# Clinical trial results:
# A randomized, multi-center, double blind (sponsor open), placebo-controlled study to assess the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of GSK3117391 in subjects with moderate to severe, active rheumatoid arthritis

## Summary

| | |
|---|---|
| EudraCT number | 2015-005800-27 |
| Trial protocol | PL |
| Global end of trial date | 14 November 2017 |

**Results information**

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 29 November 2018 |
| First version publication date | 29 November 2018 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 204957 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | GlaxoSmithKline |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, |
| 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 | 22 February 2018 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 14 November 2017 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

To assess the efficacy of GSK3117391, in participants with severe RA.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 27 December 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Poland: 1 |
| Country: Number of subjects enrolled | Romania: 2 |
| Worldwide total number of subjects | 3 |
| EEA total number of subjects | 3 |

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) | 2 |
| From 65 to 84 years | 1 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

This study was conducted in participants with severe, active rheumatoid arthritis receiving GSK3117391, 40 milligrams (mg) or placebo at one center in Poland and one in Romania.

### Pre-assignment

Screening details:

This study was terminated early by the sponsor following internal review. A total number of 26 participants were screened, of which three participants were enrolled in the study.

### 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 | Investigator, Carer, Subject |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo |

Arm description:

Eligible participants in this arm, received a matching placebo to the study drug GSK3117391, administered orally once a day as 2 capsules in the morning, following every other day, for 28-days.

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

Dosage and administration details:

Matching placebo, to the study drug, was administered, orally, as 2 capsules, in morning of every other day for 28 days.

| | |
|---|---|
| **Arm title** | GSK3117391, 40 mg |

Arm description:

Eligible participants in this arm, received a dose of 40 mg of GSK3117391, administered orally once a day as 2 capsules of 20 mg each in the morning, following every other day, for 28-days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | GSK3117391 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

The drug was administered, orally as 20 mg, as 2 capsules, in morning of every other day for 28 days.

| **Number of subjects in period 1** | Placebo | GSK3117391, 40 mg |
|---|---|---|
| Started | 2 | 1 |
| Completed | 1 | 1 |
| Not completed | 1 | 0 |
| Protocol-defined stop criteria reached | 1 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Eligible participants in this arm, received a matching placebo to the study drug GSK3117391, administered orally once a day as 2 capsules in the morning, following every other day, for 28-days. | |
| Reporting group title | GSK3117391, 40 mg |
| Reporting group description: | |
| Eligible participants in this arm, received a dose of 40 mg of GSK3117391, administered orally once a day as 2 capsules of 20 mg each in the morning, following every other day, for 28-days. | |

| Reporting group values | Placebo | GSK3117391, 40 mg | Total |
|---|---|---|---|
| Number of subjects | 2 | 1 | 3 |
| Age categorical<br>Units: Subjects | | | |
| Overall Participants | 2 | 1 | 3 |
| Age Continuous | | | |
| 99999 indicates that data could not be calculated since only one participant was analyzed | | | |
| Units: years<br>arithmetic mean<br>standard deviation | <br>58.5<br>± 14.85 | <br>46<br>± 99999 | <br><br>- |
| Sex: Female, Male<br>Units: Subjects | | | |
| Female<br>Male | 2<br>0 | 1<br>0 | 3<br>0 |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| White - White/Caucasian/European Heritage | 2 | 1 | 3 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Eligible participants in this arm, received a matching placebo to the study drug GSK3117391, administered orally once a day as 2 capsules in the morning, following every other day, for 28-days. | |
| Reporting group title | GSK3117391, 40 mg |
| Reporting group description: | |
| Eligible participants in this arm, received a dose of 40 mg of GSK3117391, administered orally once a day as 2 capsules of 20 mg each in the morning, following every other day, for 28-days. | |
| Subject analysis set title | GSK3339189 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| GSK3339189 is a metabolite of GSK3117391. Eligible participants in this arm, received a dose of 40 mg of GSK3117391, administered orally once a day as 2 capsules of 20 mg each in the morning, following every other day, for 28-days. | |

### Primary: Change from Baseline in Disease activity score for 28 different joints with (DAS28) C-reactive protein (CRP) at Day 28

| | |
|---|---|
| End point title | Change from Baseline in Disease activity score for 28 different joints with (DAS28) C-reactive protein (CRP) at Day 28[1] |
| End point description: | |
| The DAS28 score is a derived measurement with differential weighing given to each component as: Tender/Painful Joint Count (TJC28) and swollen joint count (SJC28) both scored 0-28 (higher scores indicate higher disease activity), CRP measured in milligrams per liter and Patient's Global Assessment of Arthritis (PtGA) (visual analogue scale with values from 0 [best] to 100 [worst]).The formula used to calculate DAS28 score was 0.56 multiplied by square root of TJC28 plus 0.28 multiplied by square root of SJC28 plus 0.36 log of (CRP plus 1) plus 0.014 multiplied by PtGA plus 0.96. DAS28 scores ranged from 0 (best) to 10 (worst). Baseline was defined at Day 1 (pre-dose). Change from Baseline was post-baseline value minus the value at Baseline. Safety Population consisted of all participants who received at least one dose of study medication. Individual participant data at Day 28 has been presented. 99999 indicates that data could not be calculated since only one participant was analyzed | |
| End point type | Primary |
| End point timeframe: | |
| Baseline (pre-dose, Day 1) and Day 28 | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis for this outcome measure was not performed.

| End point values | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[2] | 1[3] | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | -0.38 (± 99999) | -1.73 (± 99999) | | |

Notes:

[2] - Safety Population. Only those participants with data available at specified time point were analyzed

[3] - Safety Population. Only those participants with data available at specified time point were analyzed

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with serious adverse events (SAEs) and non-SAEs

| End point title | Number of participants with serious adverse events (SAEs) and non-SAEs |
|---|---|

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAE is defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability, is a congenital anomaly/ birth defect and other situations which involve medical or scientific judgment, and is associated with liver injury and impaired liver function.

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

End point timeframe:

Up to Day 44

| **End point values** | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2[4] | 1[5] | | |
| Units: Participants | | | | |
| Any non-SAE\| | 2 | 0 | | |
| Any SAE\| | 0 | 0 | | |

Notes:

[4] - Safety Population.

[5] - Safety Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with vital signs values of potential clinical importance (PCI)

| End point title | Number of participants with vital signs values of potential clinical importance (PCI) |
|---|---|

End point description:

Vital signs including systolic blood pressure (SBP), diastolic blood pressure (DBP), temperature and heart rate were measured in semi-supine position after 5 minutes rest. The PCI ranges for vitals were as follows; for SBP <85 or >160 millimeters of mercury (mmHg), for DBP <45 or >100 mmHg, for heart rate <40 or >110 beats per minute and for temperature <36 or >38 Celsius. The number of participants with vital signs of PCI have been presented.

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

End point timeframe:

Up to Day 44

| End point values | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2[6] | 1[7] | | |
| Units: Participants | | | | |
| SBP\| | 0 | 0 | | |
| DBP\| | 0 | 0 | | |
| Heart rate\| | 0 | 0 | | |
| Temperature\| | 0 | 0 | | |

Notes:

[6] - Safety Population.

[7] - Safety Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with abnormal electrocardiogram (ECG) findings

| End point title | Number of participants with abnormal electrocardiogram (ECG) findings |
|---|---|

End point description:

Twelve-lead ECGs were performed during the study using an automated ECG machine, after 5 minutes of rest. The number of participants with abnormal ECG findings were reported and categorized as clinically significant and not clinically significant. Any value for ECG parameters out of the following normal range was considered as clinically significant abnormality; for PR interval <110 or >220 milliseconds, for QRS interval <75 or >110 milliseconds and for QT corrected interval <450 milliseconds.

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

End point timeframe:

Up to Day 44

| End point values | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2[8] | 1[9] | | |
| Units: Participants | | | | |
| Abnormal-clinically significant\| | 0 | 0 | | |
| Abnormal-Not clinically significant\| | 1 | 0 | | |

Notes:

[8] - Safety Population.

[9] - Safety Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with values for clinical chemistry parameters of PCI

| End point title | Number of participants with values for clinical chemistry parameters of PCI |
|---|---|

End point description:

Blood samples were collected for analysis of clinical chemistry parameters. The PCI ranges were for Albumin <30 millimoles/Liter (mmol/L), Calcium (<2 or >2.75 mmol/L), Creatinine (>44.2 mmol/L),

Glucose (<3 or >9 mmol/L), Magnesium (<0.5 or >1.23 mmol/L), Phosphorus (<0.8 or > 1.6 mmol/L), Potassium (<3 or > 5.5 mmol/L), Sodium (<130 or 150 mmol/L), Total carbon-dioxide (<18 or > 32 mmol/L), Alanine aminotransferase (>= 2x Upper Limit of Normal [ULN]), Aspartate aminotransferase (>=2x ULN), alkaline phosphatase (>=2x ULN), and total bilirubin (>=1.5xULN). The number of participants with values for clinical chemistry parameters of PCI have been presented

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

End point timeframe:

Up to Day 44

| **End point values** | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2[10] | 1[11] | | |
| Units: Participants | 0 | 0 | | |

Notes:

[10] - Safety Population.

[11] - Safety Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with values for hematology parameters of PCI

| End point title | Number of participants with values for hematology parameters of PCI |
|---|---|

End point description:

Blood samples were collected for analysis of hematology parameters. PCI ranges were for platelets (< 50 or >550 × 10^9 cells/L), white blood cell count (<3 or >14 × 10^9 cells/L), hemoglobin (<90 or >180 g/L), hematocrit (if proportion of red blood cells in blood was <0.3 or >0.54), lymphocytes (<0.5 × 10^9 cells/L), neutrophils (<1.0 × 10^9 cells/L) and monocytes (<0.2 or 1.5 × 10^9 cells/L). The number of participants with values for hematology parameters of PCI have been presented.

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

End point timeframe:

Up to Day 44

| **End point values** | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2[12] | 1[13] | | |
| Units: Participants | 1 | 1 | | |

Notes:

[12] - Safety Population.

[13] - Safety Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with abnormal findings for urinalysis parameters

| End point title | Number of participants with abnormal findings for urinalysis |
|---|---|

| | |
|---|---|
| | parameters |

End point description:

Urine samples were collected for the analysis of specific gravity, potential of hydrogen (pH), glucose, protein, blood and ketones at specified time points. The number of participants with abnormal urinalysis findings have been presented.

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

End point timeframe:

Up to Day 44

| **End point values** | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2[14] | 1[15] | | |
| Units: Participants | 0 | 0 | | |

Notes:

[14] - Safety Population.

[15] - Safety Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants achieving American College of Rheumatology (ACR) 20 criteria

| End point title | Percentage of participants achieving American College of Rheumatology (ACR) 20 criteria |
|---|---|

End point description:

A participant was considered to be a responder according to the ACR20 criteria if the participant had at least 20% improvement in both the tender joint count and swollen joint count measures, and 20% improvement in at least 3 of the following 5 measures: patient and physician global assessments, pain, disability, and an acute-phase reactant. This analysis was planned but data was not collected , as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Up to Day 44

| **End point values** | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[16] | 0[17] | | |
| Units: Percentage of participants | | | | |

Notes:

[16] - Safety Population. Data was not collected and study was pre-maturely terminated

[17] - Safety Population. Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants achieving ACR 50, criteria

| End point title | Percentage of participants achieving ACR 50, criteria |
|---|---|

End point description:

A participant was considered to be a responder according to the ACR50 criteria if the participant had at least 50% improvement in both the tender joint count and swollen joint count measures, and 50% improvement in at least 3 of the following 5 measures: patient and physician global assessments, pain, disability, and an acute-phase reactant. This analysis was planned but data was not collected , as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Up to Day 44

| End point values | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[18] | 0[19] | | |
| Units: Percentage of participants | | | | |

Notes:

[18] - Safety Population. Data was not collected and study was pre-maturely terminated

[19] - Safety Population. Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants achieving ACR 70, criteria

| End point title | Percentage of participants achieving ACR 70, criteria |
|---|---|

End point description:

A participant was considered to be a responder according to the ACR70 criteria if the participant had at least 70% improvement in both the tender joint count and swollen joint count measures, and 70% improvement in at least 3 of the following 5 measures: patient and physician global assessments, pain, disability, and an acute-phase reactant. This analysis was planned but data was not collected , as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Up to Day 44

| End point values | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[20] | 0[21] | | |
| Units: Percentage of participants | | | | |

Notes:

[20] - Safety Population. Data was not collected and study was pre-maturely terminated

[21] - Safety Population. Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of swollen joints assessed using 28-joint counts

| End point title | Number of swollen joints assessed using 28-joint counts |
|---|---|

End point description:

The total number of joints ranging from 0 to 28 joints with a present swelling were assessed. The following 28 joints were taken into account for SJC28: Shoulder (2 joints), Knee (2), Elbow (2), Wrist (2), Fingers (Joints for proximal interphalangeal [PIP] and metacarpophalangeal [MCP]: 20). No missing observations were considered. Individual participant data has been presented. Only data available at specified visit with respect to the participant has been presented. 99999 indicates that data was not collected.

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

End point timeframe:

Days 1, 7, 14, 21, 28 and Follow-up (Day 44)

| End point values | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2[22] | 1[23] | | |
| Units: Number of swollen joints | | | | |
| Participant 1; Day 1; n=1,0\| | 7 | 99999 | | |
| Participant 1; Day 7; n=1,0\| | 2 | 99999 | | |
| Participant 1; Follow-up (Day 44); n=1,0\| | 1 | 99999 | | |
| Participant 2; Day 1; n=1,0\| | 8 | 99999 | | |
| Participant 2; Day 7; n=1,0\| | 7 | 99999 | | |
| Participant 2; Day 14; n=1,0\| | 4 | 99999 | | |
| Participant 2; Day 21; n=1,0\| | 1 | 99999 | | |
| Participant 2; Day 28; n=1,0\| | 1 | 99999 | | |
| Participant 2; Follow-up (Day 44); n=1,0\| | 1 | 99999 | | |
| Participant 3; Day 1;n=0,1 | 99999 | 28 | | |
| Participant 3; Day 7;n=0,1 | 99999 | 18 | | |
| Participant 3; Day 14;n=0,1\| | 99999 | 12 | | |
| Participant 3; Day 21;n=0,1\| | 99999 | 7 | | |
| Participant 3; Day 28;n=0,1\| | 99999 | 11 | | |
| Participant 3; Follow-up (Day 44);n=0,1\| | 99999 | 5 | | |

Notes:

[22] - Safety Population.

[23] - Safety Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of tender/painful joints assessed using 28-joint counts

| End point title | Number of tender/painful joints assessed using 28-joint counts |
|---|---|

End point description:

The total number of joints ranging from 0 to 28 joints with a present tenderness were assessed. The following 28 joints were taken into account for TJC28: Shoulder (2 joints), Knee (2), Elbow (2), Wrist (2), Fingers (PIP and MCP: 20). No missing observations were considered. Individual participant data

has been presented. Only data available at specified visit with respect to the participant has been presented. 99999 indicates that data was not collected.

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

End point timeframe:

Days 1, 7, 14, 21, 28 and Follow-up (Day 44)

| **End point values** | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2[24] | 1[25] | | |
| Units: Number of tender/painful joints | | | | |
| Participant 1; Day 1; n=1, 0\| | 12 | 99999 | | |
| Participant 1; Day 7; n=1, 0\| | 8 | 99999 | | |
| Participant 1; Follow-up (Day 44); n=1, 0\| | 1 | 99999 | | |
| Participant 2; Day 1; n=1, 0\| | 9 | 99999 | | |
| Participant 2; Day 7; n=1, 0\| | 7 | 99999 | | |
| Participant 2; Day 14; n=1, 0\| | 5 | 99999 | | |
| Participant 2; Day 21; n=1, 0\| | 7 | 99999 | | |
| Participant 2; Day 28; n=1, 0\| | 4 | 99999 | | |
| Participant 2; Follow-up (Day 44); n=1, 0\| | 1 | 99999 | | |
| Participant 3; Day 1; n=0,1\| | 99999 | 28 | | |
| Participant 3; Day 7; n=0,1\| | 99999 | 26 | | |
| Participant 3; Day 14; n=0,1\| | 99999 | 19 | | |
| Participant 3; Day 21; n=0,1\| | 99999 | 18 | | |
| Participant 3; Day 28; n=0,1\| | 99999 | 19 | | |
| Participant 3; Follow-up (Day 44); n=0,1\| | 99999 | 8 | | |

Notes:

[24] - Safety Population.

[25] - Safety Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in DAS28-CRP score over time

| End point title | Change from Baseline in DAS28-CRP score over time |
|---|---|

End point description:

The DAS28 score is a derived measurement with differential weighing given to each component as: TJC28 and SJC28 both scored 0-28 (higher scores indicate higher disease activity), CRP measured in milligrams per liter and PtGA (visual analogue scale with values from 0 [best] to 100 [worst]). The formula used to calculate DAS28 score was 0.56 multiplied by square root of TJC28 plus 0.28 multiplied by square root of SJC28 plus 0.36 log of (CRP plus 1) plus 0.014 multiplied by PtGA plus 0.96. DAS28 scores ranged from 0 (best) to 10 (worst). Baseline was defined at Day 1 (pre-dose). Change from Baseline was post-baseline value minus the value at Baseline. A Negative change from Baseline value indicated improvement. Only data available at specified visit with respect to the participant has been presented. 99999 indicates that data was not collected. 999999 indicates that data could not be calculated since only one participant was analyzed.

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

End point timeframe:

Baseline (pre-dose, Day 1) and Days 7, 14, 21, 28, Follow-up (Day 44)

| End point values | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2[26] | 1[27] | | |
| Units: Scores on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Participant 1; Day 7 ;n=1, 0\| | -0.48 (± 999999) | 99999 (± 99999) | | |
| Participant 1; Follow-up (Day 44) ;n=1, 0\| | -2.84 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Day 7 ;n=1, 0\| | -0.24 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Day 14 ;n=1, 0\| | -0.96 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Day 21 ;n=1, 0\| | -0.77 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Day 28 ;n=1, 0\| | -0.38 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Follow-up (Day 44) ;n=1, 0\| | -2.30 (± 999999) | 99999 (± 99999) | | |
| Participant 3; Day 7 ;n=0, 1\| | 99999 (± 99999) | -0.79 (± 999999) | | |
| Participant 3; Day 14 ;n=0, 1\| | 99999 (± 99999) | -1.35 (± 999999) | | |
| Participant 3; Day 21 ;n=0, 1\| | 99999 (± 99999) | -1.54 (± 999999) | | |
| Participant 3; Day 28 ;n=0, 1\| | 99999 (± 99999) | -1.73 (± 999999) | | |
| Participant 3; Follow-up (Day 44) ;n=0, 1\| | 99999 (± 99999) | -2.59 (± 999999) | | |

Notes:

[26] - Safety Population.

[27] - Safety Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Assessment of disease activity using patient’s global assessment of arthritis (PtGA)

| End point title | Assessment of disease activity using patient’s global assessment of arthritis (PtGA) |
|---|---|

End point description:

Participants completed the global assessment of disease activity using the PtGA item using visual analogue scale (VAS) ranging from “0” (none) to “100” (extremely active), respectively. Individual participant score has been presented. Only data available at specified visit with respect to the participant has been presented. 99999 indicates that data was not collected.

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

End point timeframe:

Days 1, 7, 14, 21, 28 and Follow-up (Day 44)

| End point values | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2[28] | 1[29] | | |
| Units: Scores on a Scale | | | | |
| Participant 1; Day 1; n=1, 0\| | 58 | 99999 | | |
| Participant 1; Day 7; n=1, 0\| | 73 | 99999 | | |
| Participant 1; Follow-up (Day 44); n=1, 0\| | 25 | 99999 | | |
| Participant 2; Day 1; n=1, 0\| | 87 | 99999 | | |
| Participant 2; Day 7; n=1, 0\| | 86 | 99999 | | |
| Participant 2; Day 14; n=1, 0\| | 71 | 99999 | | |
| Participant 2; Day 21; n=1, 0\| | 78 | 99999 | | |
| Participant 2; Day 28; n=1, 0\| | 96 | 99999 | | |
| Participant 2; Follow-up (Day 44); n=1, 0\| | 33 | 99999 | | |
| Participant 3; Day 1; n=0,1\| | 99999 | 100 | | |
| Participant 3; Day 7; n=0,1\| | 99999 | 82 | | |
| Participant 3; Day 14; n=0,1\| | 99999 | 79 | | |
| Participant 3; Day 21; n=0,1\| | 99999 | 74 | | |
| Participant 3; Day 28; n=0,1\| | 99999 | 72 | | |
| Participant 3; Follow-up (Day 44); n=0,1\| | 99999 | 62 | | |

Notes:

[28] - Safety Population.

[29] - Safety Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in CRP

| End point title | Change from Baseline in CRP |
|---|---|

End point description:

Blood samples were collected at indicated time points for the analysis of CRP. Change from Baseline, was defined as the post-baseline value minus the value at Baseline. Baseline was defined as the value from the Day 1 (pre-dose). Individual participant data has been presented. Only data available at specified visit with respect to the participant has been presented. 99999 indicates that data was not collected. 999999 indicates that data could not be calculated since only one participant was analyzed.

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

End point timeframe:

Baseline (pre-dose, Day 1) and Days 7, 14, 21, 28, Follow-up (Day 44)

| End point values | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2[30] | 1[31] | | |
| Units: Milligrams per liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Participant 1; Day 7; n=1, 0\| | 0.50 (± 999999) | 99999 (± 99999) | | |

| | | | | |
|---|---|---|---|---|
| Participant 1; Follow-up (Day 44); n=1, 0\| | -11.20 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Day 7; n=1, 0\| | 0.50 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Day 14; n=1, 0\| | -1.60 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Day 21; n=1, 0\| | 1.60 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Day 28; n=1, 0\| | 30.20 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Follow-up (Day 44); n=1, 0\| | 2.20 (± 999999) | 99999 (± 99999) | | |
| Participant 3; Day 7; n=0,1\| | 99999 (± 99999) | -14.00 (± 999999) | | |
| Participant 3; Day 14; n=0,1\| | 99999 (± 99999) | -3.10 (± 999999) | | |
| Participant 3; Day 21; n=0,1\| | 99999 (± 99999) | 23.40 (± 999999) | | |
| Participant 3; Day 28; n=0,1\| | 99999 (± 99999) | -22.40 (± 999999) | | |
| Participant 3; Follow-up (Day 44); n=0,1\| | 99999 (± 99999) | 26.70 (± 999999) | | |

Notes:

[30] - Safety Population.

[31] - Safety Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma concentrations of GSK3117391 and GSK3339189

| End point title | Plasma concentrations of GSK3117391 and GSK3339189[32] |
|---|---|

End point description:

Blood samples were planned to be collected for GSK3117391 and its acid metabolite GSK3339189, at the specified timepoints. The Pharmacokinetic (PK) Population was defined as participants in the Safety Population who received an active dose and for whom a PK sample was obtained and analyzed. This analysis was planned but was not performed as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 1) and 24 hours (Day 2) post-dose; pre-dose, 0.25, 0.5, 1, 4, and 8 hours (Day 3) post-dose; pre-dose (Day 7); pre-dose (Day 21); pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 27) and 24 hours post-dose

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: Statistical analysis for this outcome measure was not performed.

| **End point values** | GSK3117391, 40 mg | GSK3339189 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 0[33] | 0[34] | | |
| Units: Nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[33] - Data was not collected and study was pre-maturely terminated

[34] - Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum observed blood concentration (Cmax) of GSK3117391 and GSK3339189

| End point title | Maximum observed blood concentration (Cmax) of GSK3117391 and GSK3339189[35] |
|---|---|

End point description:

Cmax was defined as the maximum concentration of drug in the plasma. Blood samples were planned to be collected for GSK3117391 and its acid metabolite GSK3339189, at the specified time points. This analysis was planned but was not performed as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 1) and 24 hours (Day 2) post-dose; pre-dose, 0.25, 0.5, 1, 4, and 8 hours (Day 3) post-dose; pre-dose (Day 7); pre-dose (Day 21); pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 27) and 24 hours post-dose

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: Statistical analysis for this outcome measure was not performed.

| End point values | GSK3117391, 40 mg | GSK3339189 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 0[36] | 0[37] | | |
| Units: Nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[36] - Data was not collected and study was pre-maturely terminated

[37] - Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Cmax (tmax)of GSK3117391 and GSK3339189

| End point title | Time to Cmax (tmax)of GSK3117391 and GSK3339189[38] |
|---|---|

End point description:

Tmax was defined as time required to achieve Cmax for drug, in the plasma. Blood samples were planned to be collected for GSK3117391 and its acid metabolite GSK3339189, at the specified timepoints. This analysis was planned but was not performed as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 1) and 24 hours (Day 2) post-dose; pre-dose, 0.25, 0.5, 1, 4, and 8 hours (Day 3) post-dose; pre-dose (Day 7); pre-dose (Day 21); pre-dose, 0.25 hour, 0.5, 1, 2, 4, 6, 10 hours (Day 27) and 24 hours post-dose

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: Statistical analysis for this outcome measure was not performed.

| **End point values** | GSK3117391, 40 mg | GSK3339189 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 0[39] | 0[40] | | |
| Units: Hours | | | | |
| median (full range (min-max)) | ( to ) | ( to ) | | |

Notes:

[39] - Data was not collected and study was pre-maturely terminated

[40] - Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

## Secondary: Area under the plasma concentration-time curve from time zero to time of last quantifiable concentration (AUC[0-t]) of GSK3117391 and GSK3339189

| End point title | Area under the plasma concentration-time curve from time zero to time of last quantifiable concentration (AUC[0-t]) of GSK3117391 and GSK3339189[41] |
|---|---|

End point description:

Blood samples were planned to be collected for GSK3117391, and its acid metabolite GSK3339189, at the specified time points. This analysis was planned but was not performed as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 1) and 24 hours (Day 2) post-dose; pre-dose, 0.25, 0.5, 1, 4, and 8 hours (Day 3) post-dose; pre-dose (Day 7); pre-dose (Day 21); pre-dose, 0.25 hour, 0.5, 1, 2, 4, 6, 10 hours (Day 27) and 24 hours post-dose

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: Statistical analysis for this outcome measure was not performed.

| **End point values** | GSK3117391, 40 mg | GSK3339189 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 0[42] | 0[43] | | |
| Units: Hours* Nanogram per Milliliter | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[42] - Data was not collected and study was pre-maturely terminated

[43] - Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

## Secondary: AUC from time zero to the time of next dosing (AUC[0- tau]) of

### GSK3117391 and GSK3339189

| End point title | AUC from time zero to the time of next dosing (AUC[0- tau]) of GSK3117391 and GSK3339189[44] |
|---|---|

End point description:

Blood samples were planned to be collected for GSK3117391 and its acid metabolite GSK3339189, at the specified timepoints. This analysis was planned but was not performed as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 1) and 24 hours (Day 2) post-dose; pre-dose, 0.25, 0.5, 1, 4, and 8 hours (Day 3) post-dose; pre-dose (Day 7); pre-dose (Day 21); pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 27) and 24 hours post-dose

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: Statistical analysis for this outcome measure was not performed.

| End point values | GSK3117391, 40 mg | GSK3339189 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 0[45] | 0[46] | | |
| Units: Hours* Nanogram per Milliliter | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[45] - Data was not collected and study was pre-maturely terminated

[46] - Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

### Secondary: AUC from time zero to infinity (AUC[0-infinity]) of GSK3117391 and GSK3339189

| End point title | AUC from time zero to infinity (AUC[0-infinity]) of GSK3117391 and GSK3339189[47] |
|---|---|

End point description:

Blood samples were planned to be collected for GSK3117391 and its acid metabolite GSK3339189, at the specified timepoints. This analysis was planned but was not performed as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 1) and 24 hours (Day 2) post-dose; pre-dose, 0.25, 0.5, 1, 4, and 8 hours (Day 3) post-dose; pre-dose (Day 7); pre-dose (Day 21); pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 27) and 24 hours post-dose

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: Statistical analysis for this outcome measure was not performed.

| End point values | GSK3117391, 40 mg | GSK3339189 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 0[48] | 0[49] | | |
| Units: Hours* Nanogram per Milliliter | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[48] - Data was not collected and study was pre-maturely terminated

[49] - Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

## Secondary: Apparent terminal phase half-life (t1/2) of GSK3117391 and GSK3339189

| End point title | Apparent terminal phase half-life (t1/2) of GSK3117391 and GSK3339189[50] |
|---|---|

End point description:

Blood samples were planned to be collected for GSK3117391 and its acid metabolite GSK3339189, at the specified timepoints. This analysis was planned but was not performed as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 1) and 24 hours (Day 2) post-dose; pre-dose, 0.25, 0.5, 1, 4, and 8 hours (Day 3) post-dose; pre-dose (Day 7); pre-dose (Day 21); pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 27) and 24 hours post-dose

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: Statistical analysis for this outcome measure was not performed.

| End point values | GSK3117391, 40 mg | GSK3339189 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 0[51] | 0[52] | | |
| Units: Hour | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[51] - Data was not collected and study was pre-maturely terminated

[52] - Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

## Secondary: Trough concentration (Ctau) of GSK3117391 and GSK3339189

| End point title | Trough concentration (Ctau) of GSK3117391 and |
|---|---|

End point description:

Blood samples were planned to be collected for GSK3117391 and its acid metabolite GSK3339189, at the specified timepoints. This analysis was planned but was not performed as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 1) and 24 hours (Day 2) post-dose; pre-dose, 0.25, 0.5, 1, 4, and 8 hours (Day 3) post-dose; pre-dose (Day 7); pre-dose (Day 21); pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 27) and 24 hours post-dose

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: Statistical analysis for this outcome measure was not performed.

| **End point values** | GSK3117391, 40 mg | GSK3339189 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 0[54] | 0[55] | | |
| Units: Nanogram per milliliter | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[54] - Data was not collected and study was pre-maturely terminated

[55] - Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

## Secondary: Observed accumulation ratio (Ro) of GSK3117391 and GSK3339189

| End point title | Observed accumulation ratio (Ro) of GSK3117391 and GSK3339189[56] |
|---|---|

End point description:

Blood samples were planned to be collected for GSK3117391, and its acid metabolite GSK3339189, at the specified timepoints. Accumulation ratio was planned to be determined from the ratio of AUC from time zero to time of next dosing (AUC [0-tau]) following single dose administration /AUC (0-tau) on repeat dose administration. This analysis was planned but was not performed as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 1) and 24 hours (Day 2) post-dose; pre-dose, 0.25, 0.5, 1, 4, and 8 hours (Day 3) post-dose; pre-dose (Day 7); pre-dose (Day 21); pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 27) and 24 hours post-dose

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: Statistical analysis for this outcome measure was not performed.

| **End point values** | GSK3117391, 40 mg | GSK3339189 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 0[57] | 0[58] | | |
| Units: Ratio of AUC | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[57] - Data was not collected and study was pre-maturely terminated

[58] - Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

## Secondary: Apparent total clearance (CL/F) of GSK3117391 and GSK3339189

| End point title | Apparent total clearance (CL/F) of GSK3117391 and GSK3339189[59] |
|---|---|

End point description:

CL/F, describes the removal of drug from a volume of plasma in a given unit of time (drug loss from the body). Blood samples, were planned to be collected for GSK3117391, and its acid metabolite GSK3339189, at the specified timepoints. This analysis was planned but was not performed as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 1) and 24 hours (Day 2) post-dose; pre-dose, 0.25, 0.5, 1, 4, and 8 hours (Day 3) post-dose; pre-dose (Day 7); pre-dose (Day 21); pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 27) and 24 hours post-dose

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: Statistical analysis for this outcome measure was not performed.

| End point values | GSK3117391, 40 mg | GSK3339189 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 0[60] | 0[61] | | |
| Units: Milliliter per day | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[60] - Data was not collected and study was pre-maturely terminated

[61] - Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

## Secondary: Apparent Volume of Distribution (V/F) of GSK3117391 and GSK3339189

| End point title | Apparent Volume of Distribution (V/F) of GSK3117391 and GSK3339189[62] |
|---|---|

End point description:

V/F, is defined as the theoretical volume that would be necessary to contain the total amount of an administered drug at the same concentration that it is observed in the blood plasma. Blood samples, were planned to be collected for GSK3117391, at the specified timepoints. This analysis was planned but was not performed as the sample size was too small and study was terminated pre-maturely, by the sponsor following internal review.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 1) and 24 hours (Day 2) post-dose; pre-dose, 0.25, 0.5, 1, 4, and 8 hours (Day 3) post-dose; pre-dose (Day 7); pre-dose (Day 21); pre-dose, 0.25, 0.5, 1, 2, 4, 6, 10 hours (Day 27) and 24 hours post-dose

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: Statistical analysis for this outcome measure was not performed.

| End point values | GSK3117391, 40 mg | GSK3339189 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 0[63] | 0[64] | | |
| Units: Liters | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[63] - Data was not collected and study was pre-maturely terminated

[64] - Data was not collected and study was pre-maturely terminated

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in monocyte count

| End point title | Change from Baseline in monocyte count |
|---|---|

End point description:

Blood samples were collected at the indicated time points for the analysis of monocytes. Change from Baseline was defined as the post-Baseline value minus the value at Baseline. Baseline was defined as the value from the Day 1 (pre-dose). Individual participant data has been presented. Only data available at specified visit with respect to the participant has been presented. 99999 indicates that data was not collected. 999999 indicates that data could not be calculated since only one participant was analyzed.

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

End point timeframe:

Baseline (pre-dose, Day 1); 1, 4, 6, 10 Hours on Day 1; Day 2 (24 Hours); Pre-dose, 1, 4, 8 Hours on Day 3; Pre-dose on Day 7; Day 14; Pre-dose on Day 21; Pre-dose, 1, 4, 6, 10 Hours on Day 27; Day 28 (24 Hours); Day 30 (72 Hours) and Day 44 (Follow-up)

| End point values | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2[65] | 1[66] | | |
| Units: Giga cells per liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Participant 1; Day 1; 1 Hour; n=0,1 | -0.11 (± 999999) | 99999 (± 99999) | | |
| Participant 1;Day 1; 4 Hours; n=0,1 | -0.04 (± 999999) | 99999 (± 99999) | | |
| Participant 1;Day 1; 6 Hours; n=0,1 | -0.34 (± 999999) | 99999 (± 99999) | | |
| Participant 1;Day 1; 10 Hours; n=0,1 | -0.13 (± 999999) | 99999 (± 99999) | | |
| Participant 1;Day 3; Pre-dose; n=1,0\| | -0.68 (± 999999) | 99999 (± 99999) | | |
| Participant 1;Day 3; 1 Hour; n=0,1 | -0.59 (± 999999) | 99999 (± 99999) | | |
| Participant 1; Day 3; 4 Hours; n=0,1 | -0.56 (± 999999) | 99999 (± 99999) | | |
| Participant 1; Day 3; 8 Hours; n=0,1 | -0.02 (± 999999) | 99999 (± 99999) | | |
| Participant 1;Day 7; Pre-dose; n=0,1 | -0.25 (± 999999) | 99999 (± 99999) | | |
| Participant 1;Follow-up (Day 44); n=0,1 | 0.10 (± 999999) | 99999 (± 99999) | | |

| | | | | |
|---|---|---|---|---|
| Participant 2; Day 1; 1 Hour; n=0,1 | 0.25 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 1; 4 Hours; n=0,1 | 0.27 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 1; 6 Hours; n=0,1 | 0.24 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 1; 10 Hours; n=0,1 | 0.31 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 2; 24 Hours; n=0,1 | 0.05 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 3; Pre-dose; n=0,1 | 0.27 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 3; 1 Hour; n=0,1 | 0.27 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Day 3; 4 Hours; n=0,1 | 0.24 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Day 3; 8 Hours; n=0,1 | 0.05 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 7; Pre-dose; n=0,1 | 0.23 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 14; n=0,1 | 0.02 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 21; Pre-dose; n=0,1 | 0.12 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 27; Pre-dose; n=0,1 | 0.02 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 27; 1 Hour; n=0,1 | 0.23 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 27; 4 Hours; n=0,1 | 0.02 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 27; 6 Hours; n=0,1 | -0.28 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 27; 10 Hours; n=1,0\| | 0.28 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 28; 24 Hours; n=0,1 | 0.30 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Day 30; 72 Hours; n=0,1 | 0.02 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Follow-up (Day 44); n=0,1 | 0.09 (± 999999) | 99999 (± 99999) | | |
| Participant 3; Day 1; 1 Hour; n=1,0 | 99999 (± 99999) | -0.84 (± 999999) | | |
| Participant 3;Day 1; 4 Hours; n=1,0 | 99999 (± 99999) | -0.14 (± 999999) | | |
| Participant 3;Day 1; 6 Hours; n=1,0 | 99999 (± 99999) | 0.29 (± 999999) | | |
| Participant 3;Day 1; 10 Hours; n=1,0 | 99999 (± 99999) | 0.30 (± 999999) | | |
| Participant 3;Day 2; 24 Hours; n=1,0 | 99999 (± 99999) | 0.29 (± 999999) | | |
| Participant 3;Day 3; Pre-dose; n=1,0 | 99999 (± 99999) | -0.96 (± 999999) | | |
| Participant 3;Day 3; 1 Hour; n=1,0 | 99999 (± 99999) | -0.77 (± 999999) | | |
| Participant 3; Day 3; 8 Hours; n=1,0 | 99999 (± 99999) | -0.90 (± 999999) | | |
| Participant 3;Day 7; Pre-dose; n=1,0 | 99999 (± 99999) | -0.79 (± 999999) | | |
| Participant 3;Day 14; n=1,0 | 99999 (± 99999) | -1.11 (± 999999) | | |
| Participant 3;Day 21; Pre-dose; n=1,0 | 99999 (± 99999) | -0.91 (± 999999) | | |

| | | | | |
|---|---|---|---|---|
| Participant 3;Day 27; Pre-dose; n=1,0 | 99999 (± 99999) | 0.10 (± 999999) | | |
| Participant 3;Day 27; 1 Hour; n=1,0 | 99999 (± 99999) | -0.99 (± 999999) | | |
| Participant 3;Day 27; 4 Hours; n=1,0 | 99999 (± 99999) | -0.97 (± 999999) | | |
| Participant 3;Day 27; 6 Hours; n=1,0 | 99999 (± 99999) | -0.14 (± 999999) | | |
| Participant 3;Day 27; 10 Hours; n=1,0 | 99999 (± 99999) | -1.06 (± 999999) | | |
| Participant 3;Day 28; 24 Hours; n=1,0 | 99999 (± 99999) | -0.94 (± 999999) | | |
| Participant 3; Day 30; 72 Hours; n=1,0 | 99999 (± 99999) | -0.91 (± 999999) | | |
| Participant 3; Follow-up (Day 44); n=1,0 | 99999 (± 99999) | -0.70 (± 999999) | | |

Notes:

[65] - Safety Population.

[66] - Safety Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Changes from Baseline in soluble cytokine

| End point title | Changes from Baseline in soluble cytokine |
|---|---|

End point description:

Change from Baseline, was defined as the post-Baseline value minus the value at Baseline. Baseline was defined as the value from the Day 1 (pre-dose). Blood samples were planned to be analyzed by flow cytometry for cell markers to determine any changes after treatment with GSK3117391. This analysis was planned but the assay was not performed due to sample size being too small at the time of early study termination.

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

End point timeframe:

Baseline (pre-dose, Day 1) and up to 44 Days

| **End point values** | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[67] | 0[68] | | |
| Units: Picogram per milliliter | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[67] - Safety Population. Data was not collected due to small sample size during early study termination.

[68] - Safety Population. Data was not collected due to small sample size during early study termination.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Changes from Baseline in Myeloid-related protein 8/14 (MRP8/14)

| End point title | Changes from Baseline in Myeloid-related protein 8/14 (MRP8/14) |
|---|---|

End point description:

Blood samples were collected at the indicated time points and analyzed by flow cytometry for cell markers to determine any changes after treatment with GSK3117391. Change from Baseline was defined as the post-Baseline value minus the value at Baseline. Baseline was defined as the value from the Day 1 (pre-dose). Individual participant data has been presented. Only data available at specified visit with respect to the participant has been presented. 99999 indicates that data was not collected. 999999 indicates that data could not be calculated since only one participant was analyzed.

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

End point timeframe:

Baseline (pre-dose, Day 1); 1, 4, 10 Hours on Day 1; Day 2 (24 Hours); Pre-dose, 8 Hours on Day 3; Pre-dose on Day 7; Day 14; Pre-dose on Day 21; Pre-dose on Day 27; Day 28 (24 Hours) and Day 44 (Follow-up)

| **End point values** | Placebo | GSK3117391, 40 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2[69] | 1[70] | | |
| Units: Milligram per liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Participant 1; Day 1; 1 Hour; n=1,0\| | -0.36 (± 999999) | 99999 (± 99999) | | |
| Participant 1;Day 1; 4 Hours; n=1,0\| | -0.57 (± 999999) | 99999 (± 99999) | | |
| Participant 1;Day 1; 10 Hours; n=1,0\| | -0.46 (± 999999) | 99999 (± 99999) | | |
| Participant 1;Day 2; 24 Hours; n=1,0\| | -0.52 (± 999999) | 99999 (± 99999) | | |
| Participant 1;Day 3; Pre-dose; n=1,0\| | -0.21 (± 999999) | 99999 (± 99999) | | |
| Participant 1; Day 3; 8 Hours; n=1,0\| | -0.21 (± 999999) | 99999 (± 99999) | | |
| Participant 1;Day 7; Pre-dose; n=1,0\| | -0.39 (± 999999) | 99999 (± 99999) | | |
| Participant 1; Follow-up (Day 44); n=1,0\| | -1.22 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Day 1; 1 Hour; n=1,0\| | 0.27 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 1; 4 Hours; n=1,0\| | -1.13 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 1; 10 Hours; n=1,0\| | 0.37 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 2; 24 Hours;n=1,0\| | -2.34 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 3; Pre-dose; n=1,0\| | 0.20 (± 999999) | 99999 (± 99999) | | |
| Participant 2; Day 3; 8 Hours;n=1,0\| | -0.31 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 7; Pre-dose; n=1,0\| | 2.29 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 14;n=1,0\| | 3.76 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 21; Pre-dose; n=1,0\| | -0.78 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 27; Pre-dose; n=1,0\| | 0.67 (± 999999) | 99999 (± 99999) | | |
| Participant 2;Day 28; 24 Hours; n=1,0\| | -2.51 (± 999999) | 99999 (± 99999) | | |

| | | | | |
|---|---|---|---|---|
| Participant 2;Follow-up (Day 44); n=1,0\| | -1.43 (± 999999) | 99999 (± 99999) | | |
| Participant 3; Day 1; 1 Hour; n=0,1\| | 99999 (± 99999) | -0.53 (± 999999) | | |
| Participant 3;Day 1; 4 Hours; n=0,1\| | 99999 (± 99999) | 0.32 (± 999999) | | |
| Participant 3;Day 1; 10 Hours; n=0,1\| | 99999 (± 99999) | 0.89 (± 999999) | | |
| Participant 3;Day 2; 24 Hours; n=0,1\| | 99999 (± 99999) | 0.64 (± 999999) | | |
| Participant 3;Day 3; Pre-dose; n=0,1\| | 99999 (± 99999) | 2.95 (± 999999) | | |
| Participant 3; Day 3; 8 Hours; n=0,1\| | 99999 (± 99999) | 7.06 (± 999999) | | |
| Participant 3;Day 7; Pre-dose; n=0,1\| | 99999 (± 99999) | 5.21 (± 999999) | | |
| Participant 3;Day 14; n=0,1\| | 99999 (± 99999) | 4.14 (± 999999) | | |
| Participant 3;Day 21; Pre-dose; n=0,1\| | 99999 (± 99999) | 5.90 (± 999999) | | |
| Participant 3;Day 27; Pre-dose; n=0,1\| | 99999 (± 99999) | 1.41 (± 999999) | | |
| Participant 3;Day 28; 24 Hours; n=0,1\| | 99999 (± 99999) | -1.85 (± 999999) | | |
| Participant 3;Follow-up (Day 44); n=0,1\| | 99999 (± 99999) | -0.71 (± 999999) | | |

Notes:

[69] - Safety Population.

[70] - Safety Population.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All non-SAEs and SAEs were collected from start of the study treatment (Day 1) up to Day 44.

Adverse event reporting additional description:

The Safety Population was used to assess the non-SAEs and SAEs.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 20.1 |

### Reporting groups

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

Reporting group description:

Eligible participants in this arm, received a matching placebo to the study drug GSK3117391, administered orally once a day as 2 capsules in the morning, following every other day, for 28-days.

| | |
|---|---|
| Reporting group title | GSK3117391, 40 mg |

Reporting group description:

Eligible participants in this arm, received a dose of 40 mg of GSK3117391, administered orally once a day as 2 capsules of 20 mg each in the morning, following every other day, for 28-days.

| Serious adverse events | Placebo | GSK3117391, 40 mg | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Placebo | GSK3117391, 40 mg | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 2 (100.00%) | 0 / 1 (0.00%) | |
| Blood and lymphatic system disorders | | | |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Rheumatoid arthritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 1 / 2 (50.00%)<br>1 | 0 / 1 (0.00%)<br>0 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 15 September 2016 | Amendment 01: The changes in this amendment are to address typographical errors and inconsistency<br>between the Time and Events tables and the protocol text, particularly with respect to lab parameters (Methemoglobin [MetHb]), coagulation, requirement for clinical chemistry/urinalysis at day 7, 14 and 21 and pharmacodynamic [PD] biomarkers) |
| 08 December 2016 | Amendment 02: The changes in this amendment are to combine the Internal Safety review committee (iSRC) and Data Review Committee (DRC) interim review committees, in addition to changes for clarification between the Time and Events table and the text of the protocol. |
| 01 June 2017 | Amendment 03: This amendment, has been created to provide clarity regarding extension to the screening window for the washout of background Disease-Modifying Anti-Rheumatic Drug (DMARDs), ensuring blinding of the monocyte count during the study conduct, and other study requirements throughout the protocol. In addition, further detail has been added to some of the inclusion/exclusion criteria and assessment requirements for clarification. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported