus the alternative hypothesis that the 150mg dose of GSK3196165 differs from 05mg dose of Tofacitinib in the proportion of participants achieving ACR20 response at Week 12.

| | |
|---|--|
| Comparison groups | GSK3196165 150mg + MTX v Tofacitinib 5mg + MTX |
| Number of subjects included in analysis | 768 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0013 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.59 |
| Confidence interval | |
| level | Other: 0.95 % |
| sides | 2-sided |
| lower limit | 0.43 |
| upper limit | 0.82 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

The null hypothesis is defined as there is no difference between the 90mg dose of GSK3196165 and 05mg dose of Tofacitinib in the proportion of participants achieving ACR20 response at Week 12, versus the alternative hypothesis that the 90mg dose of GSK3196165 differs from 05mg dose of Tofacitinib in the proportion of participants achieving ACR20 response at Week 12.

| | |
|---|---|
| Comparison groups | GSK3196165 90mg + MTX v Tofacitinib 5mg + MTX |
| Number of subjects included in analysis | 771 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.023 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.69 |

| | |
|---------------------|---------------|
| Confidence interval | |
| level | Other: 0.95 % |
| sides | 2-sided |
| lower limit | 0.5 |
| upper limit | 0.95 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

The null hypothesis is defined as there is no difference between the 05mg dose of Tofacitinib and placebo in the proportion of participants achieving ACR20 response at Week 12, versus the alternative hypothesis that the 05mg dose of Tofacitinib differs from placebo in the proportion of participants achieving ACR20 response at Week 12.

| | |
|---|--|
| Comparison groups | Tofacitinib 5mg + MTX v Pooled Placebo |
| Number of subjects included in analysis | 514 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.34 |
| Confidence interval | |
| level | Other: 0.95 % |
| sides | 2-sided |
| lower limit | 1.62 |
| upper limit | 3.37 |

Secondary: Percentage of participants achieving Clinical disease activity index (CDAI) total score less than or equal to (\leq)10 [CDAI Low disease activity (LDA)] at Week 12

| | |
|-----------------|--|
| End point title | Percentage of participants achieving Clinical disease activity index (CDAI) total score less than or equal to (\leq)10 [CDAI Low disease activity (LDA)] at Week 12 ^[2] |
|-----------------|--|

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score \leq 10. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12

Notes:

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

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-----------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 20.9 | 19.8 | 32.5 | 13.9 |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|---|
| End point title | Change from Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 12 ^[3] |
|-----------------|---|

End point description:

Health Assessment Questionnaire-Disability Index (HAQ-DI) is 20-question instrument that assesses degree of difficulty in accomplishing tasks in eight functional areas: dressing and grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. Overall HAQ-DI score is sum of domain scores divided by number of domains answered. The score ranges from 0 to 3 where 0=least difficulty and 3=extreme difficulty. Higher overall score indicates greater disability. A negative change from baseline indicates an improvement. Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline. For the purpose of all analyses up to week 12, placebo arms were pooled into single placebo arm to primarily serve as reference for comparison of active treatment arms. The analysis was performed on ITT set using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: <The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-------------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | -0.46 (± 0.025) | -0.38 (± 0.024) | -0.5 (± 0.034) | -0.27 (± 0.034) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving 20% improvement in ACR20 at Week 24 (Non-Inferiority versus tofacitinib)

| | |
|-----------------|--|
| End point title | Percentage of participants achieving 20% improvement in ACR20 at Week 24 (Non-Inferiority versus tofacitinib) ^[4] |
|-----------------|--|

End point description:

ACR20 is calculated as a 20% improvement from Baseline in Tender Joint Count 68 (TJC68) and Swollen Joint Count 66 (SJC66) and a 20% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA) [visual analogue scale (VAS) with values from 0=best to 100=worst], Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst), Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty) and an acute-phase reactant [high sensitivity C-reactive Protein milligram per liter (mg/L) (hsCRP)]. The analysis was performed on the ITT set using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-----------------------------------|-----------------------|------------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 63.9 | 61.3 | 74.4 | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|--|
| Comparison groups | GSK3196165 150mg + MTX v Tofacitinib 5mg + MTX |
| Number of subjects included in analysis | 768 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Regression, Logistic |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -13 |
| Confidence interval | |
| level | Other: 0.98 % |
| sides | 2-sided |
| lower limit | -21.2 |
| upper limit | -4.8 |

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | GSK3196165 90mg + MTX v Tofacitinib 5mg + MTX |
| Number of subjects included in analysis | 771 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Regression, Logistic |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -10.4 |

| | |
|---------------------|---------------|
| Confidence interval | |
| level | Other: 0.98 % |
| sides | 2-sided |
| lower limit | -18.6 |
| upper limit | -2.3 |

Secondary: Percentage of participants achieving 50%/70% improvement in American College of Rheumatology Criteria (ACR50/70) at Week 12

| | |
|-----------------|--|
| End point title | Percentage of participants achieving 50%/70% improvement in American College of Rheumatology Criteria (ACR50/70) at Week 12 ^[5] |
|-----------------|--|

End point description:

ACR50/70 is calculated as 50%/70% improvement from Baseline in Tender Joint Count 68 (TJC68) and Swollen Joint Count 66 (SJC66) and 50%/70% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA), Physician Global Assessment of Arthritis Disease Activity (PhGA) [VAS with values from 0=best to 100=worst], Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ-DI) (ranges from 0 = least difficulty to 3 = extreme difficulty) and an acute-phase reactant (high sensitivity C-reactive Protein mg/L (hsCRP)). For the purpose of all analyses up to week 12, placebo arms were pooled into single placebo arm to primarily serve as reference for comparison of active treatment arms. The analysis was performed on the ITT set using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12

Notes:

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

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-----------------------------------|-----------------------|------------------------|-----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| ACR50, Week 12 | 23.3 | 20.0 | 34.1 | 12.2 |
| ACR70, Week 12 | 8.5 | 6.1 | 13.9 | 3.5 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving 50%/70% improvement in American College of Rheumatology Criteria (ACR50/70) at Week 24 and ACR 20/50/70 at and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Percentage of participants achieving 50%/70% improvement in American College of Rheumatology Criteria (ACR50/70) at Week 24 and ACR 20/50/70 at and Week 52 for treatment arms who started study intervention from Day 1 ^[6] |
|-----------------|---|

End point description:

ACR20/50/70 is calculated as a 20%/50%/70% improvement from Baseline in Tender Joint Count 68 (TJC68) and Swollen Joint Count 66 (SJC66) and a 20%/50%/70% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale (VAS) with values from 0=best to 100=worst), Physician Global Assessment of Arthritis Disease Activity (PhGA) [VAS with values from 0=best to 100=worst], Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ- DI) (ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty) and an acute-phase reactant [high sensitivity C-reactive Protein mg/L (hsCRP)]. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

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

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-----------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| ACR20, Week 52 | 63.9 | 61.1 | 75.8 | |
| ACR50, Week 24 | 31.4 | 29.1 | 46.7 | |
| ACR50, Week 52 | 35.0 | 34.2 | 48.4 | |
| ACR70, Week 24 | 12.5 | 10.1 | 25.1 | |
| ACR70, Week 52 | 16.7 | 14.4 | 26.9 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving ACR20/50/70 at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Percentage of participants achieving ACR20/50/70 at Week 24 and Week 52 for placebo switched arms ^[7] |
|-----------------|--|

End point description:

ACR20/50/70 is calculated as a 20%/50%/70% improvement from Baseline in Tender Joint Count 68 (TJC68) and Swollen Joint Count 66 (SJC66) and a 20%/50%/70% improvement in 3 of the following 5 measures: Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale (VAS) with values from 0=best to 100=worst), Physician Global Assessment of Arthritis Disease Activity (PhGA) [VAS with values from 0=best to 100=worst], Patient Assessment of Arthritis Pain (VAS with values from 0=no pain and 100=most severe pain), Health Assessment Questionnaire-Disability Index (HAQ- DI) (ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty) and an acute-phase reactant [high sensitivity C-reactive Protein mg/L (hsCRP)]. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

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

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| ACR20, Week 24 | 56.7 | 71.2 | 69.9 | |
| ACR20, Week 52 | 70.5 | 67.8 | 84.6 | |
| ACR50, Week 24 | 37.0 | 35.0 | 40.7 | |
| ACR50, Week 52 | 28.6 | 42.5 | 50.7 | |
| ACR70, Week 24 | 7.9 | 15.0 | 19.6 | |
| ACR70, Week 52 | 10.3 | 20.2 | 25.8 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score ≤ 10 (CDAI LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Percentage of participants achieving CDAI total score ≤ 10 (CDAI LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[8] |
|-----------------|---|

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score ≤ 10 . The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

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

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-----------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 29.9 | 29.8 | 45.9 | |
| Week 52 | 35.5 | 37.1 | 51.7 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score <=10 (CDAI LDA) at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|---|
| End point title | Percentage of participants achieving CDAI total score <=10 (CDAI LDA) at Week 24 and Week 52 for placebo switched arms ^[9] |
|-----------------|---|

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

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

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-----------------------------------|--|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 32.9 | 37.4 | 45.8 | |
| Week 52 | 38.5 | 44 | 52.4 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score ≤ 2.8 (CDAI Remission) at Week 12

| | |
|-----------------|--|
| End point title | Percentage of participants achieving CDAI total score ≤ 2.8 (CDAI Remission) at Week 12 ^[10] |
|-----------------|--|

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. CDAI remission is achieved when CDAI total score ≤ 2.8 . For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12

Notes:

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

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-----------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 3.8 | 2.4 | 5.8 | 1.0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score ≤ 2.8 (CDAI Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Percentage of participants achieving CDAI total score ≤ 2.8 (CDAI Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[11] |
|-----------------|---|

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. CDAI remission is achieved when CDAI total score ≤ 2.8 . The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-----------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 6.1 | 5.2 | 12.1 | |
| Week 52 | 9.4 | 4.4 | 15.1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving CDAI total score ≤ 2.8 (CDAI Remission) at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Percentage of participants achieving CDAI total score ≤ 2.8 (CDAI Remission) at Week 24 and Week 52 for placebo switched arms ^[12] |
|-----------------|--|

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of the sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (visual analogue scale with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale before computing the CDAI total score. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. CDAI remission is achieved when CDAI total score ≤ 2.8 . The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-----------------------------------|--|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 4.4 | 8.4 | 6.4 | |
| Week 52 | 4.6 | 9.6 | 11.1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving 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 achieving Disease Activity Score using 28 joint count and C-Reactive Protein (DAS28-CRP) ≤ 3.2 (DAS28-CRP LDA) at Week 12 ^[13] |
|-----------------|---|

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-----------------------------------|-----------------------|------------------------|-----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 20.2 | 19.4 | 33.5 | 11.3 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28 Erythrocyte Sedimentation Rate (ESR) ≤ 3.2 (DAS28-ESR LDA) at Week 12

| | |
|-----------------|---|
| End point title | Percentage of participants achieving DAS28 Erythrocyte Sedimentation Rate (ESR) ≤ 3.2 (DAS28-ESR LDA) at Week 12 ^[14] |
|-----------------|---|

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in millimeter [mm]/hour[hr]),

Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-ESR \leq 3.2. A negative change from baseline in DAS28-ESR indicates an improvement. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-----------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 13.6 | 12.2 | 19.7 | 8.2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP \leq 3.2 (DAS28-CRP LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Percentage of participants achieving DAS28-CRP \leq 3.2 (DAS28-CRP LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[15] |
|-----------------|---|

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-CRP greater than or equal to (\geq)3.2. A negative change from baseline in DAS28-CRP indicates an improvement. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-----------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 26.8 | 29.0 | 47.4 | |
| Week 52 | 32.8 | 31.3 | 49.8 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-ESR ≤ 3.2 (DAS28-ESR LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Percentage of participants achieving DAS28-ESR ≤ 3.2 (DAS28-ESR LDA) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[16] |
|-----------------|---|

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in millimeter [mm]/hour[hr]), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-ESR ≤ 3.2 . A negative change from baseline in DAS28-ESR indicates an improvement. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-----------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 17.2 | 18.3 | 28.3 | |
| Week 52 | 23.3 | 18.7 | 34.1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP ≤ 3.2 (DAS28-CRP

LDA) at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Percentage of participants achieving DAS28-CRP ≤ 3.2 (DAS28-CRP LDA) at Week 24 and Week 52 for placebo switched arms ^[17] |
|-----------------|--|

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-CRP greater than or equal to (\leq) 3.2. A negative change from baseline in DAS28-CRP indicates an improvement. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 26.3 | 31.0 | 44.9 | |
| Week 52 | 34.2 | 34.9 | 50.2 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-ESR ≤ 3.2 (DAS28-ESR LDA) at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Percentage of participants achieving DAS28-ESR ≤ 3.2 (DAS28-ESR LDA) at Week 24 and Week 52 for placebo switched arms ^[18] |
|-----------------|--|

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in millimeter [mm]/hour[hr]), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Low disease activity (LDA) is achieved when DAS28-ESR ≤ 3.2 . A negative change from baseline in DAS28-ESR indicates an improvement. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 20.7 | 22.7 | 30.4 | |
| Week 52 | 22.9 | 21.8 | 30.3 | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 12 ^[19] |
|-----------------|--|

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-----------------------------------|-----------------------|------------------------|-----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 10.3 | 8.4 | 17.1 | 5.2 |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 12 ^[20] |
|-----------------|--|

End point description:

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-----------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 6.0 | 5.3 | 11.5 | 5.2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[21] |
|-----------------|---|

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-CRP less than (<)2.6. A negative change from baseline in DAS28-CRP indicates an improvement. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-----------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 14.5 | 14.1 | 26.3 | |
| Week 52 | 19.3 | 15.3 | 34.0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[22] |
|-----------------|---|

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-ESR <2.6. A negative change from baseline in DAS28-ESR indicates an improvement. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-----------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 8.6 | 7.8 | 13.7 | |
| Week 52 | 14.1 | 8.8 | 18.7 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Percentage of participants achieving DAS28-CRP <2.6 (DAS28-CRP Remission) at Week 24 and Week 52 for placebo switched arms ^[23] |
|-----------------|--|

End point description:

The DAS28-CRP is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), C-reactive protein (CRP) (in mg/L), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-CRP scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-CRP less than (<)2.6. A negative change from baseline in DAS28-CRP indicates an improvement. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 14.7 | 20.2 | 28.2 | |
| Week 52 | 18.2 | 18.7 | 31.2 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Percentage of participants achieving DAS28 ESR <2.6 (DAS28-ESR Remission) at Week 24 and Week 52 for placebo switched arms ^[24] |
|-----------------|--|

End point description:

The DAS28-ESR is a measure of RA disease activity calculated using Tender Joint Count 28 (TJC28), Swollen Joint Count 28 (SJC28), Erythrocyte sedimentation rate (ESR) (in mm/hr), Patient's Global Assessment of Arthritis Disease Activity (PtGA) (visual analogue scale with values from 0=best to 100=worst). DAS28-ESR scores range from 1.0 to 9.4, where lower scores indicate less disease activity. Remission is achieved when DAS28-ESR <2.6. A negative change from baseline in DAS28-ESR indicates an improvement. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 10.8 | 14.8 | 12 | |
| Week 52 | 11.0 | 11.8 | 15.5 | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|---|
| End point title | Percentage of participants achieving a good/moderate (European League Against Rheumatism) EULAR response at Week 12 ^[25] |
|-----------------|---|

End point description:

DAS28-CRP and DAS28-ESR scores were categorized using EULAR response criteria. Response was defined based on combination of current DAS28 score and improvement in current score relative to Baseline. The definition of no response, moderate response and good response was as; DAS28 ≤3.2 and DAS28 decrease from Baseline (>1.2:good response, >0.6 to ≤1.2:moderate response, ≤0.6:no response); DAS28 >3.2 to ≤5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to ≤1.2:moderate response, ≤0.6:no response) and DAS28 >5.1 and DAS28 decrease from Baseline (>1.2:moderate response, >0.6 to ≤1.2:no response, ≤0.6:no response). If the post-Baseline DAS28-CRP score was missing, then the corresponding EULAR category was set to missing. For purpose of all analyses up to week 12, placebo arms were pooled into single arm to primarily serve as reference for comparison of active treatment arms. Analysis was performed on ITT set using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-----------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 73.1 | 69.3 | 83.0 | 54.5 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a good/moderate EULAR response at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Percentage of participants achieving a good/moderate EULAR response at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[26] |
|-----------------|---|

End point description:

DAS28-CRP and DAS28-ESR scores were categorized using EULAR response criteria. Response was defined based on combination of current DAS28 score and improvement in current score relative to Baseline. The definition of no response, moderate response and good response was as; DAS28 ≤ 3.2 and DAS28 decrease from Baseline (>1.2 :good response, >0.6 to ≤ 1.2 :moderate response, ≤ 0.6 :no response); DAS28 >3.2 to ≤ 5.1 and DAS28 decrease from Baseline (>1.2 :moderate response, >0.6 to ≤ 1.2 :moderate response, ≤ 0.6 :no response) and DAS28 >5.1 and DAS28 decrease from Baseline (>1.2 :moderate response, >0.6 to ≤ 1.2 :no response, ≤ 0.6 :no response). If the post-Baseline DAS28-CRP score was missing, then the corresponding EULAR category was set to missing. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-----------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 78.4 | 74.9 | 89.8 | |
| Week 52 | 79.1 | 78.6 | 89.0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a good/moderate EULAR response at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Percentage of participants achieving a good/moderate EULAR response at Week 24 and Week 52 for placebo switched arms ^[27] |
|-----------------|--|

End point description:

DAS28-CRP and DAS28-ESR scores were categorized using EULAR response criteria. Response was defined based on combination of current DAS28 score and improvement in current score relative to Baseline. The definition of no response, moderate response and good response was as; DAS28 ≤ 3.2 and DAS28 decrease from Baseline (>1.2 :good response, >0.6 to ≤ 1.2 :moderate response, ≤ 0.6 :no response); DAS28 >3.2 to ≤ 5.1 and DAS28 decrease from Baseline (>1.2 :moderate response, >0.6 to ≤ 1.2 :moderate response, ≤ 0.6 :no response) and DAS28 >5.1 and DAS28 decrease from Baseline (>1.2 :moderate response, >0.6 to ≤ 1.2 :no response, ≤ 0.6 :no response). If the post-Baseline DAS28-CRP score was missing, then the corresponding EULAR category was set to missing. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 76.3 | 82.4 | 88.9 | |
| Week 52 | 87.1 | 79.1 | 92.5 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants achieving ACR/EULAR remission at Week 12

| | |
|-----------------|---|
| End point title | Number of participants achieving ACR/EULAR remission at Week 12 ^[28] |
|-----------------|---|

End point description:

Boolean-based ACR/EULAR remission is achieved if all of the following requirements are met at the same timepoint: Tender Joint Count 68 (TJC68) ≤ 1 , Swollen Joint Count 66 (SJC66) ≤ 1 , high sensitivity C-reactive Protein (hsCRP) ≤ 1 mg/dl and patient's global assessment of disease activity (PtGA) ≤ 10 . For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set that includes all randomized participants who received at least one dose of study treatment. This population was based on the treatment the participant was randomized to. Only those participants with data available at the specified time points were analyzed.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |
| Notes: | |
| [28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. | |
| Justification: The endpoints are different for the different parts of the study. | |

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-----------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 475 | 477 | 228 | |
| Units: Participants | 11 | 9 | 11 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants achieving ACR/EULAR remission at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|--|
| End point title | Number of participants achieving ACR/EULAR remission at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[29] |
|-----------------|--|

End point description:

Boolean-based ACR/EULAR remission is achieved if all of the following requirements are met at the same timepoint: Tender Joint Count 68 (TJC68) ≤ 1 , Swollen Joint Count 66 (SJC66) ≤ 1 , high sensitivity C-reactive Protein (hsCRP) ≤ 1 mg/dl and patient's global assessment of disease activity (PtGA) ≤ 10 . The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Only those participants with data available at the specified time points were analyzed.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 24 and Week 52 | |
| Notes: | |
| [29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. | |
| Justification: The endpoints are different for the different parts of the study. | |

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-----------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 453 | 467 | 227 | |
| Units: Participants | | | | |
| Week 24 | 16 | 13 | 14 | |
| Week 52 | 24 | 13 | 18 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants achieving ACR/EULAR remission at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|---|
| End point title | Number of participants achieving ACR/EULAR remission at Week 24 and Week 52 for placebo switched arms ^[30] |
|-----------------|---|

End point description:

Boolean-based ACR/EULAR remission is achieved if all of the following requirements are met at the same timepoint: Tender Joint Count 68 (TJC68) ≤ 1 , Swollen Joint Count 66 (SJC66) ≤ 1 , high sensitivity C-reactive Protein (hsCRP) ≤ 1 mg/dl and patient's global assessment of disease activity (PtGA) ≤ 10 . The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Only those participants with data available at the specified time points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-----------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 76 | 80 | 78 | |
| Units: Participants | | | | |
| Week 24 | 2 | 4 | 3 | |
| Week 52 | 3 | 3 | 8 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving no radiographic progression (Van der Heijde modified total sharp scores (mTSS ≤ 0.5) at Week 12

| | |
|-----------------|--|
| End point title | Percentage of participants achieving no radiographic progression (Van der Heijde modified total sharp scores (mTSS ≤ 0.5) at Week 12 ^[31] |
|-----------------|--|

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score ranges from 0 to 448 for mTSS with higher values representing higher disease activity. No radiographic progression is defined as a change from Baseline in van der Heijde mTSS score of ≤ 0.5 . For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-----------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 83.8 | 82.6 | 88.9 | 76.7 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving no radiographic progression (mTSS <= 0.5) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|--|
| End point title | Percentage of participants achieving no radiographic progression (mTSS <= 0.5) at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[32] |
|-----------------|--|

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score ranges from 0 to 448 for mTSS with higher values representing higher disease activity. No radiographic progression is defined as a change from Baseline in van der Heijde mTSS score of <=0.5. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-----------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| mTSS <= 0.5, Week 24 | 79.5 | 79.6 | 84.6 | |
| mTSS <= 0.5, Week 52 | 71.8 | 72.8 | 79.7 | |

Statistical analyses

Secondary: Percentage of participants achieving no radiographic progression (mTSS <= 0.5) at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|---|
| End point title | Percentage of participants achieving no radiographic progression (mTSS <= 0.5) at Week 24 and Week 52 for placebo switched arms ^[33] |
|-----------------|---|

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score ranges from 0 to 448 for mTSS with higher values representing higher disease activity. No radiographic progression is defined as a change from Baseline in van der Heijde mTSS score of <=0.5. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 and Week 52

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| mTSS <= 0.5, Week 24 | 78.6 | 74.6 | 77.7 | |
| mTSS <= 0.5, Week 52 | 76.0 | 68.3 | 69.5 | |

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 ^[34] |
|-----------------|---|

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score <=10. Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline. For purpose of all analyses up to week 12, placebo arms were pooled into single arm to primarily serve as reference for comparison of active treatment arms. The analysis was performed on the ITT set using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-------------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | -17.85 (± 0.574) | -17.15 (± 0.563) | -21.39 (± 0.801) | -13.01 (± 0.798) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI total score at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|--|
| End point title | Change from Baseline in CDAI total score at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[35] |
|-----------------|--|

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score ≤ 10 . Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | -20.63 (± 0.561) | -19.88 (± 0.551) | -24.5 (± 0.781) | |
| Week 52 | -21.79 (± 0.558) | -21.81 (± 0.549) | -25.55 (± 0.77) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI total score at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|---|
| End point title | Change from Baseline in CDAI total score at Week 24 and Week 52 for placebo switched arms ^[36] |
|-----------------|---|

End point description:

Clinical Disease Activity Index (CDAI) total score is a composite score consisting of sum of Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), Patient's Global Assessment of Arthritis Disease Activity (PtGA) and Physician Global Assessment of Arthritis Disease Activity (PhGA) (VAS with values from 0=best to 100=worst). PtGA and PhGA are transformed to a 0-10 scale. CDAI total score ranges from 0 to 76 with higher values representing higher disease activity. Low disease activity (LDA) is achieved when CDAI total score ≤ 10 . Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline. For efficacy assessments baseline is interpreted as Day 1. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | -21.41 (\pm 1.359) | -22.93 (\pm 1.31) | -24.5 (\pm 1.307) | |
| Week 52 | -23.49 (\pm 1.365) | -22.91 (\pm 1.291) | -25.83 (\pm 1.28) | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|---|
| End point title | Change from Baseline in DAS28-CRP/DAS28-ESR at Week |
|-----------------|---|

End point description:

DAS28-CRP and DAS28-ESR are measure of RA disease activity calculated using Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), high sensitivity C-reactive Protein (hsCRP in mg/L)/Erythrocyte sedimentation rate (ESR) [ESR in millimeter/hour (mm/hr)] and patient's global assessment of disease activity (PtGA) transformed to a 0-10 scale. Total score range from 0-9.4, with higher scores indicating more disease activity. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-------------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| DAS28-CRP | -1.49 (± 0.054) | -1.44 (± 0.053) | -1.96 (± 0.076) | -1.01 (± 0.075) |
| DAS28-ESR | -1.53 (± 0.057) | -1.48 (± 0.056) | -1.97 (± 0.079) | -1.07 (± 0.079) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DAS28-CRP/DAS28-ESR at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Change from Baseline in DAS28-CRP/DAS28-ESR at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[38] |
|-----------------|---|

End point description:

DAS28-CRP and DAS28-ESR are measure of RA disease activity calculated using Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), high sensitivity C-reactive Protein (hsCRP in mg/L)/Erythrocyte sedimentation rate (ESR) [ESR in millimeter/hour (mm/hr)] and patient's global assessment of disease activity (PtGA) transformed to a 0-10 scale. Total score range from 0-9.4, with higher scores indicating more disease activity. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| DAS28-CRP, Week 24 | -1.74 (± 0.056) | -1.67 (± 0.055) | -2.31 (± 0.078) | |
| DAS28-CRP, Week 52 | -1.85 (± 0.06) | -1.82 (± 0.059) | -2.39 (± 0.083) | |
| DAS28-ESR, Week 24 | -1.79 (± 0.059) | -1.74 (± 0.057) | -2.3 (± 0.082) | |
| DAS28-ESR, Week 52 | -1.92 (± 0.063) | -1.84 (± 0.062) | -2.36 (± 0.087) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in DAS28-CRP/DAS28-ESR at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Change from Baseline in DAS28-CRP/DAS28-ESR at Week 24 and Week 52 for placebo switched arms ^[39] |
|-----------------|--|

End point description:

DAS28-CRP and DAS28-ESR are measure of RA disease activity calculated using Swollen Joint Count 28 (SJC28), Tender Joint Count 28 (TJC28), high sensitivity C-reactive Protein (hsCRP in mg/L)/Erythrocyte sedimentation rate (ESR) [ESR in millimeter/hour (mm/hr)] and patient's global assessment of disease activity (PtGA) transformed to a 0-10 scale. Total score range from 0-9.4, with higher scores indicating more disease activity. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For efficacy assessments baseline is interpreted as Day 1. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-------------------------------------|--|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |

| | | | | |
|--------------------|-----------------|-----------------|-----------------|--|
| DAS28-CRP, Week 24 | -1.77 (± 0.136) | -1.95 (± 0.131) | -2.29 (± 0.131) | |
| DAS28-CRP, Week 52 | -1.92 (± 0.146) | -1.96 (± 0.139) | -2.37 (± 0.137) | |
| DAS28-ESR, Week 24 | -1.84 (± 0.143) | -2.05 (± 0.137) | -2.23 (± 0.137) | |
| DAS28-ESR, Week 52 | -2.06 (± 0.151) | -2.06 (± 0.145) | -2.43 (± 0.145) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Van der Heijde mTSS at Week 12

| | |
|-----------------|--|
| End point title | Change from Baseline in Van der Heijde mTSS at Week 12 ^[40] |
|-----------------|--|

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score range from 0 to 448 for mTSS with higher values representing higher disease activity. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-------------------------------------|-----------------------|------------------------|-----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | 0.15 (± 0.075) | 0.19 (± 0.073) | 0.13 (± 0.104) | 0.55 (± 0.103) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Van der Heijde mTSS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Change from Baseline in Van der Heijde mTSS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[41] |
|-----------------|---|

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score range from 0 to 448 for mTSS with higher values representing higher disease activity. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | 0.25 (± 0.08) | 0.38 (± 0.078) | 0.2 (± 0.112) | |
| Week 52 | 0.61 (± 0.117) | 0.63 (± 0.114) | 0.35 (± 0.158) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Van der Heijde mTSS at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Change from Baseline in Van der Heijde mTSS at Week 24 and Week 52 for placebo switched arms ^[42] |
|-----------------|--|

End point description:

Van der Heijde mTSS is utilized for scoring radiographs of hands and feet in rheumatoid arthritis. This method includes 16 areas of erosions, and 15 areas for joint space narrowing (JSN) in each hand, and 6 areas for erosions and 6 areas JSN in each foot. The total mTSS score is the sum of erosion (maximum of 280) and JSN (maximum of 168) scores. The score range from 0 to 448 for mTSS with higher values representing higher disease activity. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For efficacy assessments baseline is interpreted as Day 1. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | 0.71 (± 0.215) | 0.77 (± 0.208) | 0.67 (± 0.208) | |
| Week 52 | 0.9 (± 0.309) | 1.24 (± 0.306) | 1.06 (± 0.297) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HAQ-DI at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|--|
| End point title | Change from Baseline in HAQ-DI at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[43] |
|-----------------|--|

End point description:

HAQ-DI is a 20-question instrument that assesses the degree of difficulty of a participant in accomplishing tasks in eight functional areas: dressing and grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. Overall HAQ-DI score was computed as sum of the domain scores divided by the number of domains answered. The total possible score ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty. Higher overall score indicates greater disability. A negative change from baseline indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-------------------------------------|-----------------------|------------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | -0.51 (± 0.027) | -0.41 (± 0.026) | -0.56 (± 0.037) | |
| Week 52 | -0.54 (± 0.028) | -0.46 (± 0.028) | -0.58 (± 0.039) | |

Statistical analyses

Secondary: Change from Baseline in HAQ-DI at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|---|
| End point title | Change from Baseline in HAQ-DI at Week 24 and Week 52 for placebo switched arms ^[44] |
|-----------------|---|

End point description:

HAQ-DI is a 20-question instrument that assesses the degree of difficulty of a participant in accomplishing tasks in eight functional areas: dressing and grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. Overall HAQ-DI score was computed as sum of the domain scores divided by the number of domains answered. The total possible score ranges from 0 to 3 where 0 = least difficulty and 3 = extreme difficulty. Higher overall score indicates greater disability. A negative change from baseline indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | -0.53 (± 0.065) | -0.46 (± 0.062) | -0.58 (± 0.062) | |
| Week 52 | -0.47 (± 0.069) | -0.45 (± 0.066) | -0.67 (± 0.065) | |

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 ^[45] |
|-----------------|---|

End point description:

For the Arthritis Pain VAS, participants assess the severity of their current arthritis pain using a continuous visual analogue scale (VAS) with anchors at "0" (no pain) and "100" (most severe pain). A negative change from baseline indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-------------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | -22 (± 1.056) | -19.56 (± 1.033) | -27.26 (± 1.473) | -14.58 (± 1.466) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Arthritis pain VAS at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|---|
| End point title | Change from Baseline in Arthritis pain VAS at Week 24 and Week 52 for placebo switched arms ^[46] |
|-----------------|---|

End point description:

For the Arthritis Pain VAS, participants assess the severity of their current arthritis pain using a continuous visual analogue scale (VAS) with anchors at "0" (no pain) and "100" (most severe pain). A negative change from baseline indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For efficacy assessments baseline is interpreted as Day 1. The analysis was performed on all randomized participants who switched from placebo to study intervention at Week 12. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-------------------------------------|--|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | -26.91 (± 2.666) | -28.02 (± 2.564) | -29.13 (± 2.566) | |
| Week 52 | -24.08 (± 2.902) | -29.22 (± 2.765) | -34.8 (± 2.742) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Short form (SF)-36 physical component scores (PCS) at Week 12

| | |
|-----------------|---|
| End point title | Change from Baseline in Short form (SF)-36 physical component scores (PCS) at Week 12 ^[47] |
|-----------------|---|

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning(PF),bodily pain(BP),role limitations due to physical/emotional issues,general health(GH),mental health,social functioning,vitality. Each of 8 domains is scored using average, 0-100; higher score represents better health.PCS was aggregated across the domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health.PCS is primarily derived from 4 domains(PF,role-physical,BP,GH) representing overall physical health.Positive change from baseline, reported using T-score change, indicates improvement in overall physical health.Quality Metric software was used for scoring.Baseline was defined as most recent pre-dose NMV, including unscheduled visits.CB=subtracting PD value from BV.For analysis up to week 12, placebo arms were pooled into single arm to serve as reference for active treatment arm comparison.ITT set was analyzed using multiple imputation to manage missing

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[47] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-------------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: T-Score | | | | |
| least squares mean (standard error) | 5.38 (± 0.305) | 4.96 (± 0.297) | 6.93 (± 0.427) | 3.19 (± 0.423) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 mental component scores (MCS) at Week 12

| | |
|-----------------|--|
| End point title | Change from Baseline in SF-36 mental component scores (MCS) at Week 12 ^[48] |
|-----------------|--|

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning,bodily pain,role limitations due to physical/emotional issues,general health,mental health(MH),social functioning(SF),vitality. Each of 8 domains is scored using average, 0-100; higher score represents better health.MCS was aggregated across the domains and scaled to T-score with mean of 50 and SD of

represents better health. MCS is primarily derived from 4 domains (SF, MH, vitality, role-emotional) representing overall mental health. Positive change from baseline, reported using T-score change, indicates improvement in overall mental health. Quality Metric software was used for scoring. Baseline was defined as most recent pre-dose NMV, including unscheduled visits. CB=subtracting PD value from BV. For analysis up to week 12, placebo arms were pooled into single arm to serve as reference for active treatment arm comparison. ITT set was analyzed using multiple imputation to manage missing data

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[48] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-------------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: T-Score | | | | |
| least squares mean (standard error) | 2.88 (\pm 0.41) | 2.54 (\pm 0.399) | 4.04 (\pm 0.574) | 2.46 (\pm 0.569) |

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 ^[49] |
|-----------------|--|

End point description:

SF-36 survey assessed health-related quality of life, covering physical functioning, bodily pain, role limitations due to physical/emotional issues, general health, mental health, social functioning, and vitality. MCS consists of four domains (MH, vitality, SF, role-emotional), and PCS consists of four domains (PF, role-physical, BP, GH). Individual question items were totaled within items under various sections, and these domain scores were then scaled from 0 to 100, with higher scores indicating better health. Positive changes from the baseline indicated improvements. Scoring of SF-36 utilized Quality Metric software. Baseline=latest pre-dose assessment with NMV, including those from unscheduled visits. CB=subtracting PD visit value from BV. For analysis up to week 12, placebo arms were pooled into single arm to serve as reference for active treatment arm comparison. ITT set was analyzed only those participants with data available at the specified time points.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[49] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|----------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 474 | 483 | 235 | |
| Units: Scores on a scale | | | | |
| arithmetic mean (standard error) | | | | |
| Bodily Pain | 15.21 (± 21.448) | 14.65 (± 21.208) | 20.83 (± 22.432) | |
| General Health | 8.23 (± 15.662) | 7.32 (± 15.462) | 11.11 (± 16.447) | |
| Mental Health | 7.03 (± 18.222) | 6.4 (± 18.993) | 10.19 (± 18.659) | |
| Physical Function | 13.2 (± 21.092) | 12.9 (± 21.564) | 17.81 (± 19.957) | |
| Role Emotional | 7.47 (± 25.231) | 7.35 (± 25.162) | 9.25 (± 25.836) | |
| Role Physical | 12.51 (± 21.751) | 12.56 (± 23.345) | 16.28 (± 22.117) | |
| Social Function | 9.2 (± 23.558) | 8.72 (± 26.227) | 14.15 (± 25.092) | |
| Vitality | 11.05 (± 20.216) | 9.82 (± 19.662) | 14.63 (± 20.185) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 PCS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Change from Baseline in SF-36 PCS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[50] |
|-----------------|---|

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning(PF), bodily pain(BP), role limitations due to physical/emotional issues, general health(GH), MH, SF, vitality. Each domains is scored using average, 0-100; higher score represents better health. PCS was aggregated across domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health. PCS is primarily derived from 4 domains(PF, role-physical, BP, GH) representing overall physical health. Positive change from baseline, reported using T-score change, indicates improvement in overall physical health. Quality Metric software was used for scoring. Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline value. ITT set was analyzed using multiple imputation to manage missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: T-Score | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | 6.26 (± 0.319) | 5.82 (± 0.313) | 8.07 (± 0.448) | |
| Week 52 | 6.5 (± 0.364) | 6.04 (± 0.358) | 8.23 (± 0.507) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 MCS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Change from Baseline in SF-36 MCS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[51] |
|-----------------|---|

End point description:

SF-36 is a health-related survey that assesses quality of life covering 8 domains: physical functioning (PF), bodily pain (BP), role limitations due to physical/emotional problems, general health (GH), mental health (MH), social functioning (SF), vitality. The MCS consists of 4 domains (SF, MH, vitality, role-emotional) and PCS consists of 4 domains (PF, role-physical, BP, GH). The individual question items are first summed for each item under the various sections. Then, those domain scores are weighted to a scale between 0 to 100, where higher score represents better health. Positive change from baseline indicates an improvement. Quality Metric software was used for scoring for SF-36. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. ITT set was analyzed for participants with data available at the indicated time points.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[51] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: T-Score | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | 3.69 (± 0.401) | 3.87 (± 0.393) | 2.92 (± 0.563) | |
| Week 52 | 3.13 (± 0.443) | 2.75 (± 0.437) | 3.53 (± 0.616) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 domain scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Change from Baseline in SF-36 domain scores at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[52] |
|-----------------|---|

End point description:

SF-36 survey assessed health-related quality of life, covering physical functioning, bodily pain, role limitations due to physical/emotional issues, general health, mental health, social functioning, and vitality. MCS consists of four domains (MH,vitality,SF,role-emotional), and PCS consists of four domains (PF,role-physical,BP,GH).Individual question items were totaled within items under various sections, and these domain scores were then scaled from 0 to 100, with higher scores indicating better health. Positive changes from the baseline indicated improvements. Scoring of SF-36 utilized Quality Metric software. Baseline was defined as most recent pre-dose non-missing value, including unscheduled visits. Change from baseline was calculated by subtracting post dose value from Baseline value. Analysis was performed on all randomized participants who received study intervention from Day01 to Week52. Only those participants with data available at the specified time points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[52] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|----------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 459 | 469 | 227 | |
| Units: Scores on a scale | | | | |
| arithmetic mean (standard error) | | | | |
| Bodily Pain, Week 24 | 18.8 (± 21.717) | 18.06 (± 21.303) | 23.07 (± 22.7) | |
| Bodily Pain, Week 52 | 18.93 (± 23.084) | 18.39 (± 22.667) | 24.87 (± 23.427) | |
| General Health, Week 24 | 9.7 (± 15.747) | 9.01 (± 15.577) | 11.46 (± 16.416) | |
| General Health, Week 52 | 10.2 (± 16.795) | 8.81 (± 17.426) | 12.4 (± 19.371) | |
| Mental Health, Week 24 | 9.14 (± 17.511) | 8.88 (± 19.515) | 9.89 (± 18.461) | |
| Mental Health, Week 52 | 8.65 (± 18.468) | 7.43 (± 20.048) | 10.44 (± 21.685) | |
| Physical Function, Week 24 | 16.35 (± 22.51) | 16.2 (± 23.122) | 20.9 (± 21.808) | |
| Physical Function, Week 52 | 16.18 (± 24.737) | 17.22 (± 23.464) | 21.77 (± 25.534) | |
| Role Emotional, Week 24 | 10.75 (± 25.123) | 10.54 (± 25.451) | 7.86 (± 25.124) | |
| Role Emotional, Week 52 | 10.08 (± 26.113) | 9.24 (± 26.689) | 9.3 (± 26.279) | |
| Role Physical, Week 24 | 15.35 (± 22.432) | 14.87 (± 23.361) | 18.81 (± 22.588) | |
| Role Physical, Week 52 | 16.5 (± 23.981) | 14.74 (± 24.325) | 19.16 (± 24.391) | |
| Social Function, Week 24 | 11.6 (± 23.543) | 12.95 (± 26.72) | 13.49 (± 24.164) | |
| Social Function, Week 52 | 11.66 (± 25.523) | 10.51 (± 26.367) | 15.29 (± 24.872) | |

| | | | | |
|-------------------|------------------|------------------|------------------|--|
| Vitality, Week 24 | 13.37 (± 19.908) | 13.02 (± 20.115) | 15.5 (± 19.854) | |
| Vitality, Week 52 | 13.37 (± 20.358) | 12.23 (± 20.712) | 15.73 (± 21.767) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 PCS at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Change from Baseline in SF-36 PCS at Week 24 and Week 52 for placebo switched arms ^[53] |
|-----------------|--|

End point description:

SF-36 survey evaluates health-related quality of life, covering physical functioning(PF), bodily pain(BP), role limitations due to physical/emotional issues, general health(GH), MH, SF, vitality. Each domains is scored using average, 0-100; higher score represents better health. PCS was aggregated across domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health. PCS is primarily derived from 4 domains(PF, role-physical, BP, GH) representing overall physical health. Positive change from baseline, reported using T-score change, indicates improvement in overall physical health. Quality Metric software was used for scoring. Baseline was defined as latest pre-dose assessment with a non-missing value, including from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline value. ITT set was analyzed using multiple imputation to manage missing data. For efficacy assessments baseline is interpreted as Day 1.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[53] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: T-Score | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | 6.31 (± 0.773) | 7.07 (± 0.746) | 8.21 (± 0.747) | |
| Week 52 | 5.68 (± 0.89) | 6.27 (± 0.852) | 8.81 (± 0.848) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 MCS at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Change from Baseline in SF-36 MCS at Week 24 and Week 52 for placebo switched arms ^[54] |
|-----------------|--|

End point description:

SF-36 survey evaluates health-related quality of life, covering PF, BP, role limitations due to physical/emotional issues, GH, mental health(MH), social functioning(SF), vitality. Each domains is scored using average, 0-100; higher score represents better health. MCS was aggregated across domains and scaled to T-score with mean of 50 and SD of 10; higher score represents better health. MCS is primarily derived from 4 domains(SF, MH, vitality, role-emotional) representing overall mental health. Positive change from baseline, reported using T-score change, indicates improvement in overall mental health. Quality Metric software was used for scoring. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. ITT set was analyzed using multiple imputation to manage missing data. For efficacy assessments baseline is interpreted as Day 1.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[54] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: T-Score | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | 3.76 (± 0.973) | 4.43 (± 0.938) | 4.2 (± 0.942) | |
| Week 52 | 3.06 (± 1.081) | 3.77 (± 1.032) | 5.47 (± 1.027) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-36 domain scores at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Change from Baseline in SF-36 domain scores at Week 24 and Week 52 for placebo switched arms ^[55] |
|-----------------|--|

End point description:

SF-36 is a health-related survey that assesses quality of life covering 8 domains: physical functioning(PF),bodily pain(BP),role limitations due to physical/emotional problems,general health(GH),mental health(MH),social functioning(SF),vitality. The MCS consists of 4 domains (SF,MH,vitality,role-emotional) and PCS consists of 4 domains (PF,role-physical,BP,GH). The individual question items are first summed, then domain scores are weighted to a scale between 0 to 100, where higher score represents better health. Positive change from baseline indicates an improvement. Quality Metric software was used for scoring for SF-36. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose value from Baseline value. For efficacy assessments baseline is interpreted as Day 1. ITT set was analyzed for participants with data available at the indicated time points.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[55] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 75 | 81 | 80 | |
| Units: Scores on a scale | | | | |
| arithmetic mean (standard error) | | | | |
| Bodily Pain, Week 24 | 20.13 (± 23.373) | 23.28 (± 20.682) | 22.23 (± 20.389) | |
| Bodily Pain, Week 52 | 21.00 (± 24.696) | 24.96 (± 22.495) | 26.68 (± 22.838) | |
| General Health, Week 24 | 9.6 (± 18.212) | 12.02 (± 15.209) | 9.44 (± 13.61) | |
| General Health, Week 52 | 9.46 (± 16.95) | 9.00 (± 15.591) | 9.38 (± 15.469) | |
| Mental Health, Week 24 | 8.67 (± 18.405) | 9.81 (± 16.21) | 6.94 (± 16.41) | |
| Mental Health, Week 52 | 9.55 (± 22.271) | 9.87 (± 18.214) | 9.14 (± 17.576) | |
| Physical Function, Week 24 | 18.2 (± 20.725) | 21.42 (± 24.94) | 20.69 (± 22.385) | |
| Physical Function, Week 52 | 15.6 (± 25.13) | 18.87 (± 26.655) | 22.89 (± 20.22) | |
| Role Emotional, Week 24 | 12.89 (± 27.478) | 14.71 (± 24.73) | 10.83 (± 26.131) | |
| Role Emotional, Week 52 | 10.07 (± 28.705) | 13.11 (± 29.612) | 13.92 (± 28.231) | |
| Role Physical, Week 24 | 17.83 (± 24.739) | 17.36 (± 24.065) | 17.58 (± 19.053) | |
| Role Physical, Week 52 | 18.38 (± 25.35) | 17.08 (± 26.443) | 21.05 (± 19.144) | |
| Social Function, Week 24 | 16.83 (± 21.503) | 16.36 (± 22.504) | 15.47 (± 23.804) | |
| Social Function, Week 52 | 16.6 (± 25.505) | 14.00 (± 25.165) | 20.56 (± 25.389) | |
| Vitality, Week 24 | 15.92 (± 19.176) | 18.36 (± 19.196) | 15.31 (± 17.731) | |
| Vitality, Week 52 | 16.14 (± 19.769) | 16.42 (± 17.671) | 16.12 (± 19.345) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Arthritis pain VAS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|--|
| End point title | Change from Baseline in Arthritis pain VAS at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[56] |
|-----------------|--|

End point description:

For the Arthritis Pain VAS, participants assess the severity of their current arthritis pain using a continuous visual analogue scale (VAS) with anchors at "0" (no pain) and "100" (most severe pain). A negative change from baseline indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on all randomized participants who received study intervention from Day 01 to Week 52. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[56] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | -25.43 (± 1.096) | -22.56 (± 1.069) | -31.02 (± 1.53) | |
| Week 52 | -28.36 (± 1.188) | -25.22 (± 1.175) | -33.34 (± 1.646) | |

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 ^[57] |
|-----------------|---|

End point description:

The Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue is a validated patient-reported measure of 13 statements regarding the feeling of fatigue. The total score ranges from 0 to 52 with higher values representing a lower fatigue and a better quality of life. A positive change from baseline in FACIT-fatigue indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the ITT set. Analysis was performed using multiple imputation method to handle missing data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[57] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-------------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 258 | 256 |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | 7.07 (± 0.41) | 6.3 (± 0.399) | 8.28 (± 0.577) | 4.72 (± 0.57) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in FACIT-Fatigue at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Change from Baseline in FACIT-Fatigue at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[58] |
|-----------------|---|

End point description:

The Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue is a validated patient-reported measure of 13 statements regarding the feeling of fatigue. The total score ranges from 0 to 52 with higher values representing a lower fatigue and a better quality of life. A positive change from baseline in FACIT-fatigue indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Participants who received study intervention from Day 1 to Week 52 were analyzed. Missing data was handled by multiple imputation method.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[58] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|-------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 513 | 510 | 258 | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | 8.52 (± 0.418) | 7.59 (± 0.406) | 8.56 (± 0.585) | |
| Week 52 | 7.71 (± 0.453) | 6.76 (± 0.446) | 8.55 (± 0.632) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in FACIT-Fatigue at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Change from Baseline in FACIT-Fatigue at Week 24 and Week 52 for placebo switched arms ^[59] |
|-----------------|--|

End point description:

The Functional Assessment of Chronic Illness Therapy (FACIT)-fatigue is a validated patient-reported measure of 13 statements regarding the feeling of fatigue. The total score ranges from 0 to 52 with higher values representing a lower fatigue and a better quality of life. A positive change from baseline in FACIT-fatigue indicates an improvement. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For efficacy assessments baseline is interpreted as Day 1. Participants who received study intervention from Week 12 to Week 52 were analyzed. Missing data was handled by multiple imputation method.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[59] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 85 | 86 | 85 | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| Week 24 | 7.57 (± 1.002) | 7.91 (± 0.965) | 9.44 (± 0.969) | |
| Week 52 | 7.08 (± 1.102) | 7.2 (± 1.051) | 11.05 (± 1.043) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events (AEs), serious adverse events (SAEs) and adverse events of special interest (AESI)

| | |
|-----------------|---|
| End point title | Number of participants with adverse events (AEs), serious adverse events (SAEs) and adverse events of special interest (AESI) ^[60] |
|-----------------|---|

End point description:

AE is defined as any untoward medical occurrence in a clinical study participant, temporally associated with use of a study intervention, whether or not considered related to study intervention. SAEs are defined as any untoward medical occurrence that, at any dose: results in death, cause life threatening events which requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability or incapacity and birth defect or congenital anomaly. Protocol defined AESIs were included. Fifteen participants in Pooled placebo received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm. The analysis was performed on Safety Set that includes all randomized participants who received at least one dose of study treatment. Pooled Placebo collected data from Day 01 to Week 12. Experimental arms collected data from Day 01 to Week 59.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to Week 59

Notes:

[60] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|-----------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 273 | 241 |
| Units: Participants | | | | |
| AE | 367 | 383 | 207 | 95 |
| SAE | 33 | 39 | 23 | 8 |
| AESI | 65 | 58 | 22 | 4 |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|---|
| End point title | Change from Baseline in white blood cell (WBC) count at Week 12 ^[61] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of hematology parameter white blood cell count. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[61] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|--|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 456 | 455 | 230 | 213 |
| Units: Giga cells per liter (10 ⁹ /L) | | | | |
| arithmetic mean (standard deviation) | -0.55 (± 2.267) | -0.63 (± 2.065) | -1.03 (± 2.16) | -0.3 (± 2.005) |

Statistical analyses

Secondary: Change from Baseline in WBC count at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Change from Baseline in WBC count at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[62] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of hematology parameter white blood cell count. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[62] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|--|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 443 | 465 | 246 | |
| Units: Giga cells per liter (10 ⁹ /L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 | -0.59 (± 2.279) | -0.5 (± 2.123) | -0.94 (± 2.31) | |
| Week 52 | -0.54 (± 2.386) | -0.52 (± 2.051) | -1.21 (± 2.407) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in WBC count at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Change from Baseline in WBC count at Week 24 and Week 52 for placebo switched arms ^[63] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of hematology parameter white blood cell count. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[63] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|--|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 78 | 78 | 63 | |
| Units: Giga cells per liter (10 ⁹ /L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 | -0.06 (± 1.94) | -0.31 (± 1.642) | -0.61 (± 2.052) | |
| Week 52 | -0.21 (± 2.129) | -0.03 (± 2.459) | -0.96 (± 2.013) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of platelet count, neutrophils, lymphocytes at Week 12

| | |
|-----------------|---|
| End point title | Change from Baseline in hematology parameter of platelet count, neutrophils, lymphocytes at Week 12 ^[64] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of hematology parameters including platelet count, neutrophils, lymphocytes. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[64] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|--|-----------------------|------------------------|-----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 453 | 454 | 229 | 211 |
| Units: Giga cells per liter (10 ⁹ /L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Lymphocytes | 0.006 (± 0.5341) | 0.016 (± 0.5552) | 0.084 (± 0.5789) | -0.009 (± 0.5367) |
| Neutrophils | -0.565 (± 2.2309) | -0.66 (± 2.0562) | -1.076 (± 2.162) | -0.268 (± 2.025) |

| | | | | |
|-----------|-----------------|-----------------|-----------------|----------------|
| Platelets | -18.6 (± 58.93) | -16.3 (± 59.51) | -26.7 (± 63.56) | -1.0 (± 58.79) |
|-----------|-----------------|-----------------|-----------------|----------------|

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of platelet count, neutrophils, lymphocytes at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|--|
| End point title | Change from Baseline in hematology parameter of platelet count, neutrophils, lymphocytes at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[65] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of hematology parameters including platelet count, neutrophils, lymphocytes. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[65] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|--|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 442 | 464 | 246 | |
| Units: Giga cells per liter (10 ⁹ /L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Lymphocytes, Week 24 | 0.031 (± 0.583) | -0.003 (± 0.5395) | 0.017 (± 0.62) | |
| Lymphocytes, Week 52 | 0.015 (± 0.5485) | -0.034 (± 0.5771) | -0.102 (± 0.5877) | |
| Neutrophils, Week 24 | -0.629 (± 2.2736) | -0.515 (± 1.9997) | -0.899 (± 2.2436) | |
| Neutrophils, Week 52 | -0.583 (± 2.3708) | -0.493 (± 1.9958) | -1.049 (± 2.3054) | |
| Platelets, Week 24 | -13.7 (± 65.69) | -15.4 (± 67.72) | -27.1 (± 70.17) | |
| Platelets, Week 52 | -18.7 (± 66.07) | -18.5 (± 64.59) | -30.2 (± 56.67) | |

Statistical analyses

Secondary: Change from Baseline in hematology parameter of platelet count, neutrophils, lymphocytes at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|---|
| End point title | Change from Baseline in hematology parameter of platelet count, neutrophils, lymphocytes at Week 24 and Week 52 for placebo switched arms ^[66] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of hematology parameters including platelet count, neutrophils, lymphocytes. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[66] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|--|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 78 | 78 | 63 | |
| Units: Giga cells per liter (10 ⁹ /L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Lymphocytes, Week 24 | -0.055 (± 0.5751) | 0.038 (± 0.5294) | 0.085 (± 0.5052) | |
| Lymphocytes, Week 52 | -0.091 (± 0.6046) | 0.09 (± 0.5744) | -0.079 (± 0.4538) | |
| Neutrophils, Week 24 | -0.053 (± 1.8784) | -0.405 (± 1.5633) | -0.685 (± 1.9031) | |
| Neutrophils, Week 52 | -0.118 (± 2.0773) | -0.289 (± 2.3914) | -0.847 (± 1.8472) | |
| Platelets, Week 24 | -11.3 (± 59.64) | -17.4 (± 63.81) | -9.3 (± 43.83) | |
| Platelets, Week 52 | -19 (± 65.35) | -11.7 (± 86.52) | -19.6 (± 51.16) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of hemoglobin at Week 12

| | |
|-----------------|---|
| End point title | Change from Baseline in hematology parameter of hemoglobin at Week 12 ^[67] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters hemoglobin level. Baseline was defined as the latest pre-dose assessment with a non-missing value,

including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set participants. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[67] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|--------------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 457 | 459 | 231 | 214 |
| Units: Grams per liter (g/L) | | | | |
| arithmetic mean (standard deviation) | -0.0 (± 8.14) | 0.5 (± 8.5) | 0.0 (± 8.56) | -1.7 (± 7.83) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of hemoglobin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|--|
| End point title | Change from Baseline in hematology parameter of hemoglobin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[68] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters hemoglobin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set participants. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[68] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|--------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 444 | 466 | 246 | |
| Units: Grams per liter (g/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 | 0.5 (± 8.96) | 1.3 (± 9.22) | 1.1 (± 9.23) | |
| Week 52 | 0.4 (± 9.5) | 0.7 (± 9.24) | -0.2 (± 9.14) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter of hemoglobin at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|---|
| End point title | Change from Baseline in hematology parameter of hemoglobin at Week 24 and Week 52 for placebo switched arms ^[69] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of change from baseline in hematology parameters hemoglobin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[69] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|--------------------------------------|--|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 78 | 78 | 63 | |
| Units: Grams per liter (g/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 | 0.7 (± 8.72) | 2 (± 9.02) | 1.8 (± 6.71) | |
| Week 52 | 1.4 (± 9.85) | 1.1 (± 10.57) | 0.8 (± 8.81) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP), Gamma-Glutamyl transpeptidase (GGT) at Week 12

| | |
|-----------------|---|
| End point title | Change from Baseline in clinical chemistry parameter of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP), Gamma-Glutamyl transpeptidase (GGT) at Week 12 ^[70] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of clinical chemistry parameters including aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP) and gamma-glutamyl transferase (GGT) levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set participants. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[70] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|---|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 468 | 475 | 242 | 220 |
| Units: International units per liter (IU/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Alkaline Phosphatase | -1.5 (± 17.97) | -1.2 (± 15.64) | -3.7 (± 16.07) | -0.7 (± 15.29) |
| ALT | 0.5 (± 15.69) | 2 (± 19.66) | 2.2 (± 15.07) | -1.1 (± 11.76) |
| AST | 1.2 (± 9.71) | 2.4 (± 13.09) | 3.1 (± 14.09) | -0.4 (± 7.38) |
| Gamma Glutamyl Transferase | -2.1 (± 17.67) | -2.3 (± 16.05) | 1.2 (± 23.21) | -0.5 (± 16.31) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of AST, ALT, AP, GGT at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Change from Baseline in clinical chemistry parameter of AST, ALT, AP, GGT at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[71] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of clinical chemistry parameters including AST, ALT, AP and GGT levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set participants. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[71] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|---|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 448 | 467 | 246 | |
| Units: International units per liter (IU/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Alkaline Phosphatase, Week 24 | 0.5 (± 17.77) | 1.8 (± 19.16) | -3.0 (± 17.41) | |
| Alkaline Phosphatase, Week 52 | 2.8 (± 19.52) | 1.5 (± 17.35) | -1.0 (± 18.12) | |
| ALT, Week 24 | 1.5 (± 22.98) | 2.5 (± 17.22) | 4.5 (± 40.51) | |
| ALT, Week 52 | 0.4 (± 12.31) | -0.2 (± 13.95) | 1.9 (± 15.72) | |
| AST, Week 24 | 1.3 (± 11.36) | 2.4 (± 11.25) | 8.6 (± 94.12) | |
| AST, Week 52 | 1 (± 8.97) | 1 (± 8.22) | 3.1 (± 14.21) | |
| Gamma Glutamyl Transferase, Week 24 | -1.7 (± 18.05) | -1.2 (± 17.71) | 0.2 (± 19.7) | |
| Gamma Glutamyl Transferase, Week 52 | -0.3 (± 22.26) | -0.4 (± 22.03) | 1.6 (± 20.52) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of AST, ALT, AP, GGT at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Change from Baseline in clinical chemistry parameter of AST, ALT, AP, GGT at Week 24 and Week 52 for placebo switched arms ^[72] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of clinical chemistry parameters including AST, ALT, AP and GGT levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[72] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|---|--|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 78 | 78 | 63 | |
| Units: International units per liter (IU/L) | | | | |
| arithmetic mean (standard deviation) | | | | |

| | | | | |
|-------------------------------------|---------------|----------------|----------------|--|
| Alkaline Phosphatase, Week 24 | 0.9 (± 13.07) | -0.3 (± 18.04) | 0.7 (± 14.91) | |
| Alkaline Phosphatase, Week 52 | 5.5 (± 24.05) | -1.9 (± 16.07) | -1 (± 14.6) | |
| ALT, Week 24 | 0.3 (± 10.76) | 3.6 (± 18.43) | 3.3 (± 13.9) | |
| ALT, Week 52 | 2.6 (± 15.59) | 2.6 (± 11.55) | 2.7 (± 15.03) | |
| AST, Week 24 | 1.5 (± 11.4) | 2.9 (± 13.53) | 3.2 (± 10.53) | |
| AST, Week 52 | 1.8 (± 6.89) | 2 (± 9.08) | 3.6 (± 9.88) | |
| Gamma Glutamyl Transferase, Week 24 | 0.8 (± 13.65) | 0.9 (± 16.68) | -0.5 (± 32.46) | |
| Gamma Glutamyl Transferase, Week 52 | 8.1 (± 55.51) | 1 (± 14.4) | -2.2 (± 35.14) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of total bilirubin at Week 12

| | |
|-----------------|--|
| End point title | Change from Baseline in clinical chemistry parameter of total bilirubin at Week 12 ^[73] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter total bilirubin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set participants. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[73] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|--------------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 468 | 475 | 242 | 220 |
| Units: Micromoles per liter (umol/L) | | | | |
| arithmetic mean (standard deviation) | 0.3 (± 2.63) | 0.4 (± 2.52) | 0.5 (± 2.96) | -0.2 (± 3.13) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of total bilirubin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Change from Baseline in clinical chemistry parameter of total |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter total bilirubin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set participants. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

End point type Secondary

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[74] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|--------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 448 | 467 | 246 | |
| Units: Micromoles per liter (umol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 | 0.5 (± 2.93) | 0.6 (± 2.79) | 0.6 (± 2.95) | |
| Week 52 | 0.5 (± 2.73) | 0.4 (± 2.81) | 0.5 (± 3.2) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of total bilirubin at Week 24 and Week 52 for placebo switched arms

End point title Change from Baseline in clinical chemistry parameter of total bilirubin at Week 24 and Week 52 for placebo switched arms^[75]

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter total bilirubin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

End point type Secondary

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[75] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|--------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 78 | 78 | 63 | |
| Units: Micromoles per liter (umol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 | 0.2 (± 2.65) | 0.6 (± 2.8) | 0.1 (± 2.62) | |
| Week 52 | 0.3 (± 3.16) | 0.6 (± 2.75) | 0.6 (± 2.64) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of albumin at Week 12

| | |
|-----------------|--|
| End point title | Change from Baseline in clinical chemistry parameter of albumin at Week 12 ^[76] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter albumin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. The analysis was performed on the Safety Set participants. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[76] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|--------------------------------------|-----------------------|------------------------|-----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 468 | 475 | 242 | 220 |
| Units: Grams per liter (g/L) | | | | |
| arithmetic mean (standard deviation) | -0.2 (± 2.7) | 0.2 (± 2.53) | 0.8 (± 3.05) | -0.7 (± 2.7) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of albumin at Week 24 and Week 52 for treatment arms who started study intervention from Day

| | |
|-----------------|---|
| End point title | Change from Baseline in clinical chemistry parameter of albumin at Week 24 and Week 52 for treatment arms who started study intervention from Day 1 ^[77] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter albumin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set participants. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Week 24 and Week 52

Notes:

[77] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|--------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 448 | 466 | 246 | |
| Units: Grams per liter (g/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 | 0.2 (± 2.85) | 0.3 (± 2.69) | 1.3 (± 3.17) | |
| Week 52 | -0.2 (± 3.08) | 0.3 (± 3.03) | 0.6 (± 2.83) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter of albumin at Week 24 and Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Change from Baseline in clinical chemistry parameter of albumin at Week 24 and Week 52 for placebo switched arms ^[78] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter albumin level. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Week 12), Week 24 and Week 52

Notes:

[78] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|--------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 78 | 78 | 63 | |
| Units: Grams per liter (g/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 | 0.3 (± 2.57) | 1.1 (± 2.54) | 1.8 (± 2.47) | |
| Week 52 | 0.3 (± 2.94) | 0.8 (± 2.77) | 1.2 (± 2.24) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 12

| | |
|-----------------|---|
| End point title | Change from Baseline in lipid profile parameter of total cholesterol at Week 12 ^[79] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For the purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as a reference for the comparison of active treatment arms. Blood samples were collected at indicated time points per schedule of activities in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 12 was a secondary objective, however for lipid profile, there is no corresponding time point in schedule of activities. Consequently, the objective cannot be assessed at the specified time points since the sample was collected at Week 4. Week 4 is not pre-specified time point to report.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[79] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|--------------------------------------|-----------------------|------------------------|-----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 0 ^[80] | 0 ^[81] | 0 ^[82] | 0 ^[83] |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | () | () | () | () |

Notes:

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

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

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

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

Statistical analyses

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 24 for treatment arms who started study intervention from Day 1

| | |
|-----------------|--|
| End point title | Change from Baseline in lipid profile parameter of total cholesterol at Week 24 for treatment arms who started study intervention from Day 1 ^[84] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of activities in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid profile, there is no corresponding time point in schedule of activities. Consequently, the objective cannot be assessed at the specified time points since the sample was collected at Week 16. Week 16 is not pre-specified time point to report.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[84] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|--------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 0 ^[85] | 0 ^[86] | 0 ^[87] | |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | () | () | () | |

Notes:

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

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

[87] - 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 lipid profile parameter of total cholesterol at Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|--|
| End point title | Change from Baseline in lipid profile parameter of total cholesterol at Week 52 for treatment arms who started study intervention from Day 1 ^[88] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set participants. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[88] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|--------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 394 | 405 | 223 | |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | 0.084 (± 0.846) | 0.074 (± 0.9528) | 0.535 (± 0.9012) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 24 for placebo switched arms

| | |
|-----------------|---|
| End point title | Change from Baseline in lipid profile parameter of total cholesterol at Week 24 for placebo switched arms ^[89] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of activities in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid profile, there is no corresponding time point in schedule of activities. Consequently, the objective cannot be assessed at the specified time points since the sample was collected at Week 16. Week 16 is not pre-specified time point to report.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[89] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|--------------------------------------|--|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[90] | 0 ^[91] | 0 ^[92] | |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | () | () | () | |

Notes:

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

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

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

Statistical analyses

Secondary: Change from Baseline in lipid profile parameter of total cholesterol at Week 52 for placebo switched arms

| | |
|-----------------|---|
| End point title | Change from Baseline in lipid profile parameter of total cholesterol at Week 52 for placebo switched arms ^[93] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of lipid profile of total cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[93] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|--------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 62 | 69 | 56 | |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | 0.334 (± 0.7608) | 0.045 (± 0.7931) | 0.486 (± 0.8974) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of low-density lipoprotein (LDL) cholesterol, high-density lipoprotein-cholesterol at Week 12

| | |
|-----------------|---|
| End point title | Change from Baseline in lipid profile parameter of low-density lipoprotein (LDL) cholesterol, high-density lipoprotein-cholesterol at Week 12 ^[94] |
|-----------------|---|

End point description:

Blood samples were collected for assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For purpose of all analyses up to week 12, placebo arms were pooled into a single placebo arm to primarily serve as reference for comparison of active treatment arms. Blood samples were collected at indicated time points per schedule of activities in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 12 was a secondary objective, however for lipid profile, there is no corresponding time point in schedule of activities. Consequently, objective cannot be assessed at the specified time points since sample was collected at Week 4. Week 4 is not pre-specified time point to report.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[94] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|--------------------------------------|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 0 ^[95] | 0 ^[96] | 0 ^[97] | 0 ^[98] |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | () | () | () | () |

Notes:

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

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

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

[98] - 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 lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 24 for treatment arms who started study intervention from Day 1

| | |
|-----------------|--|
| End point title | Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 24 for treatment arms who started study intervention from Day 1 ^[99] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of activities in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid profile, there is no corresponding time point in schedule of activities. Consequently, the objective cannot be assessed at the specified time points since the sample was collected at Week 16. Week 16 is not pre-specified time point to report.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[99] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|--------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 0 ^[100] | 0 ^[101] | 0 ^[102] | |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | () | () | () | |

Notes:

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

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

[102] - 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 lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 24 for placebo switched arms

| | |
|-----------------|--|
| End point title | Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 24 for placebo switched arms ^[103] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of activities in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid profile, there is no corresponding time point in schedule of activities. Consequently, the objective cannot be assessed at the specified time points since the sample was collected at Week 16. Week 16 is not pre-specified time point to report.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[103] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|--------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[104] | 0 ^[105] | 0 ^[106] | |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | () | () | () | |

Notes:

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

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

[106] - 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 lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 52 for treatment arms who started study intervention from Day 1 ^[107] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set participants. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[107] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|--------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 394 | 405 | 223 | |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| HDL Cholesterol, Direct | -0.046 (± 0.3024) | 0.011 (± 0.2887) | 0.117 (± 0.2986) | |
| LDL Cholesterol | 0.089 (± 0.7062) | 0.053 (± 0.736) | 0.369 (± 0.758) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Change from Baseline in lipid profile parameter of LDL cholesterol, high-density lipoprotein-cholesterol at Week 52 for placebo switched arms ^[108] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of fasting lipid profile including LDL cholesterol, HDL cholesterol levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[108] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|--------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 62 | 69 | 56 | |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| HDL Cholesterol, Direct | 0.083 (± 0.302) | 0.033 (± 0.209) | 0.092 (± 0.2701) | |
| LDL Cholesterol | 0.221 (± 0.6669) | -0.003 (± 0.697) | 0.304 (± 0.8315) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lipid profile parameter of triglycerides at Week 12

| | |
|-----------------|--|
| End point title | Change from Baseline in lipid profile parameter of triglycerides at Week 12 ^[109] |
|-----------------|--|

End point description:

Blood samples was collected for assessment of change from baseline in fasting lipid profile triglycerides levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting post dose visit value from Baseline value. For purpose of all analyses up to week 12, the placebo arms were pooled into a single placebo arm to primarily serve as reference for comparison of active treatment arms. Blood samples were collected at indicated time points per schedule of activities in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 12 was a secondary objective, however for lipid profile, there is no corresponding time point in schedule of activities. Consequently, objective cannot be assessed at the specified time points since sample was collected at Week 4. Week 4 is not pre-specified time point to report.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[109] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|--------------------------------------|-----------------------|------------------------|-----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 0 ^[110] | 0 ^[111] | 0 ^[112] | 0 ^[113] |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | () | () | () | () |

Notes:

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

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

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

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

Statistical analyses

Secondary: Change from Baseline in lipid profile parameter of triglycerides at Week 24 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Change from Baseline in lipid profile parameter of triglycerides at Week 24 for treatment arms who started study intervention from Day 1 ^[114] |
|-----------------|---|

End point description:

Blood samples were collected for the assessment of change from baseline in fasting lipid profile triglycerides levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of activities in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid profile, there is no corresponding time point in schedule of activities. Consequently, the objective cannot be assessed at the specified time points since the sample was collected at Week 16. Week 16 is not pre-specified time point to report.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[114] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|--------------------------------------|--------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 0 ^[115] | 0 ^[116] | 0 ^[117] | |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | () | () | () | |

Notes:

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

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

[117] - 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 lipid profile parameter of triglycerides at Week 24 for placebo switched arms

| | |
|-----------------|--|
| End point title | Change from Baseline in lipid profile parameter of triglycerides at Week 24 for placebo switched arms ^[118] |
|-----------------|--|

End point description:

Blood samples were collected for the assessment of change from baseline in fasting lipid profile triglycerides levels. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. Blood samples were collected at indicated time points per schedule of activities in protocol. Objectives and Endpoints section incorrectly states that Change from baseline in key laboratory parameters at Week 24 was a secondary objective, however for lipid profile, there is no corresponding time point in schedule of activities. Consequently, the objective cannot be assessed at the specified time points since the sample was collected at Week 16. Week 16 is not pre-specified time point to report.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 24

Notes:

[118] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|--------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[119] | 0 ^[120] | 0 ^[121] | |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | () | () | () | |

Notes:

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

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

[121] - 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 lipid profile parameter of triglycerides at Week 52 for treatment arms who started study intervention from Day 1

| | |
|-----------------|---|
| End point title | Change from Baseline in lipid profile parameter of triglycerides at Week 52 for treatment arms who started study intervention from Day 1 ^[122] |
|-----------------|---|

End point description:

Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. The analysis was performed on the Safety Set participants. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[122] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | |
|--------------------------------------|-----------------------|------------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 394 | 405 | 223 | |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | 0.081 (\pm 0.5531) | 0.051 (\pm 0.7413) | 0.119 (\pm 0.7325) | |

Statistical analyses

Secondary: Change from Baseline in lipid profile parameter of triglycerides at Week 52 for placebo switched arms

| | |
|-----------------|--|
| End point title | Change from Baseline in lipid profile parameter of triglycerides at Week 52 for placebo switched arms ^[123] |
|-----------------|--|

End point description:

Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting the post dose visit value from the Baseline value. For safety assessments baseline is interpreted as Week 12. The analysis was performed on the Safety Set. Only those participants with data available at the specified data points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 52

Notes:

[123] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|--------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 62 | 69 | 56 | |
| Units: Millimoles per liter (mmol/L) | | | | |
| arithmetic mean (standard deviation) | 0.066 (± 0.5071) | 0.03 (± 0.6306) | 0.241 (± 0.5357) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with National Cancer Institute-Common terminology criteria for adverse events (NCI-CTCAE) ≥Grade 3 hematological/clinical chemistry abnormalities

| | |
|-----------------|---|
| End point title | Number of participants with National Cancer Institute-Common terminology criteria for adverse events (NCI-CTCAE) ≥Grade 3 hematological/clinical chemistry abnormalities ^[124] |
|-----------------|---|

End point description:

Number of participants with NCI-CTCAE ≥Grade 3 hematological/clinical chemistry abnormalities were summarized. Hematological and Clinical chemistry parameters were summarized according to the NCI-CTCAE, version 5.0: Grade 1: mild; Grade 2: moderate; Grade 3: severe; Grade 4: life-threatening or disabling. Higher grade indicates more severity. Data is presented for only those parameters for which participants had worst case ≥Grade 3 shifts from Baseline. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. The analysis was performed on the Safety Set that includes all randomized participants who received at least one dose of study treatment. Pooled Placebo collected data till Week 12. Placebo switched arms collected data from Week 12 to 59. Experimental arm collected data from Day 01 to Week 59.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to Week 59

Notes:

[124] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX | Pooled Placebo |
|--|--------------------------|---------------------------|--------------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 513 | 510 | 273 | 241 |
| Units: Participants | | | | |
| Aspartate aminotransferase increased, Total, Grade 3 | 0 | 5 | 1 | 0 |
| Aspartate aminotransferase increased, Total, Grade 4 | 0 | 0 | 1 | 0 |
| Hypertriglyceridemia, Total, Grade 3 | 2 | 1 | 2 | 1 |
| Hypertriglyceridemia, Total, Grade 4 | 1 | 1 | 0 | 0 |
| Neutrophil count decreased, Grade 3, Grade 4 | 0 | 0 | 0 | 0 |
| Neutrophil count decreased, Grade 4, Grade 3 | 0 | 0 | 0 | 0 |
| Alanine aminotransferase increased, Total, Grade 3 | 5 | 6 | 1 | 0 |
| Alanine aminotransferase increased, Total, Grade 4 | 0 | 1 | 0 | 0 |
| Blood bilirubin increased, Total, Grade 3 | 0 | 1 | 0 | 0 |
| Cholesterol - high, Total, Grade 3 | 0 | 1 | 0 | 0 |
| Creatinine increased, Total, Grade 3 | 0 | 1 | 0 | 0 |
| Chronic Kidney Disease, Total Grade 3 | 2 | 2 | 1 | 0 |
| Chronic Kidney Disease, Total Grade 4 | 0 | 1 | 0 | 0 |
| Anemia, Total, Grade 3 | 2 | 4 | 1 | 0 |
| White blood cell decreased, Total, Grade 3 | 1 | 1 | 0 | 0 |
| Lymphocyte count decreased, Total, Grade 3 | 6 | 9 | 5 | 1 |
| Lymphocyte count decreased, Total, Grade 4 | 0 | 1 | 0 | 0 |
| Neutrophil count decreased, Total, Grade 3 | 4 | 0 | 0 | 2 |
| Neutrophil count decreased, Total, Grade 4 | 2 | 3 | 1 | 1 |
| Platelet count decreased, Total Grade 3 | 1 | 0 | 0 | 0 |
| Platelet count decreased, Total, Grade 4 | 0 | 0 | 1 | 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 ^[125] |
|-----------------|---|

End point description:

Concentrations of GM-CSF autoantibodies were determined. The analysis was performed on the Safety Set. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week

4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis. Only those participants with data available at the specified time points were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At baseline

Notes:

[125] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX |
|--------------------------------------|--------------------------------|------------------------------|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 491 | 486 | 82 | 85 |
| Units: Microgram per liter (ug/L) | | | | |
| arithmetic mean (standard deviation) | 832.827 (\pm 12355.2805) | 218.456 (\pm 632.5733) | 231.376 (\pm 446.1713) | 357.087 (\pm 629.3471) |

| End point values | Placebo + MTX and Tofacitinib 5mg + MTX | Tofacitinib 5mg + MTX | | |
|--------------------------------------|---|----------------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 70 | 264 | | |
| Units: Microgram per liter (ug/L) | | | | |
| arithmetic mean (standard deviation) | 240.109 (\pm 624.4536) | 203.31 (\pm 444.708) | | |

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 ^[126] |
|-----------------|---|

End point description:

Serum samples were collected for determination of anti-GSK3196165 antibodies (ADA) using a validated electrochemiluminescence (ECL) immunoassay. The assay involved screening, confirmation and titration steps. If serum samples tested positive in the screening assay, they were considered 'potentially positive' and were further analyzed for specificity using the confirmation assay. Samples that confirmed positive in confirmation assay were reported as 'positive'. Confirmed positive ADA samples were further characterized in the titration assay to quasi-quantitate the amount of ADA in sample. Additionally, confirmed positive ADA samples were also tested in a validated neutralizing antibody assay to determine the potential neutralizing activity of ADA. The analysis was performed on the Safety set. Fifteen participants in Pooled placebo group who received active treatment of Tofacitinib from Week 4 instead of Week 12 as planned. They were pooled with the Tofacitinib arm in safety analysis.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to Week 59

Notes:

[126] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX |
|-----------------------------|--------------------------|---------------------------|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 513 | 510 | 85 | 86 |
| Units: Participants | 7 | 7 | 0 | 1 |

| End point values | Placebo + MTX and Tofacitinib 5mg + MTX | Tofacitinib 5mg + MTX | | |
|-----------------------------|---|--------------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 70 | 273 | | |
| Units: Participants | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events (AEs), serious adverse events (SAEs) and adverse events of special interest (AESI) for placebo switched arms

| | |
|-----------------|--|
| End point title | Number of participants with adverse events (AEs), serious adverse events (SAEs) and adverse events of special interest (AESI) for placebo switched arms ^[127] |
|-----------------|--|

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. The analysis was performed on Safety Set of switched arms that collected data from Week 12 to 59.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12 to Week 59

Notes:

[127] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|-----------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 80 | 82 | 68 | |
| Units: Participants | | | | |
| Participants with AE | 49 | 52 | 44 | |
| Participants with SAE | 8 | 9 | 5 | |
| Participants with AESI | 9 | 9 | 3 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with National Cancer Institute-Common terminology criteria for adverse events (NCI-CTCAE) ≥ Grade 3 hematological/clinical chemistry abnormalities for placebo switched arms

| | |
|-----------------|--|
| End point title | Number of participants with National Cancer Institute-Common terminology criteria for adverse events (NCI-CTCAE) ≥ Grade 3 hematological/clinical chemistry abnormalities for placebo switched arms ^[128] |
|-----------------|--|

End point description:

Number of participants with NCI-CTCAE ≥ Grade 3 hematological/clinical chemistry abnormalities were summarized. Hematological and Clinical chemistry parameters were summarized according to the NCI-CTCAE, version 5.0: Grade 1: mild; Grade 2: moderate; Grade 3: severe; Grade 4: life-threatening or disabling. Higher grade indicates more severity. Data is presented for only those parameters for which participants had worst case ≥ Grade 3 shifts from Baseline. The analysis was performed on Safety Set of switched arms that collected data from Week 12 to 59.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12 to Week 59

Notes:

[128] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoints are different for the different parts of the study.

| End point values | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX | Placebo + MTX and Tofacitinib 5mg + MTX | |
|--|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 80 | 82 | 68 | |
| Units: Participants | | | | |
| Hypertriglyceridemia, Total, Grade 3 | 1 | 2 | 0 | |
| Neutrophil count decreased, Grade 3, Grade 4 | 0 | 0 | 1 | |
| Neutrophil count decreased, Grade 4, Grade 3 | 1 | 0 | 0 | |
| Creatinine increased, Total, Grade 3 | 1 | 0 | 0 | |
| Chronic Kidney Disease, Total Grade 3 | 2 | 0 | 0 | |
| Anemia, Total, Grade 3 | 1 | 2 | 0 | |
| White blood cell decreased, Total, Grade 3 | 1 | 0 | 0 | |

| | | | | |
|--|---|---|---|--|
| White blood cell decreased, Total , Grade 3 | 0 | 0 | 1 | |
| Lymphocyte count decreased, Total, Grade 4 | 0 | 1 | 0 | |
| Neutrophil count decreased, Total, Grade 3 | 2 | 0 | 0 | |
| Neutrophil count decreased, Total, Grade 4 | 0 | 0 | 2 | |
| Platelet count decreased, Total Grade 3 | 0 | 0 | 1 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The Pooled Placebo arm collected during the timeframe Week 0 to Week 12. Placebo switched to active treatment arms collected during the timeframe Week 12 to Week 59. Experimental arms collected during from Week 0 to Week 59.

Adverse event reporting additional description:

The analysis was performed on the Safety Set for pooled placebo and experimental arms. The analysis was performed on Safety Set-Period 2 for placebo switched arms.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 25.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | GSK3196165 90mg + MTX |
|-----------------------|-----------------------|

Reporting group description:

Participants received GSK3196165 90 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with methotrexate (MTX).

| | |
|-----------------------|------------------------|
| Reporting group title | GSK3196165 150mg + MTX |
|-----------------------|------------------------|

Reporting group description:

Participants received GSK3196165 150 mg subcutaneous (SC) injection once weekly for 52 weeks in combination with MTX.

| | |
|-----------------------|-----------------------|
| Reporting group title | Tofacitinib 5mg + MTX |
|-----------------------|-----------------------|

Reporting group description:

Participants received Tofacitinib 5mg capsule, orally, twice daily (BID) in combination with MTX plus placebo injection weekly to maintain the blind for 52 weeks.

| | |
|-----------------------|----------------|
| Reporting group title | Pooled Placebo |
|-----------------------|----------------|

Reporting group description:

Participants received Placebo weekly SC injection in combination with MTX until Week 12. The placebo arms are pooled into a single placebo arm.

| | |
|-----------------------|---|
| Reporting group title | Placebo + MTX and GSK3196165 90mg + MTX |
|-----------------------|---|

Reporting group description:

Participants received Placebo weekly SC injection in combination with MTX for 12 weeks. At Week 12, participants were switched from placebo to GSK3196165 90 mg, SC injection, once weekly in combination with MTX until Week 52.

| | |
|-----------------------|--|
| Reporting group title | Placebo + MTX and GSK3196165 150mg + MTX |
|-----------------------|--|

Reporting group description:

Participants received Placebo weekly SC injection in combination with MTX for 12 weeks. At Week 12, participants were switched from placebo to GSK3196165 150 mg, SC injection, once weekly in combination with MTX until Week 52.

| | |
|-----------------------|---|
| Reporting group title | Placebo + MTX and Tofacitinib 5mg + MTX |
|-----------------------|---|

Reporting group description:

Participants received Placebo tablet weekly in combination with MTX for 12 weeks. At Week 12, participants were switched from placebo tablet to Tofacitinib 5mg, capsule, orally, BID in combination with MTX plus placebo injection to maintain the blind for 52 weeks.

| Serious adverse events | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX |
|---|-----------------------|------------------------|-----------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 33 / 513 (6.43%) | 39 / 510 (7.65%) | 23 / 273 (8.42%) |

| | | | |
|---|-----------------|-----------------|-----------------|
| number of deaths (all causes) number of deaths resulting from adverse events | 2 | 7 | 3 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Laryngeal squamous cell carcinoma alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Hepatic cancer alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Endometrial adenocarcinoma alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Breast cancer alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Lung adenocarcinoma alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 2 / 273 (0.73%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenocarcinoma of colon alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |

| | | | |
|--|-----------------|-----------------|-----------------|
| Ovarian adenoma alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Ovarian fibroma alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancoast's tumour alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 | | | |
| Circulatory collapse alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Deep vein thrombosis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Hypertension alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Death | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 2 / 510 (0.39%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Intermenstrual bleeding | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epistaxis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Haemothorax | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Psychiatric disorders | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| Conversion disorder alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Product issues | | | |
| Device malfunction alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Cervical vertebral fracture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Femoral neck fracture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Femur fracture | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Forearm fracture | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Post procedural complication | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Multiple injuries | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Lower limb fracture | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Humerus fracture | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Radius fracture | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ulna fracture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Tibia fracture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tendon rupture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Rib fracture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Cardiac disorders | | | |
| Atrial fibrillation alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Acute myocardial infarction alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 513 (0.39%) | 0 / 510 (0.00%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Coronary artery disease alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Myocardial infarction alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebral infarction alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 1 / 510 (0.20%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Haemorrhagic stroke | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Headache | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Hypertensive encephalopathy | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Ischaemic stroke | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar radiculopathy | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic encephalopathy | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Neuropathy peripheral alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 1 / 510 (0.20%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 encephalopathy alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Vertebrobasilar insufficiency alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Neutropenia alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Anaemia alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 2 / 510 (0.39%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Ear and labyrinth disorders | | | |
| Meniere's disease | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Vertigo | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Eye disorders | | | |
| Optic ischaemic neuropathy | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 | | | |
| Colitis ischaemic | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Gastritis erosive | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Gastric ulcer perforation | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulum intestinal alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intussusception alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders Chronic hepatitis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Drug-induced liver injury alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Hepatic cirrhosis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Hepatorenal failure alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Neurogenic bladder | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Nephrolithiasis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Acute kidney injury | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tubulointerstitial nephritis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Endocrine disorders | | | |
| Cushing's syndrome | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Goitre | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 9 |
| Musculoskeletal and connective tissue disorders | | | |
| Fracture nonunion | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Foot deformity | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Costochondritis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc disorder | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Synovial cyst alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Rheumatoid arthritis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 2 / 513 (0.39%) | 5 / 510 (0.98%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteochondrosis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Osteoarthritis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 2 / 513 (0.39%) | 0 / 510 (0.00%) | 2 / 273 (0.73%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal chest pain alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations Arthritis bacterial alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Acinetobacter sepsis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Abscess limb alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 2 / 510 (0.39%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bursitis infective alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| COVID-19 alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 2 / 273 (0.73%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Chronic tonsillitis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis staphylococcal alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-----------------|------------------|-----------------|
| Cellulitis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 2 / 273 (0.73%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 pneumonia alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 7 / 513 (1.36%) | 10 / 510 (1.96%) | 4 / 273 (1.47%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 10 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Joint abscess alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Hepatitis E alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Gastroenteritis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Diverticulitis intestinal perforated alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 2 / 513 (0.39%) | 3 / 510 (0.59%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 2 | 2 / 3 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Sinusitis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Septic shock | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 2 / 510 (0.39%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative wound infection | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 cellulitis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |

| | | | |
|--|-----------------|-----------------|-----------------|
| Urinary tract infection alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 1 / 510 (0.20%) | 0 / 273 (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 |
| Wound infection pseudomonas alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (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 |
| Wound infection staphylococcal alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 513 (0.19%) | 0 / 510 (0.00%) | 0 / 273 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders Hyperglycaemic hyperosmolar nonketotic syndrome alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 1 / 273 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Pooled Placebo | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX |
|--|-----------------|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 241 (3.32%) | 8 / 80 (10.00%) | 9 / 82 (10.98%) |
| number of deaths (all causes) | 1 | 0 | 1 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Laryngeal squamous cell carcinoma alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |

| | | | |
|--|-----------------|----------------|----------------|
| Hepatic cancer alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 1 / 82 (1.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometrial adenocarcinoma alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Breast cancer alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Lung adenocarcinoma alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Adenocarcinoma of colon alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 241 (0.41%) | 0 / 80 (0.00%) | 0 / 82 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Ovarian adenoma alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Ovarian fibroma alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Pancoast's tumour | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 241 (0.41%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Deep vein thrombosis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Hypertension | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 | | | |
| Chest pain | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Death | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Reproductive system and breast disorders | | | |
| Intermenstrual bleeding | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Epistaxis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 1 / 82 (1.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemothorax | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Conversion disorder | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 241 (0.41%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Product issues | | | |

| | | | |
|---|-----------------|----------------|----------------|
| Device malfunction alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 | | | |
| Ankle fracture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Cervical vertebral fracture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Femoral neck fracture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Femur fracture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Forearm fracture | | | |

| | | | |
|--|-----------------|----------------|----------------|
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 1 / 80 (1.25%) | 0 / 82 (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 complication | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Multiple injuries | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Lower limb fracture | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Humerus fracture | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 1 / 80 (1.25%) | 0 / 82 (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 |
| Radius fracture | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Ulna fracture | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Tibia fracture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Tendon rupture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 241 (0.41%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Rib fracture alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 241 (0.41%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Acute myocardial infarction alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 arrest alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Coronary artery disease alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 | | | |
| Cerebral infarction alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Cerebrovascular accident alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 1 / 82 (1.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Haemorrhagic stroke alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 1 / 82 (1.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Headache | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Hypertensive encephalopathy | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Ischaemic stroke | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Lumbar radiculopathy | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Metabolic encephalopathy | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Neuropathy peripheral | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |

| | | | |
|---|-----------------|----------------|----------------|
| Syncope alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 encephalopathy alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Vertebrobasilar insufficiency alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Neutropenia alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Anaemia alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Pancytopenia alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Meniere's disease alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Vertigo alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Eye disorders Optic ischaemic neuropathy alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 1 / 82 (1.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders Colitis ischaemic alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Gastritis erosive alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Gastric ulcer perforation alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Diverticulum intestinal alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Intussusception alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Hepatobiliary disorders Chronic hepatitis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Drug-induced liver injury alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Hepatic cirrhosis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Hepatorenal failure alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Renal and urinary disorders Neurogenic bladder alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Nephrolithiasis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Acute kidney injury | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Renal failure | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Tubulointerstitial nephritis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 1 / 80 (1.25%) | 0 / 82 (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 |
| Endocrine disorders | | | |
| Cushing's syndrome | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Goitre | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 | | | |
| Fracture nonunion | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Foot deformity | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Costochondritis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Arthritis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Intervertebral disc disorder | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 1 / 80 (1.25%) | 0 / 82 (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 |
| Synovial cyst | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 241 (0.00%) | 1 / 80 (1.25%) | 0 / 82 (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 |
| Rheumatoid arthritis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 2 / 80 (2.50%) | 1 / 82 (1.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteochondrosis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 1 / 80 (1.25%) | 0 / 82 (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 |
| Osteoarthritis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 1 / 80 (1.25%) | 1 / 82 (1.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal chest pain alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 Arthritis bacterial alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Acinetobacter sepsis alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Abscess limb | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Bursitis infective | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 241 (0.41%) | 0 / 80 (0.00%) | 0 / 82 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic tonsillitis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Cellulitis staphylococcal | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Cellulitis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | | |
|--|-----------------|----------------|----------------|--|
| COVID-19 pneumonia alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 1 / 241 (0.41%) | 0 / 80 (0.00%) | 0 / 82 (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 | |
| Joint abscess alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 | |
| Hepatitis E alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 | |
| Gastroenteritis alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 | |
| Diverticulitis intestinal perforated alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 | |
| Diverticulitis alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 | |
| Pneumonia alternative dictionary used: v25.0 25.0 | | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 1 / 82 (1.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 1 / 82 (1.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Sepsis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 1 / 241 (0.41%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Postoperative wound infection alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Post procedural cellulitis alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Urinary tract infection alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |

| | | | |
|--|-----------------|----------------|----------------|
| Wound infection pseudomonas alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Wound infection staphylococcal alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 |
| Metabolism and nutrition disorders Hyperglycaemic hyperosmolar nonketotic syndrome alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (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 + MTX and Tofacitinib 5mg + MTX | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 68 (7.35%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Laryngeal squamous cell carcinoma alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic cancer alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|--|----------------|--|--|--|
| Endometrial adenocarcinoma alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Breast cancer alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung adenocarcinoma alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Adenocarcinoma of colon alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ovarian adenoma alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ovarian fibroma alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancoast's tumour alternative dictionary used: v25.0 25.0 | | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Deep vein thrombosis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertension | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Death | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Intermenstrual bleeding | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Epistaxis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemothorax | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Conversion disorder | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Product issues | | | |
| Device malfunction | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |

| | | | |
|--|----------------|--|--|
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cervical vertebral fracture | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femoral neck fracture | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femur fracture | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Forearm fracture | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Post procedural complication | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Multiple injuries | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower limb fracture | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Humerus fracture | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Radius fracture | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ulna fracture | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tibia fracture | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

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|--|----------------------------------|--|--|--|
| Tendon rupture alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | | |
| Rib fracture alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | | |
| Cardiac disorders Atrial fibrillation alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | | |
| Acute myocardial infarction alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | | |
| Cardiac arrest alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | | |
| Coronary artery disease alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | | |
| Myocardial infarction alternative dictionary used: v25.0 25.0 | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebral infarction | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebrovascular accident | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dizziness | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemorrhagic stroke | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Headache | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertensive encephalopathy | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ischaemic stroke | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lumbar radiculopathy | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metabolic encephalopathy | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neuropathy peripheral | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Syncope | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vascular encephalopathy | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

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|---|----------------------------------|--|--|
| Vertebrobasilar insufficiency alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | |
| Blood and lymphatic system disorders Neutropenia alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 68 (1.47%) 0 / 1 0 / 0 | | |
| Anaemia alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | |
| Pancytopenia alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | |
| Ear and labyrinth disorders Meniere's disease alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | |
| Vertigo alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 68 (1.47%) 0 / 1 0 / 0 | | |
| Eye disorders Optic ischaemic neuropathy | | | |

| | | | |
|--|----------------|--|--|
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Colitis ischaemic | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis erosive | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastric ulcer perforation | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diverticulum intestinal | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intussusception | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Chronic hepatitis | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | | |
|--|----------------|--|--|--|
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Drug-induced liver injury alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic cirrhosis alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatorenal failure alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal and urinary disorders | | | | |
| Neurogenic bladder alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nephrolithiasis alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute kidney injury alternative dictionary used: v25.0 25.0 | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tubulointerstitial nephritis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| Cushing's syndrome | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Goitre | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Fracture nonunion | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Foot deformity | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Costochondritis | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arthritis | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intervertebral disc disorder | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Synovial cyst | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rheumatoid arthritis | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Osteochondrosis | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | | |
|--|----------------------------------|--|--|--|
| Osteoarthritis alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | | |
| Musculoskeletal chest pain alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | | |
| Infections and infestations Arthritis bacterial alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | | |
| Acinetobacter sepsis alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | | |
| Abscess limb alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | | |
| Bursitis infective alternative dictionary used: v25.0 25.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 68 (0.00%) 0 / 0 0 / 0 | | | |
| COVID-19 alternative dictionary used: v25.0 25.0 | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chronic tonsillitis | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis staphylococcal | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| COVID-19 pneumonia | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint abscess | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatitis E | | | | |
| alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | | |
|--|----------------|--|--|--|
| Gastroenteritis alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulitis intestinal perforated alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulitis alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sinusitis alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Septic shock alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sepsis alternative dictionary used: v25.0 25.0 | | | | |

| | | | | |
|--|----------------|--|--|--|
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Postoperative wound infection alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post procedural cellulitis alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary tract infection alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Wound infection pseudomonas alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Wound infection staphylococcal alternative dictionary used: v25.0 25.0 | | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metabolism and nutrition disorders Hyperglycaemic hyperosmolar nonketotic syndrome alternative dictionary used: v25.0 25.0 | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 68 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | GSK3196165 90mg + MTX | GSK3196165 150mg + MTX | Tofacitinib 5mg + MTX |
|---|------------------------------|-------------------------------|------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 127 / 513 (24.76%) | 137 / 510 (26.86%) | 83 / 273 (30.40%) |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 23 / 513 (4.48%) | 31 / 510 (6.08%) | 12 / 273 (4.40%) |
| occurrences (all) | 29 | 36 | 15 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphopenia | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 30 / 513 (5.85%) | 35 / 510 (6.86%) | 16 / 273 (5.86%) |
| occurrences (all) | 54 | 50 | 20 |
| Musculoskeletal and connective tissue disorders | | | |
| Rheumatoid arthritis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| COVID-19 | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 43 / 513 (8.38%) | 48 / 510 (9.41%) | 29 / 273 (10.62%) |
| occurrences (all) | 44 | 48 | 29 |
| Latent tuberculosis | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 513 (0.00%) | 0 / 510 (0.00%) | 0 / 273 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 22 / 513 (4.29%) | 20 / 510 (3.92%) | 18 / 273 (6.59%) |
| occurrences (all) | 23 | 23 | 22 |
| Urinary tract infection | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 23 / 513 (4.48%) | 22 / 510 (4.31%) | 19 / 273 (6.96%) |
| occurrences (all) | 26 | 26 | 23 |

| Non-serious adverse events | Pooled Placebo | Placebo + MTX and GSK3196165 90mg + MTX | Placebo + MTX and GSK3196165 150mg + MTX |
|---|-----------------|---|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 22 / 80 (27.50%) | 29 / 82 (35.37%) |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 0 / 80 (0.00%) | 0 / 82 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 4 / 80 (5.00%) | 4 / 82 (4.88%) |
| occurrences (all) | 0 | 5 | 5 |
| Lymphopenia | | | |
| alternative dictionary used: v25.0 25.0 | | | |
| subjects affected / exposed | 0 / 241 (0.00%) | 2 / 80 (2.50%) | 2 / 82 (2.44%) |
| occurrences (all) | 0 | 2 | 3 |
| Musculoskeletal and connective tissue disorders | | | |
| Rheumatoid arthritis | | | |
| alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|---|--|---|--|
| subjects affected / exposed occurrences (all) | 0 / 241 (0.00%) 0 | 2 / 80 (2.50%) 2 | 8 / 82 (9.76%) 8 |
| Infections and infestations COVID-19 alternative dictionary used: v25.0 subjects affected / exposed occurrences (all) Latent tuberculosis alternative dictionary used: v25.0 subjects affected / exposed occurrences (all) Nasopharyngitis alternative dictionary used: v25.0 subjects affected / exposed occurrences (all) Upper respiratory tract infection alternative dictionary used: v25.0 subjects affected / exposed occurrences (all) Urinary tract infection alternative dictionary used: v25.0 subjects affected / exposed occurrences (all) | 0 / 241 (0.00%) 0 0 / 241 (0.00%) 0 0 / 241 (0.00%) 0 0 / 241 (0.00%) 0 0 / 241 (0.00%) 0 0 / 241 (0.00%) 0 | 6 / 80 (7.50%) 6 5 / 80 (6.25%) 5 0 / 80 (0.00%) 0 3 / 80 (3.75%) 4 4 / 80 (5.00%) 5 | 9 / 82 (10.98%) 9 3 / 82 (3.66%) 3 2 / 82 (2.44%) 2 4 / 82 (4.88%) 5 0 / 82 (0.00%) 0 |

| | | | |
|--|---|--|--|
| Non-serious adverse events | Placebo + MTX and Tofacitinib 5mg + MTX | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 17 / 68 (25.00%) | | |
| Investigations Alanine aminotransferase increased alternative dictionary used: v25.0 subjects affected / exposed occurrences (all) | 0 / 68 (0.00%) 0 | | |
| Blood and lymphatic system disorders Anaemia alternative dictionary used: v25.0 25.0 | | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>1 / 68 (1.47%)</p> <p>occurrences (all)</p> <p>1</p> <p>Lymphopenia</p> <p>alternative dictionary used: v25.0 25.0</p> <p>subjects affected / exposed</p> <p>4 / 68 (5.88%)</p> <p>occurrences (all)</p> <p>4</p> | | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Rheumatoid arthritis</p> <p>alternative dictionary used: v25.0 25.0</p> <p>subjects affected / exposed</p> <p>1 / 68 (1.47%)</p> <p>occurrences (all)</p> <p>1</p> | | | |
| <p>Infections and infestations</p> <p>COVID-19</p> <p>alternative dictionary used: v25.0 25.0</p> <p>subjects affected / exposed</p> <p>2 / 68 (2.94%)</p> <p>occurrences (all)</p> <p>3</p> <p>Latent tuberculosis</p> <p>alternative dictionary used: v25.0 25.0</p> <p>subjects affected / exposed</p> <p>1 / 68 (1.47%)</p> <p>occurrences (all)</p> <p>1</p> <p>Nasopharyngitis</p> <p>alternative dictionary used: v25.0 25.0</p> <p>subjects affected / exposed</p> <p>4 / 68 (5.88%)</p> <p>occurrences (all)</p> <p>4</p> <p>Upper respiratory tract infection</p> <p>alternative dictionary used: v25.0 25.0</p> <p>subjects affected / exposed</p> <p>5 / 68 (7.35%)</p> <p>occurrences (all)</p> <p>6</p> <p>Urinary tract infection</p> <p>alternative dictionary used: v25.0 25.0</p> <p>subjects affected / exposed</p> <p>2 / 68 (2.94%)</p> <p>occurrences (all)</p> <p>2</p> | | | |

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 detail revised risks, entry and stopping criteria following the update to comparator drug (tofacitinib) label. To introduce new medical device safety reporting wording, required in advance of roll out of pre-filled syringes to this study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported