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	v2 (current)
This version publication date	11 April 2019
First version publication date	29 November 2018
Version creation reason	

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	Subject, Investigator, Carer

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 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			
arithmetic mean	58.5	46	
standard deviation	± 14.85	± 99999	-
Sex: Female, Male Units: Subjects			
Female	2	1	3
Male	0	0	0
Race/Ethnicity, Customized 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				
number (not applicable)	-0.38	-1.73		

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: 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: 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				
number (not applicable)				
Participant 1; Day 7 ;n=1, 0|	-0.48	99999		
Participant 1; Follow-up (Day 44) ;n=1, 0|	-2.84	99999		
Participant 2; Day 7 ;n=1, 0|	-0.24	99999		
Participant 2; Day 14 ;n=1, 0|	-0.96	99999		
Participant 2; Day 21 ;n=1, 0|	-0.77	99999		
Participant 2; Day 28 ;n=1, 0|	-0.38	99999		
Participant 2; Follow-up (Day 44) ;n=1, 0|	-2.30	99999		
Participant 3; Day 7 ;n=0, 1|	99999	-0.79		
Participant 3; Day 14 ;n=0, 1|	99999	-1.35		
Participant 3; Day 21 ;n=0, 1|	99999	-1.54		
Participant 3; Day 28 ;n=0, 1|	99999	-1.73		
Participant 3; Follow-up (Day 44) ;n=0, 1|	99999	-2.59		

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				
number (not applicable)				
Participant 1; Day 7; n=1, 0|	0.50	99999		
Participant 1; Follow-up (Day 44); n=1, 0|	-11.20	99999		

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

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				
number (not applicable)				
Participant 1; Day 1; 1 Hour; n=0,1	-0.11	99999		
Participant 1;Day 1; 4 Hours; n=0,1	-0.04	99999		
Participant 1;Day 1; 6 Hours; n=0,1	-0.34	99999		
Participant 1;Day 1; 10 Hours; n=0,1	-0.13	99999		
Participant 1;Day 3; Pre-dose; n=1,0|	-0.68	99999		
Participant 1;Day 3; 1 Hour; n=0,1	-0.59	99999		
Participant 1; Day 3; 4 Hours; n=0,1	-0.56	99999		
Participant 1; Day 3; 8 Hours; n=0,1	-0.02	99999		
Participant 1;Day 7; Pre-dose; n=0,1	-0.25	99999		
Participant 1;Follow-up (Day 44); n=0,1	0.10	99999		
Participant 2; Day 1; 1 Hour; n=0,1	0.25	99999		
Participant 2;Day 1; 4 Hours; n=0,1	0.27	99999		
Participant 2;Day 1; 6 Hours; n=0,1	0.24	99999		
Participant 2;Day 1; 10 Hours; n=0,1	0.31	99999		
Participant 2;Day 2; 24 Hours; n=0,1	0.05	99999		
Participant 2;Day 3; Pre-dose; n=0,1	0.27	99999		
Participant 2;Day 3; 1 Hour; n=0,1	0.27	99999		
Participant 2; Day 3; 4 Hours; n=0,1	0.24	99999		
Participant 2; Day 3; 8 Hours; n=0,1	0.05	99999		
Participant 2;Day 7; Pre-dose; n=0,1	0.23	99999		

Participant 2;Day 14; n=0,1	0.02	99999		
Participant 2;Day 21; Pre-dose; n=0,1	0.12	99999		
Participant 2;Day 27; Pre-dose; n=0,1	0.02	99999		
Participant 2;Day 27; 1 Hour; n=0,1	0.23	99999		
Participant 2;Day 27; 4 Hours; n=0,1	0.02	99999		
Participant 2;Day 27; 6 Hours; n=0,1	-0.28	99999		
Participant 2;Day 27; 10 Hours; n=1,0|	0.28	99999		
Participant 2;Day 28; 24 Hours; n=0,1	0.30	99999		
Participant 2; Day 30; 72 Hours; n=0,1	0.02	99999		
Participant 2; Follow-up (Day 44); n=0,1	0.09	99999		
Participant 3; Day 1; 1 Hour; n=1,0	99999	-0.84		
Participant 3;Day 1; 4 Hours; n=1,0	99999	-0.14		
Participant 3;Day 1; 6 Hours; n=1,0	99999	0.29		
Participant 3;Day 1; 10 Hours; n=1,0	99999	0.30		
Participant 3;Day 2; 24 Hours; n=1,0	99999	0.29		
Participant 3;Day 3; Pre-dose; n=1,0	99999	-0.96		
Participant 3;Day 3; 1 Hour; n=1,0	99999	-0.77		
Participant 3; Day 3; 8 Hours; n=1,0	99999	-0.90		
Participant 3;Day 7; Pre-dose; n=1,0	99999	-0.79		
Participant 3;Day 14; n=1,0	99999	-1.11		
Participant 3;Day 21; Pre-dose; n=1,0	99999	-0.91		
Participant 3;Day 27; Pre-dose; n=1,0	99999	0.10		
Participant 3;Day 27; 1 Hour; n=1,0	99999	-0.99		
Participant 3;Day 27; 4 Hours; n=1,0	99999	-0.97		
Participant 3;Day 27; 6 Hours; n=1,0	99999	-0.14		
Participant 3;Day 27; 10 Hours; n=1,0	99999	-1.06		
Participant 3;Day 28; 24 Hours; n=1,0	99999	-0.94		
Participant 3; Day 30; 72 Hours; n=1,0	99999	-0.91		
Participant 3; Follow-up (Day 44); n=1,0	99999	-0.70		

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				
number (not applicable)				
Participant 1; Day 1; 1 Hour; n=1,0|	-0.36	99999		
Participant 1;Day 1; 4 Hours; n=1,0|	-0.57	99999		
Participant 1;Day 1; 10 Hours; n=1,0|	-0.46	99999		
Participant 1;Day 2; 24 Hours; n=1,0|	-0.52	99999		
Participant 1;Day 3; Pre-dose; n=1,0|	-0.21	99999		
Participant 1; Day 3; 8 Hours; n=1,0|	-0.21	99999		
Participant 1;Day 7; Pre-dose; n=1,0|	-0.39	99999		
Participant 1; Follow-up (Day 44); n=1,0|	-1.22	99999		
Participant 2; Day 1; 1 Hour; n=1,0|	0.27	99999		
Participant 2;Day 1; 4 Hours; n=1,0|	-1.13	99999		
Participant 2;Day 1; 10 Hours; n=1,0|	0.37	99999		
Participant 2;Day 2; 24 Hours;n=1,0|	-2.34	99999		
Participant 2;Day 3; Pre-dose; n=1,0|	0.20	99999		
Participant 2; Day 3; 8 Hours;n=1,0|	-0.31	99999		

Participant 2;Day 7; Pre-dose; n=1,0|	2.29	99999		
Participant 2;Day 14;n=1,0|	3.76	99999		
Participant 2;Day 21; Pre-dose; n=1,0|	-0.78	99999		
Participant 2;Day 27; Pre-dose; n=1,0|	0.67	99999		
Participant 2;Day 28; 24 Hours; n=1,0|	-2.51	99999		
Participant 2;Follow-up (Day 44); n=1,0|	-1.43	99999		
Participant 3; Day 1; 1 Hour; n=0,1|	99999	-0.53		
Participant 3;Day 1; 4 Hours; n=0,1|	99999	0.32		
Participant 3;Day 1; 10 Hours; n=0,1|	99999	0.89		
Participant 3;Day 2; 24 Hours; n=0,1|	99999	0.64		
Participant 3;Day 3; Pre-dose; n=0,1|	99999	2.95		
Participant 3; Day 3; 8 Hours; n=0,1|	99999	7.06		
Participant 3;Day 7; Pre-dose; n=0,1|	99999	5.21		
Participant 3;Day 14; n=0,1|	99999	4.14		
Participant 3;Day 21; Pre-dose; n=0,1|	99999	5.90		
Participant 3;Day 27; Pre-dose; n=0,1|	99999	1.41		
Participant 3;Day 28; 24 Hours; n=0,1|	99999	-1.85		
Participant 3;Follow-up (Day 44); n=0,1|	99999	-0.71		

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 occurrences (all)	1 / 2 (50.00%) 1	0 / 1 (0.00%) 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 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