Clinical trial results:
A multicentre, randomised, double-blind (sponsor-unblinded), placebo-controlled study to investigate the safety and tolerability, pharmacokinetics, pharmacodynamics, and efficacy of GSK2982772 in subjects with moderate to severe rheumatoid arthritis

Summary

EudraCT number	2016-000912-13
Trial protocol	DE ES PL GB
Global end of trial date	22 October 2018

Results information

Result version number	v1 (current)
This version publication date	28 October 2019
First version publication date	28 October 2019

Trial information

Trial identification

Sponsor protocol code	203168

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 February 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the safety and tolerability of GSK2982772 in subjects with moderate to severe Rheumatoid Arthritis

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 October 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	Germany: 7
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Poland: 26
Country: Number of subjects enrolled	Russian Federation: 9
Country: Number of subjects enrolled	Spain: 7
Worldwide total number of subjects	52
EEA total number of subjects	43

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)	45
From 65 to 84 years	7

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study evaluated safety, pharmacokinetics (PK), pharmacodynamics (PD), and efficacy of GSK2982772 in participants with rheumatoid arthritis (RA). Participants were randomly assigned to receive either GSK2982772 60 milligram (mg) or placebo to be taken orally twice daily (BID) or three times daily (TID) for 84 days.

Pre-assignment

Screening details:

A total of 99 participants were screened, of them, 47 participants were screen failures and 52 participants were enrolled. Of them, 51 participants received study treatment. One participant was enrolled in the study but never received study treatment as eligibility criteria for dose was not met.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo BID

Arm description:

Participants received placebo orally twice daily (BID) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.

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

Dosage and administration details:

Two tablets taken orally BID.

Arm title	Placebo TID

Arm description:

Participants received placebo orally three times daily (TID) (approximately 8 hours apart) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.

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

Dosage and administration details:

Two tablets taken orally TID.

Arm title	GSK2982772 60 mg BID

Arm description:

Participants received GSK2982772 orally twice daily (BID) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.

Arm type	Experimental

Investigational medicinal product name	GSK2982772
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two tablets (30 mg) taken orally BID.

Arm title	GSK2982772 60 mg TID

Arm description:

Participants received GSK2982772 orally three times daily (TID) (approximately 8 hours apart) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.

Arm type	Experimental
Investigational medicinal product name	GSK2982772
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Two tablets (30 mg) taken orally TID.

Number of subjects in period 1[1]	Placebo BID	Placebo TID	GSK2982772 60 mg BID
Started	3	15	5
Completed	3	14	5
Not completed	0	1	0
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	-	-	-
Protocol defined stopping criteria	-	-	-
Lack of efficacy	-	-	-

Number of subjects in period 1[1]	GSK2982772 60 mg TID
Started	28
Completed	22
Not completed	6
Consent withdrawn by subject	1
Adverse event, non-fatal	3
Protocol defined stopping criteria	1
Lack of efficacy	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 52 participants were enrolled. Of them, 51 participants received study treatment. One participant was enrolled in the study but never received study treatment as eligibility criteria for dose was not met.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo BID
Reporting group description:	
Participants received placebo orally twice daily (BID) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.	
Reporting group title	Placebo TID
Reporting group description:	
Participants received placebo orally three times daily (TID) (approximately 8 hours apart) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.	
Reporting group title	GSK2982772 60 mg BID
Reporting group description:	
Participants received GSK2982772 orally twice daily (BID) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.	
Reporting group title	GSK2982772 60 mg TID
Reporting group description:	
Participants received GSK2982772 orally three times daily (TID) (approximately 8 hours apart) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.	

Reporting group values	Placebo BID	Placebo TID	GSK2982772 60 mg BID
Number of subjects	3	15	5
Age categorical Units: Subjects			
Total participants	3	15	5
Age Continuous Units: Years			
arithmetic mean	53.3	53.1	53.6
standard deviation	± 4.93	± 7.80	± 7.86
Sex: Female, Male Units: Subjects			
Female	2	13	4
Male	1	2	1
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	0	0	0
White-White/Caucasian/European Heritage	3	15	5

Reporting group values	GSK2982772 60 mg TID	Total	
Number of subjects	28	51	
Age categorical Units: Subjects			
Total participants	28	51	
Age Continuous Units: Years			
arithmetic mean	55.0		
standard deviation	± 11.25	-	

Sex: Female, Male Units: Subjects			
Female	23	42	
Male	5	9	
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	1	1	
White-White/Caucasian/European Heritage	27	50	

End points

End points reporting groups

Reporting group title	Placebo BID

Reporting group description:

Participants received placebo orally twice daily (BID) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.

Reporting group title	Placebo TID

Reporting group description:

Participants received placebo orally three times daily (TID) (approximately 8 hours apart) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.

Reporting group title	GSK2982772 60 mg BID

Reporting group description:

Participants received GSK2982772 orally twice daily (BID) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.

Reporting group title	GSK2982772 60 mg TID

Reporting group description:

Participants received GSK2982772 orally three times daily (TID) (approximately 8 hours apart) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.

Primary: Number of participants with non-serious adverse events (nSAEs) and serious adverse events (SAEs) as a measure of safety and tolerability

End point title	Number of participants with non-serious adverse events (nSAEs) and serious adverse events (SAEs) as a measure of safety and tolerability[1]

End point description:

An AE was 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. Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly or birth defect or any other situation according to medical or scientific judgment was categorized as SAE. Number of participants with any nSAE or SAE are presented. Safety Population comprised of all participants who received at least one dose of the study treatment.

End point type	Primary

End point timeframe:

Up to Day 112

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: There are no statistical data to report.

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[2]	15[3]	5[4]	28[5]
Units: Participants				
Any nSAEs	3	10	3	16
Any SAEs	0	0	0	2

Notes:

[2] - Safety Population

[3] - Safety Population

[4] - Safety Population

[5] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with worst case clinical chemistry parameters of potential clinical importance (PCI)

End point title	Number of participants with worst case clinical chemistry parameters of potential clinical importance (PCI)[6]

End point description:

Clinical chemistry parameters included alanine amino transferase (ALT), albumin, alkaline phosphatase, aspartate amino transferase (AST), calcium, creatinine, glucose, potassium, sodium and total bilirubin. PCI ranges were ALT(high): >=2*Upper limit of Normal(ULN) units per liter(U/L), albumin(low): 30 millimoles per liter(mmol/L), alkaline phosphatase(high): >=2*ULN U/L, AST(high): >=2*ULN U/L, calcium: <2(low) or >2.75 mmol/L(high), creatinine (high): increase from Baseline >44.25 mmol/L, glucose: <3(low) or >9 mmol/L(high), potassium: <3(low) or >5.5 mmol/L(high), sodium: <130(low) or >150 mmol/L(high) and total bilirubin(high): >=1.5*ULN micromoles per liter(µmol/L). Participants were counted in the worst case category if their value changes (to low or to high), unless there is no change in their category. Only those clinical chemistry parameters with PCI values (to low and to high) have been presented.

End point type	Primary

End point timeframe:

Up to Day 112

Notes:

[6] - 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: There are no statistical data to report.

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[7]	15[8]	5[9]	28[10]
Units: Participants				
ALT; To low	0	0	0	0
ALT; To high	0	0	0	2
Albumin; To low	0	0	0	0
Albumin; To high	0	0	0	0
Alkaline phosphatase; To Low	0	0	0	0
Alkaline phosphatase; To high	0	0	0	0
AST; To low	0	0	0	0
AST; To high	0	0	0	1
Calcium; To low	0	0	0	0
Calcium; To high	0	0	0	0
Creatinine; To low	0	0	0	0
Creatinine; To high	0	0	0	0
Glucose; To low	0	1	0	0
Glucose; To high	0	1	0	1
Potassium; To low	0	0	0	0
Potassium; To high	0	0	0	1
Sodium; To low	0	0	0	0

Sodium; To high	0	0	0	0
Total bilirubin; To low	0	0	0	0
Total bilirubin; To high	0	0	0	0

Notes:

[7] - Safety Population

[8] - Safety Population

[9] - Safety Population

[10] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with worst case hematology parameters of PCI

End point title	Number of participants with worst case hematology parameters of PCI[11]

End point description:

Hematology parameters included hematocrit, hemoglobin, lymphocytes, platelet counts, total neutrophils and white blood cells (WBCs). PCI ranges were < 0.075 (decrease from baseline) or >0.54 proportion of red blood cells in blood (high) for hematocrit, <25 (low) or >180 grams per liter (g/L) (high) for hemoglobin, <0.8 x10^9 cells per liter (cells/L) for lymphocytes (low), <100 (low) or >550 x10^9 cells/L(high) for platelets, <1.5 x10^9 cells/L (low) for total neutrophils and < 3 (low) or >20 x10^9 cells/L (high) for WBCs. Participants were counted in the worst case category that their value changes (to low or to high), unless there is no change in their category. Only those hematology parameters with PCI values (to low and to high) have been presented.

End point type	Primary

End point timeframe:

Up to Day 112

Notes:

[11] - 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: There are no statistical data to report.

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[12]	15[13]	5[14]	28[15]
Units: Participants				
Hematocrit; To low	0	0	0	0
Hematocrit; To high	0	0	0	0
Hemoglobin; To low	0	0	0	0
Hemoglobin; To high	0	0	0	0
Lymphocytes; To Low	2	1	0	1
Lymphocytes; To high	0	0	0	0
Platelet count; To low	0	0	0	0
Platelet count; To high	0	0	0	0
Total neutrophils; To low	0	0	0	1
Total neutrophils; To high	0	0	0	0
WBC; To low	0	0	0	1
WBC; To high	0	1	0	0

Notes:

[12] - Safety Population

[13] - Safety Population

[14] - Safety Population

[15] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with worst case any increase in urinalysis results post-Baseline relative to Baseline by dipstick method

End point title	Number of participants with worst case any increase in urinalysis results post-Baseline relative to Baseline by dipstick method[16]

End point description:

Urine samples were collected to assess glucose, ketones, occult blood and protein by dipstick method. The dipstick test gave results in a semi-quantitative manner, and results for urinalysis parameters glucose, ketones, occult blood and protein were categorized as 'any increase from Baseline', which imply any increase in their concentrations in the urine sample. Only participants with worst case any increase from Baseline values are presented.

End point type	Primary

End point timeframe:

Up to Day 112

Notes:

[16] - 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: There are no statistical data to report.

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[17]	15[18]	5[19]	28[20]
Units: Participants				
Glucose; Any increase	0	0	0	0
Ketones; Any increase	1	3	3	6
Occult blood; Any increase	0	6	1	8
Protein; Any increase	1	2	0	6

Notes:

[17] - Safety Population

[18] - Safety Population

[19] - Safety Population

[20] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with worst case any increase in urinalysis results post-Baseline relative to Baseline by microscopy method

End point title	Number of participants with worst case any increase in urinalysis results post-Baseline relative to Baseline by microscopy method[21]

End point description:

Urine samples were collected to assess glucose, ketones, occult blood and protein by dipstick method.

Microscopy was performed only on urine samples showing an abnormality on the dipstick. Microscopy was performed for hyaline casts, red blood cells and white blood cells. Results for microscopy parameters hyaline casts, red blood cells and white blood cells were categorized as 'any increase from Baseline', which imply any increase in their count in the urine sample. Only participants with worst case any increase from Baseline values are presented. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). 99999 indicates data is not available.

End point type	Primary

End point timeframe:

Up to Day 112

Notes:

[21] - 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: There are no statistical data to report.

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[22]	7[23]	1[24]	11[25]
Units: Participants				
Hyaline casts;any increase;n=0,1,0,0	99999	1	99999	99999
Red blood cells;any increase;n=2,7,1,11	1	5	1	8
White blood cells;any increase;n=2,7,1,11	2	5	1	7

Notes:

[22] - Safety Population

[23] - Safety Population

[24] - Safety Population

[25] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in electrocardiogram (ECG) heart rate at indicated time points

End point title	Change from Baseline in electrocardiogram (ECG) heart rate at indicated time points[26]

End point description:

12- lead ECG was measured on each day using an ECG machine that automatically calculated the heart rate and measured PR interval, QRS duration, QT interval, QT interval corrected for heart rate according to either Bazett's formula (QTcB) and QT interval corrected for heart rate according to Fridericia's formula (QTcF). ECG was measured in semi-supine or supine position after 5 minutes rest. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1 pre-dose), Days 8, 15, 29, 43, 57, 71 and 85

Notes:

[26] - 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: There are no statistical data to report.

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[27]	14[28]	5[29]	24[30]
Units: Beats per minute				
arithmetic mean (standard deviation)				
Day 8; n=3,14,5,23	7.0 (± 5.57)	1.1 (± 10.68)	0.6 (± 7.09)	0.6 (± 7.55)
Day 15; n=3,14,5,24	0.7 (± 2.08)	-0.3 (± 11.64)	-4.6 (± 4.16)	1.0 (± 9.94)
Day 29; n=3,14,5,22	2.7 (± 4.93)	-1.4 (± 8.27)	-5.8 (± 13.66)	1.3 (± 9.14)
Day 43; n=3,13,5,23	-0.7 (± 7.57)	-3.5 (± 9.73)	-6.0 (± 7.35)	-0.2 (± 10.86)
Day 57; n=3,13,5,22	-3.7 (± 10.69)	-2.4 (± 8.79)	-4.2 (± 8.58)	0.7 (± 9.75)
Day 71; n=3,13,5,22	0.3 (± 9.29)	-3.0 (± 12.08)	-7.6 (± 7.73)	0.3 (± 9.32)
Day 85; n=3,13,5,21	-1.7 (± 5.69)	-4.1 (± 11.51)	-2.4 (± 4.72)	-1.4 (± 9.12)

Notes:

[27] - Safety Population

[28] - Safety Population

[29] - Safety Population

[30] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in ECG PR interval, QRS duration, QT interval, QTcB and QTcF at indicated time points

End point title	Change from Baseline in ECG PR interval, QRS duration, QT interval, QTcB and QTcF at indicated time points[31]

End point description:

12- lead ECG was measured on each day using an ECG machine that automatically calculated the heart rate and measured PR interval, QRS duration, QT interval QTcB and QTcF. ECG was measured in semi-supine or supine position after 5 minutes rest. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1 pre-dose), Days 8, 15, 29, 43, 57, 71 and 85

Notes:

[31] - 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: There are no statistical data to report.

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[32]	14[33]	5[34]	24[35]
Units: Millisecond				
arithmetic mean (standard deviation)				
PR interval; Day 8; n=3,14,5,23	-0.3 (± 14.36)	-1.9 (± 26.35)	-6.4 (± 19.98)	0.8 (± 18.84)
PR interval; Day 15; n=3,14,5,24	6.3 (± 12.66)	0.6 (± 29.94)	-2.0 (± 23.10)	3.0 (± 15.71)
PR interval; Day 29; n=3,14,5,22	5.3 (± 24.01)	-3.5 (± 32.15)	-0.2 (± 22.66)	-6.9 (± 28.00)
PR interval; Day 43; n=3,13,5,23	2.0 (± 17.35)	6.5 (± 14.44)	2.4 (± 5.41)	6.6 (± 15.69)
PR interval; Day 57; n=3,13,5,22	-12.0 (± 5.29)	5.8 (± 21.75)	5.0 (± 6.36)	4.1 (± 17.51)
PR interval; Day 71; n=3,13,5,22	1.0 (± 17.78)	1.2 (± 18.65)	2.2 (± 23.92)	0.8 (± 15.06)
PR interval; Day 85; n=3,13,5,21	1.3 (± 10.02)	6.2 (± 15.38)	-0.2 (± 5.26)	0.4 (± 10.29)

QRS duration; Day 8; n=3,14,5,23	-4.7 (± 5.03)	-3.3 (± 10.75)	8.2 (± 10.33)	3.7 (± 12.97)
QRS duration; Day 15; n=3,14,5,24	-3.3 (± 4.16)	-3.1 (± 10.50)	-1.2 (± 7.26)	1.1 (± 6.89)
QRS duration; Day 29; n=3,14,5,22	-1.3 (± 3.79)	-2.1 (± 10.89)	0.4 (± 5.03)	-0.5 (± 9.01)
QRS duration; Day 43; n=3,13,5,23	-3.3 (± 5.51)	-1.1 (± 9.90)	3.6 (± 8.29)	0.3 (± 10.48)
QRS duration; Day 57; n=3,13,5,22	-6.0 (± 6.00)	-4.0 (± 5.90)	3.2 (± 9.34)	1.0 (± 18.33)
QRS duration; Day 71; n=3,13,5,22	-10.0 (± 7.55)	-0.2 (± 6.68)	4.6 (± 12.26)	-0.5 (± 8.31)
QRS duration; Day 85; n=3,13,5,21	-7.3 (± 11.37)	-1.0 (± 9.07)	3.4 (± 8.68)	1.5 (± 10.68)
QT interval; Day 8; n=3,14,5,23	-25.7 (± 6.11)	6.4 (± 40.17)	-14.2 (± 22.49)	-1.0 (± 35.97)
QT interval; Day 15; n=3,14,5,24	2.7 (± 11.02)	20.7 (± 34.85)	0.0 (± 21.12)	-4.5 (± 25.27)
QT interval; Day 29; n=3,14,5,22	-9.3 (± 17.67)	7.6 (± 25.03)	-5.6 (± 22.37)	5.5 (± 31.49)
QT interval; Day 43; n=3,13,5,23	-12.7 (± 28.10)	18.5 (± 38.73)	1.0 (± 20.74)	0.6 (± 29.36)
QT interval; Day 57; n=3,13,5,22	12.3 (± 30.04)	13.6 (± 41.48)	2.4 (± 22.78)	-1.8 (± 36.44)
QT interval; Day 71; n=3,13,5,22	-9.3 (± 33.98)	13.8 (± 32.50)	10.2 (± 28.71)	-2.1 (± 22.06)
QT interval; Day 85; n=3,13,5,21	-0.3 (± 14.50)	17.2 (± 32.16)	-3.2 (± 14.60)	3.0 (± 17.28)
QTcB; Day 8; n=2,14,5,22	-12.1 (± 8.34)	10.5 (± 46.28)	-10.3 (± 14.09)	0.7 (± 33.20)
QTcB; Day 15; n=2,14,5,23	7.2 (± 7.18)	22.9 (± 46.10)	-12.9 (± 17.59)	-0.9 (± 19.63)
QTcB; Day 29; n=2,14,5,21	-2.4 (± 7.96)	4.4 (± 25.73)	-21.2 (± 29.58)	10.3 (± 29.02)
QTcB; Day 43; n=2,13,5,22	-13.0 (± 14.51)	9.1 (± 37.18)	-14.2 (± 14.64)	0.6 (± 27.77)
QTcB; Day 57; n=2,13,5,21	-1.5 (± 1.83)	7.5 (± 38.73)	-7.0 (± 11.67)	1.1 (± 47.85)
QTcB; Day 71; n=2,13,5,21	-9.3 (± 16.59)	4.6 (± 34.77)	-11.0 (± 16.47)	-1.1 (± 20.55)
QTcB; Day 85; n=2,13,5,20	4.2 (± 15.78)	7.0 (± 32.09)	-9.1 (± 12.42)	-0.7 (± 17.51)
QTcF; Day 8; n=2,14,5,22	-16.0 (± 3.35)	9.0 (± 42.58)	-11.4 (± 14.05)	0.3 (± 33.04)
QTcF; Day 15; n=2,14,5,23	7.5 (± 7.65)	22.2 (± 39.68)	-8.4 (± 18.00)	-2.3 (± 17.61)
QTcF; Day 29; n=2,14,5,21	-3.3 (± 13.16)	5.6 (± 22.87)	-15.6 (± 18.24)	8.7 (± 27.77)
QTcF; Day 43; n=2,13,5,22	-13.5 (± 23.40)	12.4 (± 35.37)	-8.7 (± 13.81)	0.7 (± 25.16)
QTcF; Day 57; n=2,13,5,21	5.9 (± 11.57)	9.6 (± 38.25)	-3.5 (± 11.35)	-0.1 (± 42.41)
QTcF; Day 71; n=2,13,5,21	-11.1 (± 27.30)	7.6 (± 30.12)	-3.5 (± 18.48)	-1.2 (± 17.15)
QTcF; Day 85; n=2,13,5,20	2.5 (± 17.46)	10.6 (± 28.46)	-7.0 (± 11.36)	0.6 (± 12.45)

Notes:

[32] - Safety Population

[33] - Safety Population

[34] - Safety Population

[35] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) at indicated time points

End point title	Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) at indicated time points[36]

End point description:

SBP and DBP were measured in a supine or semi-supine position after approximately 5 minutes rest. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data

available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1 pre-dose), Days 8, 15, 29, 43, 57, 71 and 85

Notes:

[36] - 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: There are no statistical data to report.

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[37]	15[38]	5[39]	25[40]
Units: Millimeters of Mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP; Day 8; n=3,15,5,25	-9.7 (± 5.69)	0.5 (± 12.61)	-4.6 (± 14.33)	2.7 (± 11.0)
SBP; Day 15; n=3,15,5,25	-2.0 (± 7.55)	-2.7 (± 11.21)	-13.0 (± 12.79)	4.6 (± 9.43)
SBP; Day 29; n=3,15,5,24	-9.3 (± 15.70)	-0.8 (± 10.82)	-8.2 (± 19.12)	1.9 (± 11.94)
SBP; Day 43; n=3,14,5,24	-7.0 (± 9.54)	-2.0 (± 15.11)	-11.4 (± 19.72)	-1.6 (± 10.01)
SBP; Day 57; n=3,14,5,23	-14.7 (± 17.21)	0.5 (± 16.19)	-9.6 (± 18.49)	-0.3 (± 12.84)
SBP; Day 71; n=3,14,5,23	-7.0 (± 9.85)	1.1 (± 14.35)	-8.2 (± 12.19)	1.2 (± 14.40)
SBP; Day 85; n=3,14,5,22	-4.3 (± 12.70)	-0.1 (± 14.68)	-4.8 (± 11.23)	1.9 (± 12.97)
DBP; Day 8; n=3,15,5,25	2.00 (± 5.00)	2.0 (± 11.32)	1.0 (± 8.69)	-0.4 (± 7.12)
DBP; Day 15; n=3,15,5,25	0.3 (± 6.11)	0.3 (± 7.85)	0.4 (± 4.39)	1.1 (± 7.61)
DBP; Day 29; n=3,15,5,24	-4.0 (± 8.89)	0.2 (± 8.28)	-2.0 (± 6.04)	0.7 (± 7.65)
DBP; Day 43; n=3,14,5,24	0.3 (± 14.36)	-0.3 (± 8.96)	-1.4 (± 8.76)	-0.8 (± 6.68)
DBP; Day 57; n=3,14,5,23	-3.7 (± 8.33)	0.8 (± 9.90)	1.4 (± 6.43)	-0.9 (± 7.78)
DBP; Day 71; n=3,14,5,23	-7.0 (± 9.17)	1.4 (± 8.36)	-7.2 (± 9.76)	-1.5 (± 6.90)
DBP; Day 85; n=3,14,5,22	1.0 (± 6.24)	2.1 (± 10.79)	-1.4 (± 7.67)	-0.4 (± 7.50)

Notes:

[37] - Safety Population

[38] - Safety Population

[39] - Safety Population

[40] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in respiratory rate at indicated time points

End point title	Change from Baseline in respiratory rate at indicated time points[41]

End point description:

Respiratory rate was measured in a supine or semi-supine position after approximately 5 minutes rest. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1 pre-dose), Days 8, 15, 29, 43, 57, 71 and 85

Notes:

[41] - 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: There are no statistical data to report.

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[42]	15[43]	5[44]	25[45]
Units: Breaths per minute				
arithmetic mean (standard deviation)				
Day 8; n=3,15,5,25	0.7 (± 1.53)	0.1 (± 1.13)	-0.4 (± 2.61)	0.0 (± 1.14)
Day 15; n=3,15,5,25	1.0 (± 1.73)	0.2 (± 1.08)	-1.2 (± 1.79)	0.2 (± 1.91)
Day 29; n=3,15,5,24	1.0 (± 1.00)	-0.2 (± 1.47)	-1.6 (± 1.67)	0.1 (± 1.28)
Day 43; n=3,14,5,24	1.7 (± 0.58)	0.3 (± 1.33)	-0.8 (± 1.10)	0.5 (± 2.70)
Day 57; n=3,14,5,23	1.7 (± 2.08)	0.2 (± 0.70)	0.4 (± 3.29)	0.6 (± 2.00)
Day 71; n=3,14,5,23	1.7 (± 0.58)	0.5 (± 0.65)	0.0 (± 2.45)	0.7 (± 2.07)
Day 85; n=3,14,5,22	0.7 (± 0.58)	0.4 (± 0.84)	-0.4 (± 2.61)	0.5 (± 1.60)

Notes:

[42] - Safety Population

[43] - Safety Population

[44] - Safety Population

[45] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in body temperature at indicated time points

End point title	Change from Baseline in body temperature at indicated time points[46]

End point description:

Body temperature was measured in a supine or semi-supine position after approximately 5 minutes rest. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1 pre-dose), Days 8, 15, 29, 43, 57, 71 and 85

Notes:

[46] - 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: There are no statistical data to report.

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[47]	15[48]	5[49]	25[50]
Units: Degrees Celsius				
arithmetic mean (standard deviation)				
Day 8; n=3,15,5,25	0.60 (± 0.529)	-0.03 (± 0.209)	-0.06 (± 0.261)	0.06 (± 0.222)
Day 15; n=3,15,5,25	0.80 (± 0.500)	-0.07 (± 0.171)	-0.04 (± 0.219)	0.06 (± 0.251)

Day 29; n=3,15,5,24	0.60 (± 0.656)	-0.02 (± 0.204)	0.10 (± 0.187)	0.11 (± 0.249)
Day 43; n=3,14,5,24	0.53 (± 0.513)	-0.01 (± 0.251)	0.04 (± 0.270)	0.06 (± 0.286)
Day 57; n=3,14,5,23	0.53 (± 0.462)	-0.02 (± 0.226)	-0.02 (± 0.239)	0.16 (± 0.310)
Day 71; n=3,14,5,23	0.27 (± 0.404)	-0.06 (± 0.210)	-0.00 (± 0.141)	0.17 (± 0.255)
Day 85; n=3,14,5,22	0.53 (± 0.379)	-0.10 (± 0.162)	-0.12 (± 0.356)	0.14 (± 0.353)

Notes:

[47] - Safety Population

[48] - Safety Population

[49] - Safety Population

[50] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in vital sign-heart rate at indicated time points

End point title	Change from Baseline in vital sign-heart rate at indicated time points[51]

End point description:

Vital sign-heart rate was planned to be assessed as a measure of safety and tolerability. The data for assessment of vital sign-heart rate was not collected.

End point type	Primary

End point timeframe:

Baseline (Day 1 pre-dose), Days 8, 15, 29, 43, 57, 71 and 85

Notes:

[51] - 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: There are no statistical data to report.

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[52]	0[53]	0[54]	0[55]
Units: Beats per minute				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[52] - Safety Population

[53] - Safety Population

[54] - Safety Population

[55] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose plasma concentrations of GSK2982772 on Days 8 and 43

End point title	Pre-dose plasma concentrations of GSK2982772 on Days 8 and 43[56]

End point description:

Blood samples were collected on Day 8 and Day 43 for determining pre-dose plasma concentrations of GSK2982772. Pharmacokinetic parameters were determined using standard non-compartmental

methods. Pharmacokinetic GSK298772 Population comprised of participants in the safety population who received an active dose and for whom a GSK2982772 pharmacokinetic sample was obtained and analyzed. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Pre-dose on Day 8 and Day 43

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

End point values	GSK2982772 60 mg BID	GSK2982772 60 mg TID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[57]	24[58]		
Units: Nanogram per milliliter				
arithmetic mean (standard deviation)				
Day 8;n=5,24	88.332 (± 96.5705)	181.774 (± 322.8428)		
Day 43;n=5,23	33.994 (± 51.1033)	142.792 (± 176.2630)		

Notes:

[57] - Pharmacokinetic GSK298772 Population

[58] - Pharmacokinetic GSK298772 Population

Statistical analyses

No statistical analyses for this end point

Secondary: Post-dose plasma concentrations of GSK2982772 on Days 1, 8, and 43 at 1, 2, 4 and 6 hours

End point title	Post-dose plasma concentrations of GSK2982772 on Days 1, 8, and 43 at 1, 2, 4 and 6 hours[59]

End point description:

Blood samples were collected on Day 1, Day 8 and Day 43 for determining post-dose plasma concentrations of GSK2982772. Pharmacokinetic parameters were determined using standard non-compartmental methods. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Days 1, 8 and 43: 1, 2, 4 and 6 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: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	GSK2982772 60 mg BID	GSK2982772 60 mg TID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[60]	27[61]		
Units: Nanogram per milliliter				
arithmetic mean (standard deviation)				

Day 1;1 hour;n=5,27	851.000 (± 375.5110)	953.037 (± 556.4630)		
Day 1;2 hour;n=5,27	656.000 (± 386.5741)	911.630 (± 376.7128)		
Day 1;4 hour;n=5,27	269.600 (± 156.3052)	421.215 (± 211.7969)		
Day 1;6 hour;n=5,27	120.240 (± 54.6881)	382.419 (± 485.6076)		
Day 8;1 hour;n=5,23	796.600 (± 397.7120)	881.783 (± 550.4666)		
Day 8;2 hour;n=5,24	689.000 (± 317.5602)	930.958 (± 446.0379)		
Day 8;4 hour;n=5,24	265.000 (± 129.6360)	520.958 (± 324.4127)		
Day 8;6 hour;n=5,23	112.280 (± 78.0491)	444.470 (± 358.1685)		
Day 43;1 hour;n=5,23	672.200 (± 165.4470)	862.487 (± 501.4882)		
Day 43;2 hour;n=5,23	598.600 (± 253.0036)	872.652 (± 354.1155)		
Day 43;4 hour;n=5,23	313.200 (± 226.0845)	553.783 (± 430.5811)		
Day 43;6 hour;n=5,23	177.980 (± 192.6731)	332.522 (± 240.9716)		

Notes:

[60] - Pharmacokinetic GSK298772 Population

[61] - Pharmacokinetic GSK298772 Population

Statistical analyses

No statistical analyses for this end point

Secondary: Trough plasma concentration of GSK2982772 on Day 85

End point title	Trough plasma concentration of GSK2982772 on Day 85[62]

End point description:

Blood samples were collected to evaluate plasma concentration of GSK2982772. Pharmacokinetic parameters including trough plasma concentration was determined using standard non-compartmental methods. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Day 85

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

End point values	GSK2982772 60 mg BID	GSK2982772 60 mg TID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[63]	17[64]		
Units: Nanogram per milliliter				
arithmetic mean (standard deviation)	54.64 (± 50.714)	391.11 (± 694.270)		

Notes:

[63] - Pharmacokinetic GSK298772 Population

[64] - Pharmacokinetic GSK298772 Population

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose plasma concentrations of methotrexate on Days 1, 8 and 43

End point title	Pre-dose plasma concentrations of methotrexate on Days 1, 8 and 43

End point description:

Blood samples were collected on Day 1, Day 8 and Day 43 for determining pre-dose plasma concentrations of methotrexate. Pharmacokinetic parameters were determined using standard non-compartmental methods. Only participants who received methotrexate during the study were included. Pharmacokinetic Methotrexate Population comprised of participants in the safety population who received an active dose and for whom a Methotrexate pharmacokinetic sample was obtained and analyzed. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Pre-dose on Days 1, 8 and 43

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[65]	13[66]	5[67]	22[68]
Units: Nanogram per milliliter				
arithmetic mean (standard deviation)				
Day 1;n=3,13,5,22	0.450 (± 0.7794)	16.236 (± 56.4280)	0.546 (± 0.7909)	6.309 (± 15.4993)
Day 8;n=3,12,5,17	1.117 (± 1.9341)	0.509 (± 0.9879)	4.640 (± 10.3754)	11.939 (± 47.4493)
Day 43;n=3,11,5,19	36.000 (± 62.3538)	0.909 (± 2.0658)	1.512 (± 3.3809)	1.445 (± 3.1606)

Notes:

[65] - Pharmacokinetic Methotrexate Population

[66] - Pharmacokinetic Methotrexate Population

[67] - Pharmacokinetic Methotrexate Population

[68] - Pharmacokinetic Methotrexate Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Baseline in C-Reactive Protein (CRP)

End point title	Percent change from Baseline in C-Reactive Protein (CRP)

End point description:

CRP is an inflammatory biomarker present in blood. Blood samples were collected at indicated time points for the assessment of CRP. Baseline was defined as the latest pre-dose assessment (Day 1 pre-

dose). Percent change from Baseline was calculated by 100*[(post-dose value minus Baseline value)/ Baseline value]. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[69]	14[70]	5[71]	24[72]
Units: Percent change				
arithmetic mean (standard deviation)				
Day 43;n=3,14,5,24	-24.02 (± 53.259)	63.02 (± 331.286)	-10.37 (± 94.318)	12.68 (± 107.207)
Day 85;n=3,14,5,22	-43.62 (± 49.968)	220.05 (± 828.334)	-16.42 (± 70.096)	274.25 (± 879.900)

Notes:

[69] - Safety Population

[70] - Safety Population

[71] - Safety Population

[72] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Baseline in Interleukin 6 (IL6)

End point title	Percent change from Baseline in Interleukin 6 (IL6)

End point description:

IL6 is an inflammatory biomarker present in blood. Blood samples were collected at indicated time points for the assessment of IL6. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Percent change from Baseline was calculated by 100*[(post-dose value minus Baseline value)/ Baseline value]. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[73]	14[74]	5[75]	24[76]
Units: Percent change				
arithmetic mean (standard deviation)				
Day 43;n=3,14,5,24	89.12 (± 96.649)	55.00 (± 257.661)	-3.95 (± 66.008)	74.49 (± 358.187)
Day 85;n=3,14,5,22	5.21 (± 16.978)	27.52 (± 97.215)	-24.44 (± 67.817)	0.52 (± 106.029)

Notes:

[73] - Safety Population

[74] - Safety Population

[75] - Safety Population

[76] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Baseline in Matrix metalloproteinase-1 (MMP-1), MMP-3, and MMP-13

End point title	Percent change from Baseline in Matrix metalloproteinase-1 (MMP-1), MMP-3, and MMP-13

End point description:

MMP-1, MMP-3, and MMP-13 are an inflammatory biomarkers present in blood. Blood samples were collected at indicated time points for the assessment of MMP-1, MMP-3, and MMP-13. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Percent change from Baseline was calculated by 100*[(post-dose value minus Baseline value)/ Baseline value]. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[77]	14[78]	5[79]	24[80]
Units: Percent change				
arithmetic mean (standard deviation)				
MMP-1;Day 43;n=3,14,5,24	-11.25 (± 6.591)	-4.04 (± 23.016)	-15.36 (± 13.399)	-4.07 (± 27.244)
MMP-1;Day 85;n=3,14,5,22	-19.77 (± 28.013)	9.75 (± 41.645)	-20.21 (± 19.417)	-1.61 (± 28.420)
MMP-3;Day 43;n=3,14,5,24	8.86 (± 27.501)	6.07 (± 27.883)	-26.82 (± 20.757)	-4.07 (± 36.176)
MMP-3;Day 85;n=3,14,5,22	32.61 (± 32.849)	11.98 (± 42.337)	-38.26 (± 19.306)	-2.14 (± 34.751)
MMP-13;Day 43;n=3,12,5,22	-6.45 (± 7.000)	32.94 (± 139.157)	-7.27 (± 34.373)	-3.55 (± 29.506)
MMP-13;Day 85;n=3,11,5,17	-34.65 (± 35.926)	114.18 (± 223.386)	-21.16 (± 31.372)	67.91 (± 157.027)

Notes:

[77] - Safety Population

[78] - Safety Population

[79] - Safety Population

[80] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Baseline in tissue inhibitor of metalloproteinases-1 (TIMP-1)

End point title	Percent change from Baseline in tissue inhibitor of metalloproteinases-1 (TIMP-1)

End point description:

TIMP-1 is an inflammatory biomarker present in blood. Blood samples were collected at indicated time points for the assessment of TIMP-1. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Percent change from Baseline was calculated by 100*[(post-dose value minus Baseline value)/ Baseline value]. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[81]	14[82]	5[83]	24[84]
Units: Percent change				
arithmetic mean (standard deviation)				
Day 43;n=3,14,5,24	-1.82 (± 6.578)	-9.89 (± 37.032)	-7.39 (± 11.298)	-5.59 (± 23.922)
Day 85;n=3,14,5,22	35.61 (± 73.383)	-2.63 (± 57.144)	49.38 (± 114.161)	-1.75 (± 33.789)

Notes:

[81] - Safety Population

[82] - Safety Population

[83] - Safety Population

[84] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Baseline in monocyte chemo attractant protein-1 (MCP-1)

End point title	Percent change from Baseline in monocyte chemo attractant protein-1 (MCP-1)

End point description:

MCP-1 is an inflammatory biomarker present in blood. Blood samples were collected at indicated time points for the assessment of MCP-1. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Percent change from Baseline was calculated by 100*[(post-dose value minus Baseline value)/ Baseline value]. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[85]	14[86]	5[87]	23[88]
Units: Percent change				
arithmetic mean (standard deviation)				
Day 43;n=3,14,5,23	-4.57 (± 19.262)	388.23 (± 565.617)	-4.37 (± 11.309)	156.79 (± 297.549)
Day 85;n=3,14,5,21	-33.39 (± 49.411)	422.45 (± 514.842)	-30.35 (± 36.118)	199.94 (± 392.590)

Notes:

[85] - Safety Population

[86] - Safety Population

[87] - Safety Population

[88] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Baseline in migration inhibitory factor (MIF)

End point title	Percent change from Baseline in migration inhibitory factor (MIF)

End point description:

MIF is an inflammatory biomarker present in blood. Blood samples were collected at indicated time points for the assessment of MIF. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Percent change from Baseline was calculated by 100*[(post-dose value minus Baseline value)/ Baseline value]. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[89]	14[90]	5[91]	24[92]
Units: Percent change				
arithmetic mean (standard deviation)				
Day 43;n=3,14,5,24	8.98 (± 29.041)	4.69 (± 46.772)	120.23 (± 362.931)	34.46 (± 160.400)
Day 85;n=3,14,5,22	15.39 (± 26.888)	-15.72 (± 49.080)	-11.80 (± 47.351)	-5.76 (± 49.377)

Notes:

[89] - Safety Population

[90] - Safety Population

[91] - Safety Population

[92] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Baseline in Myeloid-related Protein 8/14 (MRP8/14)

End point title	Percent change from Baseline in Myeloid-related Protein 8/14 (MRP8/14)

End point description:

MRP8/14 is an inflammatory biomarker present in blood. Blood samples were collected at indicated time points for the assessment of MRP8/14. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Percent change from Baseline was calculated by 100*[(post-dose value minus Baseline value)/ Baseline value]. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[93]	14[94]	5[95]	24[96]
Units: Percent change				
arithmetic mean (standard deviation)				
Day 43;n=3,14,5,24	3.15 (± 47.472)	25.14 (± 75.189)	-49.21 (± 19.168)	-22.95 (± 38.992)
Day 85;n=3,14,5,22	13.84 (± 66.492)	70.37 (± 199.467)	-28.27 (± 17.112)	-11.35 (± 77.927)

Notes:

[93] - Safety Population

[94] - Safety Population

[95] - Safety Population

[96] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in bone erosion total score by "Outcome Measures in Rheumatology, Rheumatoid Arthritis Magnetic Resonance Image Scoring System (OMERACT-RAMRIS)" scoring system

End point title	Change from Baseline in bone erosion total score by "Outcome Measures in Rheumatology, Rheumatoid Arthritis Magnetic Resonance Image Scoring System (OMERACT-RAMRIS)" scoring system

End point description:

A total of 25 locations in the hand and wrist were evaluated for RAMRIS bone erosions. Individual location scores range from 0 (no erosions) to 10 (91 to 100 percent of bone eroded) based on the proportion of eroded bone compared to the “assessed bone volume” on all available images. The final bone erosion score was the sum of the individual location scores. The total score from the 25 locations ranges from 0 to 250, with 0 implying no bone erosion and 250 implying 91 to 100 percent bone eroded. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[97]	13[98]	5[99]	24[100]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Day 43;n=3,13,5,24	0.7 (± 1.15)	0.6 (± 1.04)	0.4 (± 1.52)	-0.2 (± 1.83)
Day 85;n=3,13,5,22	1.7 (± 2.89)	1.3 (± 2.43)	0.4 (± 1.52)	-0.1 (± 2.21)

Notes:

[97] - Safety Population

[98] - Safety Population

[99] - Safety Population

[100] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in bone erosions by the Rheumatoid arthritis MRI quantitative (RAMRIQ) scoring system

End point title	Change from Baseline in bone erosions by the Rheumatoid arthritis MRI quantitative (RAMRIQ) scoring system

End point description:

RAMRIQ bone erosions (normalized) was a quantitative measurement from the bones and synovial capsules of the joints from the most affected (or dominant hand if equally affected). It was calculated as the sum of the individual measurements of the volume of bone erosions divided by sum of the individual measurements of the bone volume. The total score ranged from 0 to 1, with 0 implying no erosive damage. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[101]	13[102]	5[103]	23[104]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Day 43;n=2,13,5,23	-0.00160 (± 0.002550)	-0.00110 (± 0.002265)	-0.00072 (± 0.001662)	-0.00069 (± 0.004145)
Day 85;n=2,13,5,21	-0.00069 (± 0.001134)	-0.00075 (± 0.001301)	-0.00273 (± 0.003505)	0.00059 (± 0.003946)

Notes:

[101] - Safety Population

[102] - Safety Population

[103] - Safety Population

[104] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in bone erosions by modified Cartilage Loss Scoring System (CARLOS)

End point title	Change from Baseline in bone erosions by modified Cartilage Loss Scoring System (CARLOS)

End point description:

Change from Baseline in bone erosions was planned to be assessed by modified CARLOS. Data was not collected for this outcome measure, as bone erosion is not a part of modified CARLOS and it was measured by OMERACT-RAMRIS scoring system in another outcome measure.

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[105]	0[106]	0[107]	0[108]
Units: Scores on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[105] - Safety Population

[106] - Safety Population

[107] - Safety Population

[108] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in synovitis by OMERACT-RAMRIS scoring system

End point title	Change from Baseline in synovitis by OMERACT-RAMRIS scoring system

End point description:

A total of 8 joints in the hand and wrist were evaluated for RAMRIS synovitis. Individual joint scores were assessed on a scale of 0 (no synovitis) to 3 (67 to 100 percent volume enhancement). The final synovitis score was the sum of the individual joint scores. The total score from 8 joints ranges from 0 to 24, with 0 implying normal (no synovitis) and 24 implying 67 to 100 percent volume enhancement. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[109]	13[110]	5[111]	24[112]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Day 43;n=3,13,5,24	0.0 (± 1.73)	0.3 (± 1.55)	-0.4 (± 1.52)	-0.3 (± 1.90)
Day 85;n=3,13,5,22	0.3 (± 1.15)	0.5 (± 2.67)	-0.4 (± 1.52)	-0.5 (± 2.20)

Notes:

[109] - Safety Population

[110] - Safety Population

[111] - Safety Population

[112] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in synovitis by RAMRIQ scoring system

End point title	Change from Baseline in synovitis by RAMRIQ scoring system

End point description:

RAMRIQ synovitis (normalised) was a quantitative measurement from the bones and synovial capsules of the joints from the most affected (or dominant hand if equally affected). It was calculated as the sum of the individual measurements of the volume of enhancing pannus (VEP) divided by sum of the individual measurements of the joint volume. The total score ranged from 0 to 1, with 0 implying no synovitis. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[113]	13[114]	5[115]	23[116]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Day 43;n=2,13,5,23	-0.0570 (± 0.02302)	-0.0165 (± 0.04302)	-0.0592 (± 0.06931)	-0.0084 (± 0.10490)
Day 85;n=2,13,5,21	-0.0659 (± 0.01625)	0.0251 (± 0.12286)	-0.0270 (± 0.07061)	-0.0107 (± 0.11472)

Notes:

[113] - Safety Population

[114] - Safety Population

[115] - Safety Population

[116] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in synovitis by modified CARLOS

End point title	Change from Baseline in synovitis by modified CARLOS

End point description:

Change from Baseline in synovitis was planned to be assessed by modified CARLOS. Data was not collected for this outcome measure, as synovitis is not a part of modified CARLOS and it was measured by OMERACT-RAMRIS scoring system in another outcome measure.

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[117]	0[118]	0[119]	0[120]
Units: Scores on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[117] - Safety Population

[118] - Safety Population

[119] - Safety Population

[120] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in bone edema by OMERACT-RAMRIS scoring system

End point title	Change from Baseline in bone edema by OMERACT-RAMRIS scoring system

End point description:

A total of 25 locations in the hand and wrist were evaluated for RAMRIS bone edema or osteitis. Individual location scores range from 0 (no edema) to 3 (67 to 100 percent involvement of original articular bone) based on the proportion of estimated originally non-eroded bone involved. The final bone edema or osteitis score is the sum of the individual location scores. The total score from the 25 locations ranges from 0 to 75, with 0 implying no bone edema or osteitis and 75 implying 67 to 100 percent involvement of original articular bone. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[121]	13[122]	5[123]	24[124]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Day 43;n=3,13,5,24	-1.0 (± 1.73)	-0.2 (± 1.52)	-0.8 (± 3.27)	-0.9 (± 2.47)
Day 85;n=3,13,5,22	0.3 (± 0.58)	0.3 (± 1.38)	-4.4 (± 6.80)	-1.1 (± 2.59)

Notes:

[121] - Safety Population

[122] - Safety Population

[123] - Safety Population

[124] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in bone edema by RAMRIQ scoring system

End point title	Change from Baseline in bone edema by RAMRIQ scoring system

End point description:

RAMRIQ bone edema (normalised) was a quantitative measurement from the bones and synovial capsules of the joints from the most affected (or dominant hand if equally affected). It was calculated as the sum of the individual measurements of the Volume of bone edema divided by sum of the individual measurements of the bone volume.. The total score ranged from 0 to 1, with 0 implying no bone marrow lesions. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[125]	13[126]	5[127]	22[128]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Day 43;n=2,13,5,22	-0.00396 (± 0.000647)	-0.00463 (± 0.007465)	-0.01963 (± 0.031481)	-0.00095 (± 0.018745)
Day 85;n=2,13,5,21	0.00116 (± 0.010166)	-0.00229 (± 0.010143)	-0.03921 (± 0.055431)	-0.00384 (± 0.016126)

Notes:

[125] - Safety Population

[126] - Safety Population

[127] - Safety Population

[128] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in bone edema by modified CARLOS

End point title	Change from Baseline in bone edema by modified CARLOS

End point description:

Change from Baseline in bone edema was planned to be assessed by modified CARLOS. Data was not collected for this outcome measure, as bone edema is not a part of modified CARLOS and it was measured by OMERACT-RAMRIS scoring system in another outcome measure.

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[129]	0[130]	0[131]	0[132]
Units: Scores on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[129] - Safety Population

[130] - Safety Population

[131] - Safety Population

[132] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in joint space narrowing by OMERACT-RAMRIS scoring system

End point title	Change from Baseline in joint space narrowing by OMERACT-RAMRIS scoring system

End point description:

Change from Baseline in joint space narrowing was planned to be assessed by OMERACT-RAMRIS scoring system. Data was not collected for this outcome measure, as joint space narrowing is not a part of OMERACT-RAMRIS scoring system and it was measured by modified CARLOS in another outcome.

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[133]	0[134]	0[135]	0[136]
Units: Scores on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[133] - Safety Population

[134] - Safety Population

[135] - Safety Population

[136] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in joint space narrowing by RAMRIQ scoring system

End point title	Change from Baseline in joint space narrowing by RAMRIQ scoring system

End point description:

RAMRIQ joint space narrowing was a quantitative measurement from the bones and synovial capsules of the joints from the most affected (or dominant hand if equally affected). It was calculated as the sum of the individual measurements (in millimeter) for the joints measured. The minimum possible total score is 0 implying complete loss of the joint space. The maximum possible total score will be largest possible joint space. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[137]	13[138]	5[139]	23[140]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Day 43;n=2,13,5,23	1.121 (± 1.4793)	0.378 (± 1.3394)	0.484 (± 2.8980)	-0.335 (± 1.4365)
Day 85;n=2,13,5,21	0.534 (± 0.8910)	0.216 (± 0.6974)	0.235 (± 2.2525)	-0.433 (± 1.1205)

Notes:

[137] - Safety Population

[138] - Safety Population

[139] - Safety Population

[140] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in joint space narrowing by modified CARLOS

End point title	Change from Baseline in joint space narrowing by modified CARLOS

End point description:

A total of 20 locations in the hand and wrist were evaluated for CARLOS joint space narrowing/cartilage loss. Individual location scores range from 0 (no cartilage loss or Joint Space Narrowing) to 4 (complete

ankylosis) in increments of 0.5 based on the amount of narrowing present in a given joint. The final cartilage loss score was the sum of the individual location scores. The total score from 20 location ranged from 0 to 80, with 0 implying no cartilage loss at any location and 80 implying complete ankylosis. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[141]	13[142]	5[143]	24[144]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Day 43;n=3,13,5,24	0.00 (± 0.00)	0.00 (± 0.00)	0.00 (± 0.00)	0.08 (± 0.408)
Day 85;n=3,13,5,22	0.00 (± 0.00)	0.00 (± 0.00)	0.00 (± 0.00)	0.09 (± 0.426)

Notes:

[141] - Safety Population

[142] - Safety Population

[143] - Safety Population

[144] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in exchange rate (Ktrans)

End point title	Change from Baseline in exchange rate (Ktrans)

End point description:

Contrast agent volume transfer constant (Ktrans) relates to the exchange of contrast agent between the blood plasma and the tissue extravascular extracellular spaces and reflects blood flow and capillary permeability. Ktrans was measured by dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) tracer kinetic modeling in the most affected hand/wrist at indicated time points. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[145]	9[146]	5[147]	19[148]
Units: Per minute				
arithmetic mean (standard deviation)				
Day 43;n=2,9,5,19	0.0012 (± 0.00076)	0.0022 (± 0.01214)	-0.0095 (± 0.01716)	-0.0018 (± 0.01443)

Day 85;n=2,9,5,17	0.0002 (± 0.01726)	-0.0021 (± 0.01385)	-0.0073 (± 0.00618)	-0.0043 (± 0.01747)

Notes:

[145] - Safety Population

[146] - Safety Population

[147] - Safety Population

[148] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in interstitial volume (Ve)

End point title	Change from Baseline in interstitial volume (Ve)

End point description:

Interstitial volume (Ve) is the fractional volume of the extravascular extracellular (EC) space per unit volume tissue within which contrast agent can accumulate. Ve was measured by DCE-MRI in most affected hand/wrist at indicated time points. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[149]	9[150]	5[151]	18[152]
Units: Ratio of EC space to tissue volume				
arithmetic mean (standard deviation)				
Day 43;n=2,9,5,18	-0.305 (± 0.3128)	-0.066 (± 0.3615)	-0.140 (± 0.4825)	0.073 (± 0.4044)
Day 85;n=2,9,5,15	0.009 (± 0.7840)	-0.024 (± 0.2450)	-0.278 (± 0.5170)	0.113 (± 0.4664)

Notes:

[149] - Safety Population

[150] - Safety Population

[151] - Safety Population

[152] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in fractional volume of blood plasma (Vp)

End point title	Change from Baseline in fractional volume of blood plasma (Vp)

End point description:

Fractional volume of blood plasma (Vp) is the fractional volume of blood plasma per unit volume of tissue. Vp was measured by DCE-MRI in most affected hand/wrist at indicated time points. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by

subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[153]	9[154]	5[155]	19[156]
Units: Ratio of plasma volume to tissue volume				
arithmetic mean (standard deviation)				
Day 43;n=2,9,5,19	0.0018 (± 0.00166)	0.0007 (± 0.00678)	-0.0023 (± 0.00786)	-0.0007 (± 0.00358)
Day 85;n=2,9,5,17	0.0000 (± 0.00019)	-0.0022 (± 0.00407)	-0.0001 (± 0.00272)	-0.0007 (± 0.00282)

Notes:

[153] - Safety Population

[154] - Safety Population

[155] - Safety Population

[156] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in initial rate of enhancement (IRE)

End point title	Change from Baseline in initial rate of enhancement (IRE)

End point description:

Initial Rate of Enhancement (IRE) is a measure of how quickly tissue enhances over 60 seconds following administration of contrast agent. IRE was measured by DCE-MRI in most affected hand/wrist at indicated time points. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[157]	9[158]	5[159]	19[160]
Units: Millimole per second				
arithmetic mean (standard deviation)				
Day 43;n=2,9,5,19	-0.00002 (± 0.000044)	0.00008 (± 0.000538)	-0.00043 (± 0.000750)	-0.00008 (± 0.000575)
Day 85;n=2,9,5,17	-0.00011 (± 0.000566)	-0.00010 (± 0.000542)	-0.00037 (± 0.000271)	-0.00014 (± 0.000735)

Notes:

[157] - Safety Population

[158] - Safety Population

[159] - Safety Population

[160] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in maximal signal intensity enhancement (ME)

End point title	Change from Baseline in maximal signal intensity enhancement (ME)

End point description:

Maximum enhancement (ME) is a measure of the maximum concentration of contrast agent in the tissue over the duration of the DCE-MRI time series. ME was measured by DCE-MRI in most affected hand/wrist at indicated time points. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[161]	9[162]	5[163]	19[164]
Units: Millimole				
arithmetic mean (standard deviation)				
Day 43;n=2,9,5,19	-0.0300 (± 0.00994)	0.0029 (± 0.05405)	-0.0531 (± 0.06876)	0.0007 (± 0.06159)
Day 85;n=2,9,5,17	-0.0533 (± 0.00473)	-0.0138 (± 0.05168)	-0.0584 (± 0.06009)	-0.0074 (± 0.07180)

Notes:

[161] - Safety Population

[162] - Safety Population

[163] - Safety Population

[164] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Disease Activity Score 28-C-Reactive Protein (DAS28-CRP) scores

End point title	Change from Baseline in Disease Activity Score 28-C-Reactive Protein (DAS28-CRP) scores

End point description:

The DAS28-CRP is a composite measure of inflammation in rheumatoid arthritis calculated from the sum of tender joint count 28 (TJC28), swollen joint count (SJC28), CRP and patient global assessment of disease activity (PtGA). 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. Scores of DAS28-CRP ranged from 0.96 to 9.4 with higher scores indicating greater disease burden. A DAS28-CRP score of <=2.6 suggested remission, <3.2 suggested a low level of disease activity, while a score of >5.1 suggested a high level of disease activity. Baseline was defined as the latest pre-dose assessment (Day 1 pre-dose). Change from Baseline was calculated by subtracting post-dose value from Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1 pre-dose) and Day 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[165]	12[166]	5[167]	22[168]
Units: Scores on a scale				
least squares mean (confidence interval 95%)	-1.00 (-2.45 to 0.46)	-0.87 (-1.57 to -0.17)	-1.47 (-2.60 to 0.35)	-1.23 (-1.75 to 0.71)

Notes:

[165] - Safety Population

[166] - Safety Population

[167] - Safety Population

[168] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants achieving categorical DAS28-CRP response using European League Against Rheumatism [EULAR] response

End point title	Number of participants achieving categorical DAS28-CRP response using European League Against Rheumatism [EULAR] response

End point description:

DAS28-CRP scores were categorized using EULAR response criteria. Response at a given time point was defined based on the combination of current DAS28 score and the improvement in the current DAS28 score relative to Baseline. The definition of no response, moderate response and good response was as; if current DAS28 <=3.2 and DAS28 decrease from Baseline (>1.2: good response), (>0.6 to <=1.2: moderate response) and (<=0.6: no response); if current DAS28 >3.2 to <=5.1 and DAS28 decrease from Baseline value (>1.2: moderate response), (>0.6 to <=1.2: moderate response) and (<=0.6: no response) and if current DAS28 >5.1 and DAS28 decrease from Baseline value (>1.2: moderate response), (>0.6 to <=1.2: no response) and (<=0.6: no response). If the post-Baseline DAS28-CRP score was missing, then the corresponding EULAR category was set to missing. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Day 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[169]	12[170]	5[171]	22[172]
Units: Participants				
No response	2	6	1	7
Moderate response	0	4	2	8
Good response	1	2	2	7

Notes:

[169] - Safety Population

[170] - Safety Population

[171] - Safety Population

[172] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants achieving categorical American college of rhumatology20/50/70 (ACR20/50/70) response

End point title	Number of participants achieving categorical American college of rhumatology20/50/70 (ACR20/50/70) response

End point description:

The ACR score was based on improvement from Baseline in tender joint counts and swollen joint counts. A participant had achieved ACR20 if he experienced >=20 percent improvement from Baseline in Tender Joint count 28 (TJC28) and Swollen Joint Count 28 (SJC28) and a >=20 percent improvement from Baseline in 3 out of 5 of the following assessments: participant pain assessment on a 100 millimeter (mm) visual analog scale (VAS), participant global assessment on a 100 mm VAS scale, physician global assessment on a 100 mm VAS scale, C-reactive protein and Health Assessment Questionnaire – Disability Index (HAQ-DI). Similarly, ACR50 and ACR70 are calculated using 50 or 70 percent improvement from baseline respectively. For all visits, if any of the component scores were missing; then those scores were considered as not having met the criteria for improvement.

End point type	Secondary

End point timeframe:

Day 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[173]	15[174]	5[175]	28[176]
Units: Participants				
ACR20	1	6	3	12
ACR50	1	2	0	5
ACR70	1	1	0	4

Notes:

[173] - Safety Population

[174] - Safety Population

[175] - Safety Population

[176] - Safety Population

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in joint volume

End point title	Change from Baseline in joint volume

End point description:

Joint volume was planned to be measured by DCE-MRI in most affected hand/wrist at indicated time points. This was an other pre-specified outcome measure. Data will not be analyzed and reported.

End point type	Other pre-specified

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[177]	0[178]	0[179]	0[180]
Units: Cubic millimeter				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[177] - Safety Population

[178] - Safety Population

[179] - Safety Population

[180] - Safety Population

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in enhancing volume

End point title	Change from Baseline in enhancing volume

End point description:

Enhancing volume was planned to be measured by DCE-MRI in most affected hand/wrist at indicated time points. This was an other pre-specified outcome measure. Data will not be analyzed and reported.

End point type	Other pre-specified

End point timeframe:

Baseline (Day 1 pre-dose), Days 43 and 85

End point values	Placebo BID	Placebo TID	GSK2982772 60 mg BID	GSK2982772 60 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[181]	0[182]	0[183]	0[184]
Units: Cubic millimeter				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[181] - Safety Population

[182] - Safety Population

[183] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
On-therapy non-SAEs and SAEs were reported from start of study treatment and up to 112 days	
Adverse event reporting additional description:	
Non-SAE and SAEs were reported for Safety Population. Adverse events were presented treatment-wise.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	Placebo BID
Reporting group description:	
Participants received placebo orally twice daily (BID) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.	
Reporting group title	Placebo TID
Reporting group description:	
Participants received placebo orally three times daily (TID) (approximately 8 hours apart) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.	
Reporting group title	GSK2982772 60mg BID
Reporting group description:	
Participants received GSK2982772 orally twice daily (BID) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.	
Reporting group title	GSK2982772 60mg TID
Reporting group description:	
three times daily (TID) (approximately 8 hours apart) for 84 days (12 weeks). Participants received methotrexate for the treatment of RA during conduct of the study, if required.	

Serious adverse events	Placebo BID	Placebo TID	GSK2982772 60mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Tibia fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			

subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	GSK2982772 60mg TID		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 28 (7.14%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Tibia fracture			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ulna fracture			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal vein thrombosis			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo BID	Placebo TID	GSK2982772 60mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	10 / 15 (66.67%)	3 / 5 (60.00%)
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Transaminases increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Cardiac disorders			

Bundle branch block left			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ventricular arrhythmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vascular headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			

subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia areata			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Macule			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0

Synovial cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Genital herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pertussis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection viral			

subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Viral infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

Non-serious adverse events	GSK2982772 60mg TID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 28 (57.14%)		
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			

Ovarian cyst subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Investigations Blood pressure increased subjects affected / exposed occurrences (all) Transaminases increased subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2 1 / 28 (3.57%) 1		
Cardiac disorders Bundle branch block left subjects affected / exposed occurrences (all) Palpitations subjects affected / exposed occurrences (all) Ventricular arrhythmia subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0 1 / 28 (3.57%) 1 0 / 28 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all) Somnolence	1 / 28 (3.57%) 1 2 / 28 (7.14%) 3 0 / 28 (0.00%) 0		

subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Vascular headache			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Visual impairment			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia areata			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Dermatitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Macule			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pollakiuria			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Synovial cyst			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Bronchitis			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Genital herpes			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Pertussis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Respiratory tract infection viral			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Skin infection			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Viral infection			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Hypercholesterolaemia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 May 2016	Protocol Amendment 01 incorporates the addition of risk text for drug interaction with Pglycoprotein (Pgp) inhibitors and narrow therapeutic index (NTI) CYP3A4 substrates, an updated list of prohibited medications plus some minor protocol clarifications and administrative changes.
14 July 2016	Protocol Amendment 02 incorporates addition of suicidal ideation and behaviour (SIB) withdrawal criteria plus other minor protocol clarifications and administrative changes.
20 April 2017	Protocol Amendment 03 incorporates change in dosing regimen from 60 mg BID to 60 mg TID, restrictions on Janus Kinase (JAK) inhibitors, defined non-reproductive potential criteria in Exclusion 11, change to clinical laboratory criteria in Exclusion 23, addition of evaluation of joint space narrowing with MRI, flexibility in scheduling with MRI and synovial biopsy, some minor protocol clarifications and administrative changes.
03 August 2017	A country specific amendment for Germany (only applicable in Germany) which reinstates the clinical laboratory criteria in Exclusion 23 and Haematologic Stopping Criteria in Section 5.4.5 that was changed in Amendment 03.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported