Clinical trial results:
A randomized, double-blind, multi-dose, placebo-controlled study to evaluate the efficacy, safety and tolerability of GSK2330672 administration for the treatment of pruritus in patients with primary biliary cholangitis (GLIMMER: GSK2330672 triaL of Ibat inhibition with Multidose Measurement for Evaluation of Response)

Summary

EudraCT number	2016-002416-41
Trial protocol	ES GB PL IT
Global end of trial date	15 April 2020

Results information

Result version number	v1 (current)
This version publication date	24 April 2021
First version publication date	24 April 2021

Trial information

Trial identification

Sponsor protocol code	201000

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the dose response of oral GSK2330672 on itch in primary biliary cholangitis (PBC) participants with moderate to severe pruritus at Baseline

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 January 2017
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	Australia: 4
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Japan: 38
Country: Number of subjects enrolled	Poland: 17
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 25
Country: Number of subjects enrolled	United States: 20
Worldwide total number of subjects	147
EEA total number of subjects	49

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	111
From 65 to 84 years	36
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted across 66 centers in 10 countries. The 40 milligrams (mg) twice daily dose group was added and recruitment into the 20 mg twice daily dose group was discontinued following the pre-specified interim analysis.

Pre-assignment

Screening details:

A total of 147 adult participants were randomized in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Eligible participants were randomized to receive GSK2330672 matching placebo via oral route for 16 weeks including the Main Study Period and Final Study period. Participants were then followed up for 4 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo was available as white-film coated tablets to be administered orally.

Arm title	GSK2330672 20 mg QD

Arm description:

Eligible participants were randomized to receive GSK2330672 20 milligrams (mg) once daily (QD) for 12 weeks in the Main Study period followed by matching placebo for 4 weeks in the Final Study period. Participants were then followed up for 4 weeks. All doses were administered via oral route.

Arm type	Experimental
Investigational medicinal product name	GSK2330672
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GSK2330672 was available as white-film coated tablets at unit dose strength of 10 and 45 milligrams (mg) to be administered orally.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo was available as white-film coated tablets to be administered orally.

Arm title	GSK2330672 90 mg QD

Arm description:

Eligible participants were randomized to receive GSK2330672 90 mg QD for 12 weeks in the Main study period followed by matching placebo for 4 weeks in the Final Study Period. Participants were then followed up for 4 weeks. All doses were administered via oral route.

Arm type	Experimental
Investigational medicinal product name	GSK2330672
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GSK2330672 was available as white-film coated tablets at unit dose strength of 10 and 45 milligrams (mg) to be administered orally.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo was available as white-film coated tablets to be administered orally.

Arm title	GSK2330672 180 mg QD

Arm description:

Eligible participants were randomized to receive GSK2330672 180 mg QD for 12 weeks in the Main study period followed by matching placebo for 4 weeks in the Final study period. Participants were then followed up for 4 weeks. All doses were administered via oral route.

Arm type	Experimental
Investigational medicinal product name	GSK2330672
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GSK2330672 was available as white-film coated tablets at unit dose strength of 10 and 45 milligrams (mg) to be administered orally.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo was available as white-film coated tablets to be administered orally.

Arm title	GSK2330672 40 mg BID

Arm description:

Eligible participants were randomized to receive GSK2330672 40 mg twice daily (BID) for 12 weeks in the Main study period followed by matching placebo for 4 weeks in the Final study period. Participants were then followed up for 4 weeks. All doses were administered via oral route.

Arm type	Experimental

Investigational medicinal product name	GSK2330672
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GSK2330672 was available as white-film coated tablets at unit dose strength of 10 and 45 milligrams (mg) to be administered orally.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo was available as white-film coated tablets to be administered orally.

Arm title	GSK2330672 90 mg BID

Arm description:

Eligible participants were randomized to receive GSK2330672 90 mg BID for 12 weeks in the Main study period followed by matching placebo for 4 weeks in the Final Study Period. Participants were then followed up for 4 weeks All doses were administered via oral route.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo was available as white-film coated tablets to be administered orally.

Investigational medicinal product name	GSK2330672
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GSK2330672 was available as white-film coated tablets at unit dose strength of 10 and 45 milligrams (mg) to be administered orally.

Number of subjects in period 1	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD
Started	36	16	23
Completed	35	16	22
Not completed	1	0	1
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	1
Lack of efficacy	1	-	-
Protocol deviation	-	-	-

Number of subjects in period 1	GSK2330672 180 mg QD	GSK2330672 40 mg BID	GSK2330672 90 mg BID

Started	27	23	22
Completed	22	22	21
Not completed	5	1	1
Consent withdrawn by subject	2	-	-
Adverse event, non-fatal	2	1	1
Lack of efficacy	-	-	-
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Eligible participants were randomized to receive GSK2330672 matching placebo via oral route for 16 weeks including the Main Study Period and Final Study period. Participants were then followed up for 4 weeks.	
Reporting group title	GSK2330672 20 mg QD
Reporting group description:	
Eligible participants were randomized to receive GSK2330672 20 milligrams (mg) once daily (QD) for 12 weeks in the Main Study period followed by matching placebo for 4 weeks in the Final Study period. Participants were then followed up for 4 weeks. All doses were administered via oral route.	
Reporting group title	GSK2330672 90 mg QD
Reporting group description:	
Eligible participants were randomized to receive GSK2330672 90 mg QD for 12 weeks in the Main study period followed by matching placebo for 4 weeks in the Final Study Period. Participants were then followed up for 4 weeks. All doses were administered via oral route.	
Reporting group title	GSK2330672 180 mg QD
Reporting group description:	
Eligible participants were randomized to receive GSK2330672 180 mg QD for 12 weeks in the Main study period followed by matching placebo for 4 weeks in the Final study period. Participants were then followed up for 4 weeks. All doses were administered via oral route.	
Reporting group title	GSK2330672 40 mg BID
Reporting group description:	
Eligible participants were randomized to receive GSK2330672 40 mg twice daily (BID) for 12 weeks in the Main study period followed by matching placebo for 4 weeks in the Final study period. Participants were then followed up for 4 weeks. All doses were administered via oral route.	
Reporting group title	GSK2330672 90 mg BID
Reporting group description:	
Eligible participants were randomized to receive GSK2330672 90 mg BID for 12 weeks in the Main study period followed by matching placebo for 4 weeks in the Final Study Period. Participants were then followed up for 4 weeks All doses were administered via oral route.	

Reporting group values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD
Number of subjects	36	16	23
Age categorical Units: Subjects			
All participants	36	16	23
Age Continuous Units: Years			
arithmetic mean	54.4	58.5	52.5
standard deviation	± 11.06	± 7.35	± 12.32
Sex: Female, Male Units: Participants			
Female	34	16	21
Male	2	0	2
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	0	0	0
Asian - Japanese Heritage	8	6	6

White - White/Caucasian/European Heritage	26	10	17
Multiple	0	0	0
Unknown	2	0	0

Reporting group values	GSK2330672 180 mg QD	GSK2330672 40 mg BID	GSK2330672 90 mg BID
Number of subjects	27	23	22
Age categorical Units: Subjects			
All participants	27	23	22
Age Continuous Units: Years			
arithmetic mean	58.9	55.6	56.2
standard deviation	± 11.10	± 11.23	± 11.32
Sex: Female, Male Units: Participants			
Female	25	22	20
Male	2	1	2
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	0	1	0
Asian - Japanese Heritage	7	4	7
White - White/Caucasian/European Heritage	19	16	15
Multiple	1	0	0
Unknown	0	2	0

Reporting group values	Total		
Number of subjects	147		
Age categorical Units: Subjects			
All participants	147		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	138		
Male	9		
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	1		
Asian - Japanese Heritage	38		
White - White/Caucasian/European Heritage	103		
Multiple	1		
Unknown	4		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Eligible participants were randomized to receive GSK2330672 matching placebo via oral route for 16 weeks including the Main Study Period and Final Study period. Participants were then followed up for 4 weeks.	
Reporting group title	GSK2330672 20 mg QD
Reporting group description:	
Eligible participants were randomized to receive GSK2330672 20 milligrams (mg) once daily (QD) for 12 weeks in the Main Study period followed by matching placebo for 4 weeks in the Final Study period. Participants were then followed up for 4 weeks. All doses were administered via oral route.	
Reporting group title	GSK2330672 90 mg QD
Reporting group description:	
Eligible participants were randomized to receive GSK2330672 90 mg QD for 12 weeks in the Main study period followed by matching placebo for 4 weeks in the Final Study Period. Participants were then followed up for 4 weeks. All doses were administered via oral route.	
Reporting group title	GSK2330672 180 mg QD
Reporting group description:	
Eligible participants were randomized to receive GSK2330672 180 mg QD for 12 weeks in the Main study period followed by matching placebo for 4 weeks in the Final study period. Participants were then followed up for 4 weeks. All doses were administered via oral route.	
Reporting group title	GSK2330672 40 mg BID
Reporting group description:	
Eligible participants were randomized to receive GSK2330672 40 mg twice daily (BID) for 12 weeks in the Main study period followed by matching placebo for 4 weeks in the Final study period. Participants were then followed up for 4 weeks. All doses were administered via oral route.	
Reporting group title	GSK2330672 90 mg BID
Reporting group description:	
Eligible participants were randomized to receive GSK2330672 90 mg BID for 12 weeks in the Main study period followed by matching placebo for 4 weeks in the Final Study Period. Participants were then followed up for 4 weeks All doses were administered via oral route.	
Subject analysis set title	Placebo -Main Study Period
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Eligible participants were randomized to receive GSK2330672 matching placebo via oral route for 12 weeks in Main Study Period.	
Subject analysis set title	GSK2330672 20 mg QD - Main Study Period
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Eligible participants were randomized to receive GSK2330672 20 milligrams (mg) once daily (QD) for 12 weeks in the Main Study period.	
Subject analysis set title	GSK2330672 90 mg QD - Main Study Period
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Eligible participants were randomized to receive GSK2330672 90 mg QD for 12 weeks in the Main study period.	
Subject analysis set title	GSK2330672 180 mg QD - Main Study Period
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Eligible participants were randomized to receive GSK2330672 180 mg QD for 12 weeks in the Main study period.	
Subject analysis set title	GSK2330672 40 mg BID - Main Study Period
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants were randomized to receive GSK2330672 40 mg twice daily (BID) for 12 weeks in the Main study period.

Subject analysis set title	GSK2330672 90 mg BID - Main Study Period
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants were randomized to receive GSK2330672 90 mg BID for 12 weeks in the Main study period

Subject analysis set title	Placebo - Final Study Period
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants were randomized to receive GSK2330672 matching placebo via oral route for 4 weeks in Final Study Period.

Subject analysis set title	GSK2330672 20 mg QD - Final Study Period
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants were randomized to receive GSK2330672 matching placebo via oral route for 4 weeks in Final Study Period. Participants received GSK2330672 20 mg QD during Main study period.

Subject analysis set title	GSK2330672 90 mg QD - Final Study Period
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants were randomized to receive GSK2330672 matching placebo via oral route for 4 weeks in Final Study Period. Participants received GSK2330672 90 mg QD during Main study period.

Subject analysis set title	GSK2330672 180 mg QD - Final Study Period
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants were randomized to receive GSK2330672 matching placebo via oral route for 4 weeks in Final Study Period. Participants received GSK2330672 180 mg QD during Main study period.

Subject analysis set title	GSK2330672 40 mg BID - Final Study Period
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants were randomized to receive GSK2330672 matching placebo via oral route for 4 weeks in Final Study Period. Participants received GSK2330672 40 mg BID during Main study period.

Subject analysis set title	GSK2330672 90 mg BID - Final Study Period
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants were randomized to receive GSK2330672 matching placebo via oral route for 4 weeks in Final Study Period. Participants received GSK2330672 90 mg BID during Main study period.

Subject analysis set title	Placebo - Follow-up
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received GSK2330672 matching placebo in Main study period and Final study period entered in a 4-week no-treatment follow-up period.

Subject analysis set title	GSK2330672 20 mg QD - Follow-up
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received treatment (active or placebo) in Main study period and Final study period entered in a 4-week no-treatment follow-up period.

Subject analysis set title	GSK2330672 90 mg QD - Follow-up
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received treatment (active or placebo) in Main study period and Final study period entered in a 4-week no-treatment follow-up period.

Subject analysis set title	GSK2330672 180 mg QD - Follow-up
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received treatment (active or placebo) in Main study period and Final study period entered in a 4-week no-treatment follow-up period.

Subject analysis set title	GSK2330672 40 mg BID - Follow-up
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received treatment (active or placebo) in Main study period and Final study period entered in a 4-week no-treatment follow-up period.

Subject analysis set title	GSK2330672 90 mg BID - Follow-up
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received treatment (active or placebo) in Main study period and Final study period entered in a 4-week no-treatment follow-up period.

Primary: Mean change from Baseline at Week 16 in the Mean Worst Daily Itch Score

End point title	Mean change from Baseline at Week 16 in the Mean Worst Daily Itch Score

End point description:

Participants were required to score the severity of their itching using a 0-10 numerical rating scale (NRS) where 0 represents no itching and 10 indicates the worst imaginable itching. The Worst Daily Itch Score is the most severe (highest) NRS recorded on a given day. Mean Worst Daily Itch score was calculated as the average of the worst daily itch scores provided in the 7 days prior to the Week 16 visit. Baseline is the average of the scores in the 7 days prior to the Week 4 (Visit 3 [V3]). Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Analysis was done using Analysis of covariance (ANCOVA) including treatment group and centered Mean Worst Daily Itch score at Baseline. Intent-to-Treat (ITT) Population comprised of all randomized participants who received at least one dose of study treatment, had a Baseline and at least one on-treatment assessment. Only those participants with data available at the specified data points were analyzed.

End point type	Primary

End point timeframe:

Baseline and Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35[1]	16[2]	20[3]	22[4]
Units: Scores on a scale				
least squares mean (confidence interval 95%)	-1.73 (-2.44 to -1.01)	-2.19 (-3.26 to -1.12)	-2.60 (-3.55 to -1.65)	-2.60 (-3.51 to -1.70)

Notes:

[1] - ITT Population

[2] - ITT Population

[3] - ITT Population

[4] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[5]	21[6]		
Units: Scores on a scale				
least squares mean (confidence interval 95%)	-2.86 (-3.76 to -1.95)	-2.25 (-3.19 to -1.32)		

Notes:
[5] - ITT Population
[6] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.75
upper limit	0.82

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.07
upper limit	0.31

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.03
upper limit	0.28

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.29
upper limit	0.03

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.71
upper limit	0.65

Secondary: Mean change from Baseline at Week 16 in Primary Biliary Cholangitis-40 (PBC-40) scale

End point title	Mean change from Baseline at Week 16 in Primary Biliary Cholangitis-40 (PBC-40) scale

End point description:

PBC-40 questionnaire consists of 40 questions arranged in 6 domains with 3 to 11 questions in each domain. Each question is scored from 1 (least impact) to 5 (greatest impact). All questions within a domain are summed to obtain individual domain score. Domains were: Symptoms (7 questions) with score range 7-35, Itch (3 questions) with score range 3-15, Fatigue (11 questions) with score range 11-55, Cognitive (6 questions) with score range 6-30, Emotional (3 questions) with score range 3-15, and Social (10 questions) with score range 10-50. Higher scores for individual domains represent a poor quality of life. Baseline is the assessment performed at Week 4 (V3) which is conducted prior to first dosing of randomized medication that evening. Change from Baseline was calculated as post-Baseline value minus Baseline value. Analysis was performed using ANCOVA including treatment group and Baseline. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35[7]	16[8]	21[9]	22[10]
Units: Scores on a scale				
least squares mean (confidence interval 95%)				
Symptoms	0.2 (-1.0 to 1.4)	0.4 (-1.3 to 2.2)	0.7 (-0.8 to 2.3)	-0.9 (-2.4 to 0.6)
Itch	-2.3 (-3.3 to -1.4)	-1.9 (-3.3 to -0.4)	-2.6 (-3.9 to -1.3)	-2.7 (-3.9 to -1.4)
Fatigue	-1.8 (-4.0 to 0.4)	-2.4 (-5.6 to 0.7)	-1.1 (-3.8 to 1.7)	1.7 (-1.0 to 4.5)
Cognitive	-0.3 (-1.7 to 1.1)	-0.3 (-2.4 to 1.8)	-0.9 (-2.7 to 0.9)	-0.1 (-1.9 to 1.6)
Emotional	-0.5 (-1.2 to 0.1)	-1.4 (-2.4 to -0.4)	-0.4 (-1.3 to 0.5)	-0.6 (-1.5 to 0.3)
Social	-0.8 (-2.3 to 0.8)	-0.5 (-2.7 to 1.8)	0.4 (-1.5 to 2.4)	-0.6 (-2.5 to 1.3)

Notes:

[7] - ITT Population

[8] - ITT Population

[9] - ITT Population

[10] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[11]	20[12]		
Units: Scores on a scale				
least squares mean (confidence interval 95%)				
Symptoms	0.3 (-1.2 to 1.8)	0.2 (-1.4 to 1.8)		
Itch	-3.4 (-4.6 to -2.1)	-2.7 (-4.0 to -1.4)		
Fatigue	-0.1 (-2.8 to 2.6)	-1.8 (-4.6 to 1.1)		
Cognitive	0.1 (-1.6 to 1.9)	-0.1 (-2.0 to 1.7)		
Emotional	-1.4 (-2.2 to -0.5)	-0.6 (-1.5 to 0.3)		
Social	-3.1 (-5.1 to -1.2)	-1.0 (-3.0 to 1.0)		

Notes:

[11] - ITT Population

[12] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Symptoms

Comparison groups	Placebo v GSK2330672 20 mg QD

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	2.3

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Symptoms	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	2.5

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Symptoms	
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	0.8

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Symptoms	

Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	2

Statistical analysis title	Statistical Analysis 5
Statistical analysis description: Symptoms	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	1.9

Statistical analysis title	Statistical Analysis 6
Statistical analysis description: Itch	
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	2.2

Statistical analysis title	Statistical Analysis 7

Statistical analysis description: Itch	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	1.3

Statistical analysis title	Statistical Analysis 8
Statistical analysis description: Itch	
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	1.2

Statistical analysis title	Statistical Analysis 9
Statistical analysis description: Itch	
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	0.5

Statistical analysis title	Statistical Analysis 10
Statistical analysis description: Itch	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	1.3

Statistical analysis title	Statistical Analysis 11
Statistical analysis description: Fatigue	
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	3.2

Statistical analysis title	Statistical Analysis 12
Statistical analysis description: Fatigue	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	4.2

Statistical analysis title	Statistical Analysis 13
Statistical analysis description: Fatigue	
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	7

Statistical analysis title	Statistical Analysis 14
Statistical analysis description: Fatigue	
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	5.1

Statistical analysis title	Statistical Analysis 15
Statistical analysis description: Fatigue	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	3.6

Statistical analysis title	Statistical Analysis 16
Statistical analysis description: Cognitive	
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	2.6

Statistical analysis title	Statistical Analysis 17
Statistical analysis description: Cognitive	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	1.7

Statistical analysis title	Statistical Analysis 18
Statistical analysis description: Cognitive	
Comparison groups	Placebo v GSK2330672 180 mg QD

Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	2.5

Statistical analysis title	Statistical Analysis 19
Statistical analysis description: Cognitive	
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	2.8

Statistical analysis title	Statistical Analysis 20
Statistical analysis description: Cognitive	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	2.5

Statistical analysis title	Statistical Analysis 21
Statistical analysis description: Emotional	

Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	0.4

Statistical analysis title	Statistical Analysis 22
Statistical analysis description: Emotional	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1.3

Statistical analysis title	Statistical Analysis 23
Statistical analysis description: Emotional	
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	1.1

Statistical analysis title	Statistical Analysis 24

Statistical analysis description: Emotional	
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.3

Statistical analysis title	Statistical Analysis 25
Statistical analysis description: Emotional	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	1.1

Statistical analysis title	Statistical Analysis 26
Statistical analysis description: Social	
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	3

Statistical analysis title	Statistical Analysis 27
Statistical analysis description: Social	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	3.7

Statistical analysis title	Statistical Analysis 28
Statistical analysis description: Social	
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	2.7

Statistical analysis title	Statistical Analysis 29
Statistical analysis description: Social	
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	0.1

Statistical analysis title	Statistical Analysis 30
Statistical analysis description:	
Social	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	2.4

Secondary: Mean change from Baseline at Week 16 in serum alkaline phosphatase (ALP) concentrations, in participants with high risk of PBC progression

End point title	Mean change from Baseline at Week 16 in serum alkaline phosphatase (ALP) concentrations, in participants with high risk of PBC progression

End point description:

Criteria for high risk of PBC progression is defined as serum ALP concentrations more than or equal to (>=)1.67 times upper limit of normal (ULN) range and/or total bilirubin concentrations more than (>)ULN at Day 1. Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 (Day 1) or Visit 1 (Screening), excluding unscheduled visits. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Analysis was performed using ANCOVA including treatment group and Baseline. High Risk Population comprised of subset of the ITT population who were assigned to the High Risk stratum for randomization (based upon serum ALP concentrations >=1.67 times ULN and/or total bilirubin concentrations >ULN at Day 1 (Visit 2). Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[13]	5[14]	11[15]	7[16]
Units: International units per Liter				
least squares mean (confidence interval 95%)	49.1 (-29.3 to 127.6)	-57.7 (-179.6 to 64.3)	-38.2 (-117.0 to 40.5)	49.6 (-49.1 to 148.2)

Notes:

[13] - High Risk Population

[14] - High Risk Population

[15] - High Risk Population

[16] - High Risk Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[17]	5[18]		
Units: International units per Liter				
least squares mean (confidence interval 95%)	-29.2 (-136.7 to 78.3)	19.1 (-97.7 to 136.0)		

Notes:

[17] - High Risk Population

[18] - High Risk Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-106.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-251.7
upper limit	38.2

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-87.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-198.5
upper limit	23.8

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD

Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-125.6
upper limit	126.5

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-78.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-211.5
upper limit	54.8

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-30
Confidence interval	
level	95 %
sides	2-sided
lower limit	-170.7
upper limit	110.7

Secondary: Number of participants with serum ALP concentrations less than (<)1.67 times ULN and total bilirubin concentrations less than or equal to (<=) ULN at Week 16

End point title	Number of participants with serum ALP concentrations less than (<)1.67 times ULN and total bilirubin concentrations less than or equal to (<=) ULN at Week 16

End point description:

Number of participants with ALP < 1.67 times ULN and total bilirubin <= ULN at Week 16 is presented.

The endpoint was analyzed in Restricted High Risk Population. Restricted High Risk Population comprised of a subset of the High Risk population, i.e. all those participants assigned to the High Risk stratum for randomization who met the ALP/bilirubin criteria at both Visit 2 (Day 1) and Visit 3 (Week 4).

End point type	Secondary

End point timeframe:

At Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[19]	5[20]	9[21]	9[22]
Units: Participants	0	0	0	0

Notes:

[19] - Restricted High Risk Population

[20] - Restricted High Risk Population

[21] - Restricted High Risk Population

[22] - Restricted High Risk Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[23]	7[24]		
Units: Participants	0	1		

Notes:

[23] - Restricted High Risk Population

[24] - Restricted High Risk Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline at Week 16 in serum alanine aminotransferase (ALT) among those with a high risk of PBC progression

End point title	Mean change from Baseline at Week 16 in serum alanine aminotransferase (ALT) among those with a high risk of PBC progression

End point description:

Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 or Visit 1, excluding unscheduled visits. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Analysis was performed using ANCOVA model including Treatment group and Baseline. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[25]	5[26]	11[27]	7[28]
Units: International Units per Liter				
least squares mean (confidence interval 95%)	13.0 (-7.9 to 33.9)	-8.4 (-39.5 to 22.7)	0.3 (-20.7 to 21.2)	-2.0 (-29.0 to 25.1)

Notes:

[25] - High Risk Population

[26] - High Risk Population

[27] - High Risk Population

[28] - High Risk Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[29]	5[30]		
Units: International Units per Liter				
least squares mean (confidence interval 95%)	-13.5 (-42.8 to 15.9)	13.2 (-17.4 to 43.7)		

Notes:

[29] - High Risk Population

[30] - High Risk Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-21.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-58.4
upper limit	15.5

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-12.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.9
upper limit	16.4

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.9
upper limit	20

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-26.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-63.3
upper limit	10.4

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.7
upper limit	37.1

Secondary: Mean change from Baseline at Week 16 in serum aspartate

aminotransferase (AST) among those with a high risk of PBC progression	
End point title	Mean change from Baseline at Week 16 in serum aspartate aminotransferase (AST) among those with a high risk of PBC progression

End point description:

Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 or Visit 1, excluding unscheduled visits. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Analysis was performed using ANCOVA model including Treatment group and Baseline. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[31]	5[32]	11[33]	7[34]
Units: International Units per Liter				
least squares mean (confidence interval 95%)	13.96 (-4.55 to 32.46)	-6.04 (-34.20 to 22.12)	-10.75 (-28.90 to 7.40)	-8.66 (-32.24 to 14.93)

Notes:

[31] - High Risk Population

[32] - High Risk Population

[33] - High Risk Population

[34] - High Risk Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[35]	5[36]		
Units: International Units per Liter				
least squares mean (confidence interval 95%)	-17.72 (-42.77 to 7.34)	8.16 (-18.72 to 35.04)		

Notes:

[35] - High Risk Population

[36] - High Risk Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-20
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52.73
upper limit	12.74

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-24.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.8
upper limit	1.39

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-22.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53.39
upper limit	8.16

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-31.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-63.44
upper limit	0.09

Statistical analysis title	Statistical Analysis 5

Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-5.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.33
upper limit	26.74

Secondary: Mean change from Baseline at Week 16 in serum gamma glutamyl transferase (GGT), among those with a high risk of PBC progression

End point title	Mean change from Baseline at Week 16 in serum gamma glutamyl transferase (GGT), among those with a high risk of PBC progression

End point description:

Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 or Visit 1, excluding unscheduled visits. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Analysis was performed using ANCOVA model including treatment group and Baseline. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[37]	5[38]	11[39]	7[40]
Units: International Units per Liter				
least squares mean (confidence interval 95%)	47.5 (-9.9 to 104.8)	-58.5 (-142.5 to 25.5)	-18.0 (-74.9 to 38.9)	4.6 (-66.5 to 75.8)

Notes:

[37] - High Risk Population

[38] - High Risk Population

[39] - High Risk Population

[40] - High Risk Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[41]	5[42]		
Units: International Units per Liter				
least squares mean (confidence interval 95%)	-18.4 (-93.6 to 56.8)	-6.7 (-89.1 to 75.8)		

Notes:

[41] - High Risk Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-106
Confidence interval	
level	95 %
sides	2-sided
lower limit	-205.1
upper limit	-6.8

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-65.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-148.5
upper limit	17.6

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-42.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-136.5
upper limit	50.9

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-65.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-161.2
upper limit	29.5

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-54.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-153.6
upper limit	45.3

Secondary: Mean change from Baseline at Week 16 in total bilirubin concentration, among those with a high risk of PBC progression

End point title	Mean change from Baseline at Week 16 in total bilirubin concentration, among those with a high risk of PBC progression

End point description:

Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 or Visit 1, excluding unscheduled visits. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Analysis was performed using ANCOVA including treatment group and Baseline. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[43]	5[44]	11[45]	7[46]
Units: Micromoles per Liter				
least squares mean (confidence interval 95%)	1.258 (-2.068 to 4.583)	-4.841 (-9.693 to 0.011)	-1.079 (-4.345 to 2.187)	-0.975 (-5.150 to 3.201)

Notes:

[43] - High Risk Population

[44] - High Risk Population

[45] - High Risk Population

[46] - High Risk Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[47]	5[48]		
Units: Micromoles per Liter				
least squares mean (confidence interval 95%)	-0.234 (-4.914 to 4.446)	6.494 (1.622 to 11.365)		

Notes:

[47] - High Risk Population

[48] - High Risk Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-6.099
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.929
upper limit	-0.268

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-2.337
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.962
upper limit	2.289

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-2.232
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.679
upper limit	3.215

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-1.492
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.413
upper limit	4.43

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	5.236
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.591
upper limit	11.063

Secondary: Mean change from Baseline at Week 16 in albumin concentration,

among those with a high risk of PBC progression	
End point title	Mean change from Baseline at Week 16 in albumin concentration, among those with a high risk of PBC progression

End point description:

Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 or Visit 1, excluding unscheduled visits. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Analysis was performed using ANCOVA including treatment group and Baseline. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11[49]	5[50]	11[51]	7[52]
Units: Grams per Liter				
least squares mean (confidence interval 95%)	0.0 (-1.2 to 1.3)	-0.5 (-2.3 to 1.3)	0.3 (-1.0 to 1.6)	0.8 (-0.8 to 2.3)

Notes:

[49] - High Risk Population

[50] - High Risk Population

[51] - High Risk Population

[52] - High Risk Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[53]	5[54]		
Units: Grams per Liter				
least squares mean (confidence interval 95%)	0.0 (-1.7 to 1.7)	0.7 (-1.1 to 2.5)		

Notes:

[53] - High Risk Population

[54] - High Risk Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	1.6

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	2.1

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	2.7

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	2

Statistical analysis title	Statistical Analysis 5

Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	2.9

Secondary: Mean change from Baseline at Week 16 in prothrombin international normalized ratio (INR), among those with a high risk of PBC progression

End point title	Mean change from Baseline at Week 16 in prothrombin international normalized ratio (INR), among those with a high risk of PBC progression

End point description:

Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 or Visit 1, excluding unscheduled visits. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Analysis was performed using ANCOVA model including treatment group and Baseline. Only those participants with data available at the specified data points were analyzed

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[55]	5[56]	11[57]	6[58]
Units: Ratio				
least squares mean (confidence interval 95%)	0.01 (-0.03 to 0.05)	-0.01 (-0.06 to 0.04)	-0.03 (-0.06 to 0.00)	0.01 (-0.04 to 0.05)

Notes:

[55] - High Risk Population

[56] - High Risk Population

[57] - High Risk Population

[58] - High Risk Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7[59]	5[60]		
Units: Ratio				
least squares mean (confidence interval 95%)	-0.02 (-0.07 to 0.02)	-0.03 (-0.08 to 0.02)		

Notes:

[59] - High Risk Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.04

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.01

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.05

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.02

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.02

Secondary: Mean change from Baseline at Week 16 in prothrombin time, among those with a high risk of PBC progression

End point title	Mean change from Baseline at Week 16 in prothrombin time, among those with a high risk of PBC progression

End point description:

Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 or Visit 1, excluding unscheduled visits. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Analysis was performed using ANCOVA model including treatment group and Baseline. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[61]	5[62]	11[63]	6[64]
Units: Seconds				
least squares mean (confidence interval 95%)	-0.10 (-0.40 to 0.20)	0.05 (-0.33 to 0.44)	-0.21 (-0.47 to 0.05)	0.02 (-0.33 to 0.37)

Notes:

[61] - High Risk Population

[62] - High Risk Population

[63] - High Risk Population

[64] - High Risk Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7[65]	5[66]		
Units: Seconds				
least squares mean (confidence interval 95%)	-0.18 (-0.51 to 0.15)	-0.17 (-0.55 to 0.22)		

Notes:

[65] - High Risk Population

[66] - High Risk Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.33
upper limit	0.63

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	0.3

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	0.58

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.38

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.41

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

serious adverse events (SAEs) -Main study period

End point title	Number of participants with non-serious adverse events (Non-SAEs) and serious adverse events (SAEs) -Main study period

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study treatment, whether or not considered related to the study treatment. Any untoward event resulting in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in persisting disability/incapacity, congenital anomaly/birth defect or any other situation according to medical or scientific judgment is categorized as SAE. Safety Population comprised of all randomized participants who received at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Up to 12 weeks

End point values	Placebo -Main Study Period	GSK2330672 20 mg QD - Main Study Period	GSK2330672 90 mg QD - Main Study Period	GSK2330672 180 mg QD - Main Study Period
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	36[67]	16[68]	23[69]	27[70]
Units: Participants				
Any non-SAE	17	11	19	24
Any SAE	0	0	1	0

Notes:

[67] - Safety Population

[68] - Safety Population

[69] - Safety Population

[70] - Safety Population

End point values	GSK2330672 40 mg BID - Main Study Period	GSK2330672 90 mg BID - Main Study Period		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23[71]	22[72]		
Units: Participants				
Any non-SAE	16	18		
Any SAE	0	0		

Notes:

[71] - Safety Population

[72] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with non-SAEs and SAEs -Final study period

End point title	Number of participants with non-SAEs and SAEs -Final study period

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study treatment, whether or not considered related to the study treatment. Any untoward event resulting in death, is life threatening, requires hospitalization or prolongation of existing hospitalization,

results in persisting disability/incapacity, congenital anomaly/birth defect or any other situation according to medical or scientific judgment is categorized as SAE.

End point type	Secondary

End point timeframe:

Up to 4 weeks

End point values	Placebo - Final Study Period	GSK2330672 20 mg QD - Final Study Period	GSK2330672 90 mg QD - Final Study Period	GSK2330672 180 mg QD - Final Study Period
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35[73]	16[74]	19[75]	19[76]
Units: Participants				
Any non-SAE	2	6	8	2
Any SAE	0	0	0	0

Notes:

[73] - Safety Population

[74] - Safety Population

[75] - Safety Population

[76] - Safety Population

End point values	GSK2330672 40 mg BID - Final Study Period	GSK2330672 90 mg BID - Final Study Period		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21[77]	17[78]		
Units: Participants				
Any non-SAE	2	2		
Any SAE	0	0		

Notes:

[77] - Safety Population

[78] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with non-SAEs and SAEs - Follow-up period

End point title	Number of participants with non-SAEs and SAEs - Follow-up period

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study treatment, whether or not considered related to the study treatment. Any untoward event resulting in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in persisting disability/incapacity, congenital anomaly/birth defect or any other situation according to medical or scientific judgment is categorized as SAE.

End point type	Secondary

End point timeframe:

Up to 4 weeks

End point values	Placebo - Follow-up	GSK2330672 20 mg QD - Follow-up	GSK2330672 90 mg QD - Follow-up	GSK2330672 180 mg QD - Follow-up
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35[79]	16[80]	23[81]	27[82]
Units: Participants				
Any non-SAE	0	0	0	0
Any SAE	0	1	0	1

Notes:

[79] - Safety Population

[80] - Safety Population

[81] - Safety Population

[82] - Safety Population

End point values	GSK2330672 40 mg BID - Follow-up	GSK2330672 90 mg BID - Follow-up		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22[83]	22[84]		
Units: Participants				
Any non-SAE	0	0		
Any SAE	0	0		

Notes:

[83] - Safety Population

[84] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinical chemistry data of potential clinical importance

End point title	Number of participants with clinical chemistry data of potential clinical importance

End point description:

Blood samples were collected to measure analyze the following parameters: albumin, calcium, Glomerular filtration rate (GFR) from creatinine, glucose, potassium and sodium. Participants were counted in the worst case category that their value changes to (low, within range [w/in] or no change, or high), unless there is no change in their category. Participants whose laboratory value category was unchanged (for example [e.g.], high to high), or whose value became within range, were recorded in the "To w/in Range or No Change" category. Participants were counted twice if the participant had values that changed "To Low" and "To High", so the percentages may not add to 100 percent (%). Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Only “To Low” and/or “To High” categories with potential clinical importance data have been presented.

End point type	Secondary

End point timeframe:

At Weeks 8, 12, 16 and 20

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[85]	16[86]	23[87]	27[88]
Units: Participants				
Albumin, To Low, Week 8, n=36, 16, 21, 21, 22, 19	0	0	0	0
Albumin, To Low, Week 12, n=35, 16, 21, 23, 22, 21	0	0	0	0
Albumin, To Low, Week 16, n=35, 16, 21, 22, 21, 20	0	0	0	0
Albumin, To Low, Week 20, n=35, 16, 22, 22, 22, 21	0	0	0	0
Calcium, To Low, Week 8, n=36, 16, 21, 21, 22, 19	0	0	0	0
Calcium, To High, Week 8, n=36, 16, 21, 21, 22, 19	0	0	0	0
Calcium, To Low, Week 12, n=35, 16, 21, 23, 22, 21	0	0	0	0
Calcium, To High, Week 12, n=35, 16, 21, 23, 22,21	0	0	0	0
Calcium, To Low, Week 16, n=35, 16, 21, 22, 21, 20	0	0	0	0
Calcium, To High, Week 16,n=35, 16, 21, 22, 21, 20	0	0	0	0
Calcium, To Low, Week 20, n=35,16, 22, 22, 22, 21	0	0	0	0
Calcium, To High, Week 20, n=35,16, 22, 22, 22, 21	1	0	0	0
GFR, To Low, Week 8, n=36, 16, 21, 21, 22, 19	0	0	0	0
GFR, To Low, Week 12, n=35, 15, 21, 23, 22, 21	0	0	0	0
GFR, To Low, Week 16, n=35, 16, 21, 22, 21, 21	0	0	0	0
GFR, To Low, Week 20, n=35, 16, 22, 22, 22, 21	0	0	0	1
Glucose ,To Low, Week 8, n=36, 16, 21, 21, 22, 19	0	0	0	0
Glucose ,To High, Week 8, n=36, 16, 21, 21, 22, 19	1	0	0	0
Glucose ,To Low, Week 12, n=35, 16, 21, 23, 22, 21	0	0	0	0
Glucose, To High, Week 12, n=35,16, 21, 23, 22, 21	0	0	0	0
Glucose ,To Low, Week 16, n=35, 16, 21, 22, 21,20	0	0	0	0
Glucose, To High, Week 16, n=35,16, 21, 22, 21, 20	0	0	0	0
Glucose ,To Low, Week 20, n=35, 16, 22, 22, 22, 21	0	0	0	0
Glucose, To High, Week 20, n=35,16, 22, 22, 22, 21	1	0	0	0
Potassium,To Low, Week 8, n=36, 16, 21, 21, 22, 19	0	0	0	0
Potassium, To High, Week 8, n=36,16, 21, 21, 22,19	0	0	0	0
Potassium,To Low, Week 12, n=35,16, 21, 23, 22, 21	0	0	0	0
Potassium,To High, Week 12,n=35,16, 21, 23, 22, 21	0	0	0	0

Potassium,To Low, Week 16, n=35,16, 21, 22, 21, 20	0	0	0	0
Potassium, To High, Week 16, n=35,16,21, 22, 21,20	0	0	0	0
Potassium,To Low, Week 20, n=35,16, 22, 22, 22, 21	0	0	0	0
Potassium, To High,Week 20, n=35,16, 22,22, 22, 21	0	0	0	0
Sodium, To Low, Week 8, n=36, 16, 21, 21, 22, 19	0	0	0	0
Sodium, To High, Week 8, n=36, 16, 21, 21, 22, 19	0	0	0	0
Sodium, To Low, Week 12, n=35, 16, 21, 23, 22, 21	0	0	0	0
Sodium, To High, Week 12, n=35,16, 21, 23, 22, 21	0	0	0	0
Sodium, To Low, Week 16, n=35, 16, 21, 22, 21, 20	0	0	0	0
Sodium, To High, Week 16, n=35,16, 21, 22, 21, 20	0	0	1	0
Sodium, To Low, Week 20, n=35, 16, 22, 22, 22, 21	0	0	0	0
Sodium, To High, Week 20, n=35,16, 22, 22, 22, 21	0	0	0	0

Notes:

[85] - Safety Population

[86] - Safety Population

[87] - Safety Population

[88] - Safety Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[89]	22[90]		
Units: Participants				
Albumin, To Low, Week 8, n=36, 16, 21, 21, 22, 19	0	0		
Albumin, To Low, Week 12, n=35, 16, 21, 23, 22, 21	0	0		
Albumin, To Low, Week 16, n=35, 16, 21, 22, 21, 20	0	0		
Albumin, To Low, Week 20, n=35, 16, 22, 22, 22, 21	0	0		
Calcium, To Low, Week 8, n=36, 16, 21, 21, 22, 19	0	0		
Calcium, To High, Week 8, n=36, 16, 21, 21, 22, 19	0	0		
Calcium, To Low, Week 12, n=35, 16, 21, 23, 22, 21	0	0		
Calcium, To High, Week 12, n=35, 16, 21, 23, 22,21	0	0		
Calcium, To Low, Week 16, n=35, 16, 21, 22, 21, 20	0	0		
Calcium, To High, Week 16,n=35, 16, 21, 22, 21, 20	0	0		
Calcium, To Low, Week 20, n=35,16, 22, 22, 22, 21	0	0		
Calcium, To High, Week 20, n=35,16, 22, 22, 22, 21	0	0		

GFR, To Low, Week 8, n=36, 16, 21, 21, 22, 19	0	0		
GFR, To Low, Week 12, n=35, 15, 21, 23, 22, 21	0	0		
GFR, To Low, Week 16, n=35, 16, 21, 22, 21, 21	0	0		
GFR, To Low, Week 20, n=35, 16, 22, 22, 22, 21	0	0		
Glucose ,To Low, Week 8, n=36, 16, 21, 21, 22, 19	0	0		
Glucose ,To High, Week 8, n=36, 16, 21, 21, 22, 19	0	1		
Glucose ,To Low, Week 12, n=35, 16, 21, 23, 22, 21	0	0		
Glucose, To High, Week 12, n=35,16, 21, 23, 22, 21	0	0		
Glucose ,To Low, Week 16, n=35, 16, 21, 22, 21,20	0	0		
Glucose, To High, Week 16, n=35,16, 21, 22, 21, 20	0	0		
Glucose ,To Low, Week 20, n=35, 16, 22, 22, 22, 21	0	0		
Glucose, To High, Week 20, n=35,16, 22, 22, 22, 21	0	0		
Potassium,To Low, Week 8, n=36, 16, 21, 21, 22, 19	0	0		
Potassium, To High, Week 8, n=36,16, 21, 21, 22,19	0	0		
Potassium,To Low, Week 12, n=35,16, 21, 23, 22, 21	0	0		
Potassium,To High, Week 12,n=35,16, 21, 23, 22, 21	0	0		
Potassium,To Low, Week 16, n=35,16, 21, 22, 21, 20	0	0		
Potassium, To High, Week 16, n=35,16,21, 22, 21,20	0	0		
Potassium,To Low, Week 20, n=35,16, 22, 22, 22, 21	0	0		
Potassium, To High,Week 20, n=35,16, 22,22, 22, 21	0	0		
Sodium, To Low, Week 8, n=36, 16, 21, 21, 22, 19	0	0		
Sodium, To High, Week 8, n=36, 16, 21, 21, 22, 19	0	0		
Sodium, To Low, Week 12, n=35, 16, 21, 23, 22, 21	0	0		
Sodium, To High, Week 12, n=35,16, 21, 23, 22, 21	0	0		
Sodium, To Low, Week 16, n=35, 16, 21, 22, 21, 20	0	0		
Sodium, To High, Week 16, n=35,16, 21, 22, 21, 20	0	0		
Sodium, To Low, Week 20, n=35, 16, 22, 22, 22, 21	0	0		
Sodium, To High, Week 20, n=35,16, 22, 22, 22, 21	0	0		

Notes:

[89] - Safety Population

[90] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with hematology data of potential clinical importance

End point title	Number of participants with hematology data of potential clinical importance

End point description:

Blood samples were collected to analyze the following parameters: hematocrit, hemoglobin, leukocytes, lymphocytes, neutrophils and platelets. Participants were counted in the worst case category that their value changes to (low, w/in or no change, or high), unless there is no change in their category. Participants whose laboratory value category was unchanged (e.g., high to high), or whose value became within range, were recorded in the "To w/in Range or No Change" category. Participants were counted twice if the participant had values that changed "To Low" and "To High", so the percentages may not add to 100%. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles). Only "To Low" and/or "To High" categories with potential clinical importance data have been presented.

End point type	Secondary

End point timeframe:

At Weeks 8, 12, 16 and 20

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[91]	16[92]	23[93]	27[94]
Units: Participants				
Hematocrit, To High, Week 8,n=36,16,21, 21, 22, 19	0	0	0	0
Hematocrit,To High, Week 12, n=33,15,21, 23, 22,20	0	0	0	0
Hematocrit,To High, Week 16, n=35,15,21,22,21,21	0	0	0	0
Hematocrit,To High, Week 20, n=34,16,22,22,22,20	0	0	0	0
Hemoglobin, To High, Week 8,n=36,16, 21,21, 22,19	0	0	0	0
Hemoglobin, To High, Week 12, n=33,15,21,23,22,20	0	0	0	0
Hemoglobin, To High, Week 16, n=35,15,21,22,21,21	0	0	0	0
Hemoglobin, To High, Week 20, n=34,16, 22,22,22,20	0	0	0	0
Leukocytes, To Low, Week 8, n=36,15, 21,21, 22,19	1	0	0	0
Leukocytes,To High, Week 8, n=36,15,21,21,22,19	0	0	0	0
Leukocytes,To Low,Week 12, n=33,15,21,23,22,20	1	1	1	0
Leukocytes,To High, Week 12, n=33,15,21,23, 22,20	0	0	0	0
Leukocytes, To Low, Week 16, n=34,15,21, 22, 20,21	1	0	3	1
Leukocytes,To High, Week 16, n=34,15,21,22, 20,21	0	0	0	0
Leukocytes, To Low, Week 20, n=34,16,22,21,22,19	0	1	1	0
Leukocytes, To High, Week 20, n=34,16,22,21,22,19	0	0	0	0

Lymphocytes, To Low, Week 8, n=35,15,21,21,22,19	2	0	0	0
Lymphocytes, To Low, Week 12, n=32,15,21,23,22,20	1	0	0	2
Lymphocytes, To Low, Week 16, n=34,15,21,22,20,21	0	0	0	1
Lymphocytes, To Low, Week 20, n=34,16,22,21,22,19	0	0	1	0
Neutrophils, To Low, Week 8,n=35,15,21,21,22,19	1	1	0	1
Neutrophils, To Low, Week 12, n=32,15,21,23,22,20	0	1	0	1
Neutrophils, To Low, Week 16, n=34,15,21,22,20,21	1	0	2	0
Neutrophils, To Low, Week 20, n=34,16,22,21,22,19	0	0	1	0
Platelets, To Low, Week 8,n=36,15,20,21,22,19	0	0	0	0
Platelets, To High, Week 8,n=36,15,20,21,22,19	0	0	0	0
Platelets, To Low, Week 12, n=33,14,19,23,22,20	0	0	0	0
Platelets,To High, Week 12, n=33,14,19,23,22,20	0	0	0	0
Platelets, To Low, Week 16, n=35,14,19,22, 21,21	1	0	0	0
Platelets,To High, Week 16, n=35,14,19,22, 21,21	1	0	0	0
Platelets, To Low, Week 20, n=33,16,21,21,22,20	0	0	0	0
Platelets,To High, Week 20, n=33,16,21,21,22,20	0	0	0	0

Notes:

[91] - Safety Population

[92] - Safety Population

[93] - Safety Population

[94] - Safety Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[95]	22[96]		
Units: Participants				
Hematocrit, To High, Week 8,n=36,16,21, 21, 22, 19	0	0		
Hematocrit,To High, Week 12, n=33,15,21, 23, 22,20	0	0		
Hematocrit,To High, Week 16, n=35,15,21,22,21,21	0	0		
Hematocrit,To High, Week 20, n=34,16,22,22,22,20	0	0		
Hemoglobin, To High, Week 8,n=36,16, 21,21, 22,19	0	0		
Hemoglobin, To High, Week 12, n=33,15,21,23,22,20	0	0		
Hemoglobin, To High, Week 16, n=35,15,21,22,21,21	0	0		
Hemoglobin, To High, Week 20, n=34,16, 22,22,22,20	0	0		

Leukocytes, To Low, Week 8, n=36,15, 21,21, 22,19	1	0		
Leukocytes,To High, Week 8, n=36,15,21,21,22,19	0	0		
Leukocytes,To Low,Week 12, n=33,15,21,23,22,20	0	0		
Leukocytes,To High, Week 12, n=33,15,21,23, 22,20	0	0		
Leukocytes, To Low, Week 16, n=34,15,21, 22, 20,21	1	0		
Leukocytes,To High, Week 16, n=34,15,21,22, 20,21	0	0		
Leukocytes, To Low, Week 20, n=34,16,22,21,22,19	0	0		
Leukocytes, To High, Week 20, n=34,16,22,21,22,19	0	0		
Lymphocytes, To Low, Week 8, n=35,15,21,21,22,19	0	0		
Lymphocytes, To Low, Week 12, n=32,15,21,23,22,20	0	0		
Lymphocytes, To Low, Week 16, n=34,15,21,22,20,21	0	0		
Lymphocytes, To Low, Week 20, n=34,16,22,21,22,19	0	0		
Neutrophils, To Low, Week 8,n=35,15,21,21,22,19	1	1		
Neutrophils, To Low, Week 12, n=32,15,21,23,22,20	0	1		
Neutrophils, To Low, Week 16, n=34,15,21,22,20,21	1	0		
Neutrophils, To Low, Week 20, n=34,16,22,21,22,19	0	0		
Platelets, To Low, Week 8,n=36,15,20,21,22,19	0	0		
Platelets, To High, Week 8,n=36,15,20,21,22,19	0	0		
Platelets, To Low, Week 12, n=33,14,19,23,22,20	0	1		
Platelets,To High, Week 12, n=33,14,19,23,22,20	0	0		
Platelets, To Low, Week 16, n=35,14,19,22, 21,21	0	1		
Platelets,To High, Week 16, n=35,14,19,22, 21,21	0	0		
Platelets, To Low, Week 20, n=33,16,21,21,22,20	0	0		
Platelets,To High, Week 20, n=33,16,21,21,22,20	0	0		

Notes:

[95] - Safety Population

[96] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal 12-Lead Electrocardiogram (ECG) parameters

End point title	Number of participants with abnormal 12-Lead Electrocardiogram (ECG) parameters

End point description:

A 12-lead ECG was recorded with the participant in a semi-supine position. 12-lead ECGs were obtained by using an automated ECG machine. Data for abnormal, not clinically significant (NCS) and clinically significant (CS) ECG findings are presented. CS abnormal findings are those which are not associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition. 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:

At Weeks 8, 12, 16 and 20

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[97]	16[98]	23[99]	27[100]
Units: Participants				
Abnormal, NCS, Week 8, n=36, 16, 21, 21, 22,19	10	2	1	7
Abnormal, CS, Week 8, n=36, 16, 21, 21, 22, 19	0	0	0	1
Abnormal, NCS, Week 12, n= 35, 16, 20, 23, 22, 21	9	3	3	8
Abnormal, CS, Week 12, n=35, 16, 20, 23, 22, 21	0	0	0	0
Abnormal, NCS, Week 16, n= 35, 16, 21, 21, 22 ,21	9	3	2	5
Abnormal, CS, Week 16, n=35, 16, 21, 21, 22, 21	0	0	0	0
Abnormal, NCS, Week 20, n=35, 16, 22, 22, 22, 20	8	3	2	7
Abnormal, CS, Week 20, n=35, 16, 22, 22, 22, 20	0	0	0	0

Notes:

[97] - Safety Population

[98] - Safety Population

[99] - Safety Population

[100] - Safety Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[101]	22[102]		
Units: Participants				
Abnormal, NCS, Week 8, n=36, 16, 21, 21, 22,19	8	4		
Abnormal, CS, Week 8, n=36, 16, 21, 21, 22, 19	0	0		
Abnormal, NCS, Week 12, n= 35, 16, 20, 23, 22, 21	8	4		
Abnormal, CS, Week 12, n=35, 16, 20, 23, 22, 21	0	0		
Abnormal, NCS, Week 16, n= 35, 16, 21, 21, 22 ,21	7	4		
Abnormal, CS, Week 16, n=35, 16, 21, 21, 22, 21	0	0		

Abnormal, NCS, Week 20, n=35, 16, 22, 22, 22, 20	8	3		
Abnormal, CS, Week 20, n=35, 16, 22, 22, 22, 20	0	0		

Notes:

[101] - Safety Population

[102] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)

End point title	Change From Baseline in Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)

End point description:

SBP and DBP were measured in the semi-supine position with a completely automated device after at least 5 minutes of rest for the participant in a quiet setting without distractions. Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 or Visit 1, excluding unscheduled visits. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 20

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35[103]	16[104]	22[105]	22[106]
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP	-3.3 (± 13.33)	-2.1 (± 11.47)	0.1 (± 12.78)	0.7 (± 10.42)
DBP	-1.3 (± 8.99)	0.3 (± 7.75)	-0.3 (± 9.16)	-0.7 (± 5.51)

Notes:

[103] - Safety Population

[104] - Safety Population

[105] - Safety Population

[106] - Safety Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[107]	21[108]		
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP	-0.3 (± 15.16)	2.0 (± 15.43)		
DBP	2.5 (± 8.64)	2.3 (± 7.23)		

Notes:

[107] - Safety Population

[108] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pulse Rate

End point title	Change from Baseline in Pulse Rate

End point description:

Pulse rate was measured in a semi-supine position after 5 minutes of rest. Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 or Visit 1, excluding unscheduled visits. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 20

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35[109]	16[110]	22[111]	22[112]
Units: Beats per minute				
arithmetic mean (standard deviation)	1.5 (± 7.19)	-2.6 (± 10.35)	1.2 (± 10.91)	-0.2 (± 7.93)

Notes:

[109] - Safety Population

[110] - Safety Population

[111] - Safety Population

[112] - Safety Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[113]	21[114]		
Units: Beats per minute				
arithmetic mean (standard deviation)	3.4 (± 8.92)	0.5 (± 8.03)		

Notes:

[113] - Safety Population

[114] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Gastrointestinal Symptom Rating Scale (GSRS) assessment

End point title	Change from Baseline in Gastrointestinal Symptom Rating Scale (GSRS) assessment

End point description:

GSRS was measured for all 5 domains: Average Diarrhea Syndrome Score, Average Indigestion Syndrome Score, Average Constipation Syndrome Score, Average Abdominal Pain Syndrome Score, Average Reflux Syndrome Score. All individual domains are scored on a 7-point Likert scale ranging from 1(not at all) to 7(extremely). Higher score indicate more severe symptoms. The Average Total GSRS score was mean of these 5 domains and ranges from 1 to 7. Higher score indicates worst possible degree of symptoms. The responses summarized at each visit are those given during the week prior to the visit, with exception of Day 1. Baseline is the most recent assessment completed by participant prior

to randomization. Change from Baseline was calculated as post-Baseline value minus the Baseline value. Data has been presented for each domain along with the average Total GSRS score. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 20

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33[115]	16[116]	20[117]	21[118]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Average Diarrhea Syndrome Score	0.22 (± 1.343)	0.15 (± 1.587)	0.23 (± 1.180)	-0.13 (± 0.637)
Average Indigestion Syndrome Score	-0.01 (± 1.138)	0.09 (± 0.865)	-0.03 (± 0.811)	-0.14 (± 0.820)
Average Constipation Syndrome Score	-0.03 (± 1.045)	-0.15 (± 0.989)	0.32 (± 1.370)	-0.02 (± 0.934)
Average Abdominal Pain Syndrome Score	-0.05 (± 1.074)	0.06 (± 0.712)	-0.02 (± 1.000)	-0.06 (± 0.629)
Average Reflux Syndrome Score	-0.09 (± 1.208)	-0.13 (± 0.619)	-0.20 (± 1.332)	-0.26 (± 0.664)
Average Total Score	0.01 (± 0.830)	0.02 (± 0.668)	0.07 (± 0.802)	-0.11 (± 0.433)

Notes:

[115] - Safety Population

[116] - Safety Population

[117] - Safety Population

[118] - Safety Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[119]	20[120]		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Average Diarrhea Syndrome Score	-0.23 (± 1.729)	0.22 (± 1.565)		
Average Indigestion Syndrome Score	-0.31 (± 1.046)	-0.54 (± 1.007)		
Average Constipation Syndrome Score	-0.32 (± 1.215)	-0.37 (± 0.772)		
Average Abdominal Pain Syndrome Score	-0.08 (± 0.885)	-0.25 (± 0.904)		
Average Reflux Syndrome Score	-0.16 (± 0.762)	-0.43 (± 0.847)		
Average Total Score	-0.23 (± 0.690)	-0.28 (± 0.695)		

Notes:

[119] - Safety Population

[120] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Mean Worst Daily Itch Score of <4 at Week 16

End point title	Number of participants with Mean Worst Daily Itch Score of <4 at Week 16

End point description:

Participants were required to score the severity of their itching using a 0-10 NRS where 0 represents no itching and 10 indicates the worst imaginable itching. The Worst Daily Itch Score is the most severe (highest) NRS recorded on a given day. Mean Worst Daily Itch score was calculated as the average of the worst daily itch scores provided in the 7 days prior to the Week 16 visit. Number of participants with Mean Worst Daily Itch Score of <4 at Week 16 is presented.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[121]	16[122]	23[123]	27[124]
Units: Participants	21	13	14	18

Notes:

[121] - ITT Population

[122] - ITT Population

[123] - ITT Population

[124] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[125]	22[126]		
Units: Participants	18	14		

Notes:

[125] - ITT Population

[126] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed using Logistic regression. No covariates were used.

Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	2.89

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	12.02

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Analysis was performed using Logistic regression. No covariates were used.	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	5.02

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Analysis was performed using Logistic regression. No covariates were used.	
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	10.76

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Analysis was performed using Logistic regression. No covariates were used.	
Comparison groups	Placebo v GSK2330672 40 mg BID

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	10.76

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Analysis was performed using Logistic regression. No covariates were used	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	4.13

Secondary: Number of participants with improvement of >= 30 percent (%) in the Mean Worst Daily Itch Score at Week 16 from Baseline

End point title	Number of participants with improvement of >= 30 percent (%) in the Mean Worst Daily Itch Score at Week 16 from Baseline

End point description:

Participants were required to score the severity of their itching using a 0-10 NRS where 0 represents no itching and 10 indicates the worst imaginable itching. The Worst Daily Itch Score is the most severe (highest) NRS recorded on a given day. Mean Worst Daily Itch score was calculated as the average of the worst daily itch scores provided in the 7 days prior to the Week 16 visit. Baseline is the most recent assessment completed by the participant prior to randomization. Number of participants with improvement of >= 30% in the Mean Worst Daily Itch Score at Week 16 from Baseline is presented.

End point type	Secondary

End point timeframe:

Baseline and At Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[127]	16[128]	23[129]	27[130]
Units: Participants	17	9	15	14

Notes:

[127] - ITT Population

[128] - ITT Population

[129] - ITT Population

[130] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[131]	22[132]		
Units: Participants	15	14		

Notes:

[131] - ITT Population

[132] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Analysis was performed using Logistic regression. No covariates were used.	
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	4.47

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Analysis was performed using Logistic regression. No covariates were used.	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	3.18

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	10.65

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Analysis was performed using Logistic regression. No covariates were used.	
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	5.53

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Analysis was performed using Logistic regression. No covariates were used.	
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	2.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	6.92

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Analysis was performed using Logistic regression. No covariates were used.	
Comparison groups	Placebo v GSK2330672 90 mg BID

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	2.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	6.51

Secondary: Number of participants with improvement of >=2 in the Mean Worst Daily Itch Score at Week 16 from Baseline

End point title	Number of participants with improvement of >=2 in the Mean Worst Daily Itch Score at Week 16 from Baseline

End point description:

Participants were required to score the severity of their itching using a 0-10 NRS where 0 represents no itching and 10 indicates the worst imaginable itching. The Worst Daily Itch Score is the most severe (highest) NRS recorded on a given day. Mean Worst Daily Itch score was calculated as the average of the worst daily itch scores provided in the 7 days prior to the Week 16 visit. Baseline is the most recent assessment completed by the participant prior to randomization. Number of participants with improvement of >=2 in the Mean Worst Daily Itch Score at Week 16 from Baseline is presented.

End point type	Secondary

End point timeframe:

Baseline and At Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[133]	16[134]	23[135]	27[136]
Units: Participants	14	6	12	9

Notes:

[133] - ITT Population

[134] - ITT Population

[135] - ITT Population

[136] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[137]	22[138]		
Units: Participants	13	12		

Notes:

[137] - ITT Population

[138] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Analysis was performed using Logistic regression. No covariates were used.	
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	3.04

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Analysis was performed using Logistic regression. No covariates were used.	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	2.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	6.91

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Analysis was performed using Logistic regression. No covariates were used.	
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	3.08

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Analysis was performed using Logistic regression. No covariates were used.	
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	2.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	6.42

Statistical analysis title	Statistical Analysis 5
Statistical analysis description: Analysis was performed using Logistic regression. No covariates were used.	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Odds ratio (OR)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	5.99

Secondary: Percentage of responder days with Worst Daily Itch Score of <4

End point title	Percentage of responder days with Worst Daily Itch Score of <4
End point description: Percentage of Responder Days with Worst Daily Itch score was calculated as: (number of days response from Visit 3+1 to Visit 6-1 divided by number of days from Visit 3+1 to Visit 6-1 with worst daily itch scores available) times 100. Days for which no worst daily itch score was available did not contribute to either the numerator or the denominator. Analysis was performed using ANCOVA model including treatment group. Percentage of responder days with Worst Daily Itch Score of <4 is presented.	
End point type	Secondary
End point timeframe: Up to Week 16	

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[139]	16[140]	23[141]	27[142]
Units: Percentage of days				
least squares mean (confidence interval 95%)	40.32 (28.79 to 51.86)	58.53 (41.23 to 75.83)	51.38 (36.95 to 65.81)	58.76 (45.45 to 72.08)

Notes:

[139] - ITT Population

[140] - ITT Population

[141] - ITT Population

[142] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[143]	22[144]		
Units: Percentage of days				
least squares mean (confidence interval 95%)	65.80 (51.37 to 80.23)	53.58 (38.83 to 68.34)		

Notes:

[143] - ITT Population

[144] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	18.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.59
upper limit	39

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	11.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.42
upper limit	29.53

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	18.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	36.06

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	25.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	7
upper limit	43.95

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	13.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.47
upper limit	31.99

Secondary: Percentage of responder days with improvement of >= 30% in the Mean Worst Daily Itch Score at Week 16 from Baseline

End point title	Percentage of responder days with improvement of >= 30% in the Mean Worst Daily Itch Score at Week 16 from Baseline

End point description:

Percentage of Responder Days with Worst Daily Itch score was calculated as: (number of days response from Visit 3+1 to Visit 6-1 divided by number of days from Visit 3+1 to Visit 6-1 with worst daily itch scores available) times 100. Days for which no worst daily itch score was available did not contribute to either the numerator or the denominator. Analysis was performed using ANCOVA model including treatment group. Baseline is the most recent assessment completed by the participant prior to randomization. Percentage of responder days with improvement of >= 30% in the Mean Worst Daily Itch Score at Week 16 from Baseline is presented.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[145]	16[146]	23[147]	27[148]
Units: Percentage of days				
least squares mean (confidence interval 95%)	38.46 (27.30 to 49.61)	53.44 (36.71 to 70.18)	45.43 (31.47 to 59.39)	50.23 (37.35 to 63.12)

Notes:

[145] - ITT Population

[146] - ITT Population

[147] - ITT Population

[148] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[149]	22[150]		
Units: Percentage of days				
least squares mean (confidence interval 95%)	60.29 (46.33 to 74.25)	60.03 (45.76 to 74.31)		

Notes:
[149] - ITT Population
[150] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	14.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.13
upper limit	35.1

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	6.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.9
upper limit	24.84

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	11.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.27
upper limit	28.82

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	21.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.96
upper limit	39.7

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	21.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.46
upper limit	39.69

Secondary: Percentage of responder days with improvement of >=2 in the Mean Worst Daily Itch Score at Week 16 from Baseline

End point title	Percentage of responder days with improvement of >=2 in the Mean Worst Daily Itch Score at Week 16 from Baseline

End point description:

Percentage of Responder Days with Worst Daily Itch score was calculated as: (number of days response from Visit 3+1 to Visit 6-1 divided by number of days from Visit 3+1 to Visit 6-1 with worst daily itch scores available) times 100. Days for which no worst daily itch score was available did not contribute to either the numerator or the denominator. Analysis was performed using ANCOVA model including treatment group. Baseline is the most recent assessment completed by the participant prior to randomization. Percentage of responder days with improvement of >=2 in the Mean Worst Daily Itch Score at Week 16 from Baseline is presented.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[151]	16[152]	23[153]	27[154]
Units: Percentage of days				
least squares mean (confidence interval 95%)	31.56 (19.96 to 43.16)	37.71 (20.31 to 55.11)	38.82 (24.31 to 53.33)	40.69 (27.29 to 54.08)

Notes:

[151] - ITT Population

[152] - ITT Population

[153] - ITT Population

[154] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[155]	22[156]		
Units: Percentage of days				
least squares mean (confidence interval 95%)	51.49 (36.98 to 66.00)	58.60 (43.76 to 73.43)		

Notes:

[155] - ITT Population

[156] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	6.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.76
upper limit	27.06

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	7.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.32
upper limit	25.84

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	9.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.59
upper limit	26.85

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	19.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.36
upper limit	38.51

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	27.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.2
upper limit	45.87

Secondary: Change from Baseline in the Mean Daily Sleep Score at Week 16

End point title	Change from Baseline in the Mean Daily Sleep Score at Week 16

End point description:

Mean Daily Sleep Score is defined as the average of the daily sleep scores provided in the 7 days prior to the relevant visit. Participants sleep quality was recorded in an electronic diary each morning using a 0-10 NRS in which 0: good sleep to 10:worst possible sleep. Higher score indicates worse possible sleep. Baseline is the average of the scores in the 7 days prior to the Week 4 (V3) visit. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Analysis was performed using ANCOVA including treatment group and Baseline. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35[157]	16[158]	20[159]	22[160]
Units: Scores on a scale				
least squares mean (confidence interval 95%)	-1.39 (-2.06 to -0.72)	-1.66 (-2.64 to -0.67)	-1.87 (-2.75 to -0.99)	-1.85 (-2.69 to -1.01)

Notes:

[157] - ITT Population

[158] - ITT Population

[159] - ITT Population

[160] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[161]	20[162]		
Units: Scores on a scale				
least squares mean (confidence interval 95%)	-2.35 (-3.19 to -1.50)	-1.69 (-2.57 to -0.81)		

Notes:

[161] - ITT Population

[162] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.46
upper limit	0.92

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.58
upper limit	0.62

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.53
upper limit	0.61

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.03
upper limit	0.12

Statistical analysis title	Statistical Analysis 5

Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.8

Secondary: Change from Baseline in the Mean Daily Fatigue Score at Week 16

End point title	Change from Baseline in the Mean Daily Fatigue Score at Week 16

End point description:

Mean Daily Fatigue Score is defined as the average of the daily fatigue scores provided in the 7 days prior to the relevant visit. Participants fatigue level was recorded in an electronic diary each evening using a 0-10 NRS in which 0: no fatigue to 10:worst possible fatigue. Higher score indicates worse possible fatigue. Baseline is the average of the scores in the 7 days prior to the Week 4 (V3) visit. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Analysis was performed using ANCOVA model including treatment group and Baseline. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35[163]	16[164]	20[165]	22[166]
Units: Scores on a scale				
least squares mean (confidence interval 95%)	-0.79 (-1.39 to -0.18)	-1.18 (-2.08 to -0.27)	-1.19 (-2.00 to -0.37)	-1.04 (-1.81 to -0.28)

Notes:

[163] - ITT Population

[164] - ITT Population

[165] - ITT Population

[166] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[167]	21[168]		
Units: Scores on a scale				
least squares mean (confidence interval 95%)	-1.20 (-1.97 to -0.44)	-1.07 (-1.86 to -0.29)		

Notes:
[167] - ITT Population
[168] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	0.71

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.41
upper limit	0.61

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.24
upper limit	0.72

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	0.56

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.28
upper limit	0.7

Secondary: Change from Baseline in the Five Dimensional (5-D) Itch Scale at Week 16

End point title	Change from Baseline in the Five Dimensional (5-D) Itch Scale at Week 16

End point description:

The 5-D itch scale is instrument for multidimensional quantification of itch that is sensitive to change over time. It has data to support its validity in pruritus participants and covers five dimensions of itch: duration, degree, direction, disability and distribution. Each domain was scored on a 5-point scale, ranging from 1 (Not present/resolved/never) to 5 (unbearable/getting worse/always), higher scores indicates worst itching. The scores of each of five domains were achieved separately and then summed together to obtain a total 5-D score. A total 5-D scores ranged between 5 (no pruritus) and 25 (most severe pruritus) where higher score indicates worse possible itching. Baseline is assessment performed at Week 4 (V3) which is conducted prior to first dosing of randomized medication that evening. Change from Baseline was calculated as post-Baseline value minus Baseline value. Only those participants with data available at the specified data points were analyzed

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35[169]	16[170]	21[171]	21[172]
Units: Scores on a scale				
least squares mean (confidence interval 95%)				
Duration	-0.8 (-1.1 to -0.4)	-0.9 (-1.3 to -0.4)	-0.4 (-0.8 to 0.0)	-1.2 (-1.6 to -0.8)
Degree	-0.7 (-1.0 to -0.4)	-0.9 (-1.4 to -0.5)	-0.7 (-1.1 to -0.3)	-0.7 (-1.2 to -0.3)
Direction	-0.7 (-1.1 to -0.3)	-0.7 (-1.3 to -0.1)	-0.7 (-1.2 to -0.2)	-0.9 (-1.4 to -0.4)
Disability	-0.4 (-0.7 to 0.0)	-0.8 (-1.4 to -0.2)	-0.5 (-1.0 to 0.0)	-0.7 (-1.2 to -0.2)
Distribution	-0.4 (-0.7 to -0.1)	-0.7 (-1.2 to -0.2)	-0.7 (-1.1 to -0.3)	-0.9 (-1.3 to -0.5)
5-D Itch Total Score	-3.0 (-4.2 to -1.7)	-4.0 (-5.9 to -2.0)	-3.0 (-4.7 to -1.3)	-4.4 (-6.0 to -2.7)

Notes:

[169] - ITT Population

[170] - ITT Population

[171] - ITT Population

[172] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[173]	20[174]		
Units: Scores on a scale				
least squares mean (confidence interval 95%)				
Duration	-0.6 (-1.0 to -0.2)	-0.7 (-1.1 to -0.3)		
Degree	-0.9 (-1.3 to -0.5)	-0.8 (-1.2 to -0.4)		
Direction	-1.1 (-1.6 to -0.6)	-0.7 (-1.2 to -0.2)		
Disability	-0.7 (-1.2 to -0.2)	-0.7 (-1.2 to -0.1)		
Distribution	-0.7 (-1.2 to -0.3)	-0.6 (-1.0 to -0.2)		
5-D Itch Total Score	-3.8 (-5.4 to -2.2)	-3.5 (-5.2 to -1.8)		

Notes:

[173] - ITT Population

[174] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Duration

Comparison groups	Placebo v GSK2330672 20 mg QD

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.5

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Duration	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.9

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Duration	
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.1

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Duration	

Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.7

Statistical analysis title	Statistical Analysis 5
Statistical analysis description: Duration	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.6

Statistical analysis title	Statistical Analysis 6
Statistical analysis description: Degree	
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.3

Statistical analysis title	Statistical Analysis 7

Statistical analysis description:	
Degree	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.5

Statistical analysis title	Statistical Analysis 8
Statistical analysis description:	
Degree	
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.5

Statistical analysis title	Statistical Analysis 9
Statistical analysis description:	
Degree	
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.3

Statistical analysis title	Statistical Analysis 10
Statistical analysis description: Degree	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.4

Statistical analysis title	Statistical Analysis 11
Statistical analysis description: Direction	
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.7

Statistical analysis title	Statistical Analysis 12
Statistical analysis description: Direction	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.6

Statistical analysis title	Statistical Analysis 13
Statistical analysis description: Direction	
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.5

Statistical analysis title	Statistical Analysis 14
Statistical analysis description: Direction	
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.2

Statistical analysis title	Statistical Analysis 15
Statistical analysis description: Direction	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.6

Statistical analysis title	Statistical Analysis 16
Statistical analysis description: Disability	
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.3

Statistical analysis title	Statistical Analysis 17
Statistical analysis description: Disability	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.5

Statistical analysis title	Statistical Analysis 18
Statistical analysis description: Disability	
Comparison groups	Placebo v GSK2330672 180 mg QD

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.3

Statistical analysis title	Statistical Analysis 19
Statistical analysis description: Disability	
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.3

Statistical analysis title	Statistical Analysis 20
Statistical analysis description: Disability	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.3

Statistical analysis title	Statistical Analysis 21
Statistical analysis description: Distribution	

Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.3

Statistical analysis title	Statistical Analysis 22
Statistical analysis description: Distribution	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.2

Statistical analysis title	Statistical Analysis 23
Statistical analysis description: Distribution	
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0

Statistical analysis title	Statistical Analysis 24

Statistical analysis description: Distribution	
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.2

Statistical analysis title	Statistical Analysis 25
Statistical analysis description: Distribution	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.3

Statistical analysis title	Statistical Analysis 26
Statistical analysis description: 5-D Itch Total Score	
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	1.3

Statistical analysis title	Statistical Analysis 27
Statistical analysis description: 5-D Itch Total Score	
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	2.1

Statistical analysis title	Statistical Analysis 28
Statistical analysis description: 5-D Itch Total Score	
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	0.7

Statistical analysis title	Statistical Analysis 29
Statistical analysis description: 5-D Itch Total Score	
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	1.2

Statistical analysis title	Statistical Analysis 30
Statistical analysis description: 5-D Itch Total Score	
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	1.6

Secondary: Mean change from Baseline at Week 16 in serum total bile acid concentration

End point title	Mean change from Baseline at Week 16 in serum total bile acid concentration
End point description: Blood samples were collected for evaluating total bile acid concentration as a biomarker of PBC. Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 or Visit 1, excluding unscheduled visits. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Only those participants with data available at the specified data points were analyzed.	
End point type	Secondary
End point timeframe: Baseline and at Week 16	

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35[175]	16[176]	20[177]	22[178]
Units: Micromoles per Liter				
arithmetic mean (standard deviation)	-4.274 (± 20.0163)	-0.469 (± 6.5466)	-3.878 (± 40.1857)	-1.114 (± 6.9359)

Notes:

[175] - ITT Population

[176] - ITT Population

[177] - ITT Population

[178] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[179]	21[180]		

Units: Micromoles per Liter				
arithmetic mean (standard deviation)	-2.133 (± 8.9308)	7.379 (± 38.8282)		

Notes:

[179] - ITT Population

[180] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline at Week 16 in serum 7-alpha hydroxy-4-cholesten-3-one (C4)

End point title	Mean change from Baseline at Week 16 in serum 7-alpha hydroxy-4-cholesten-3-one (C4)

End point description:

Blood samples were collected for evaluating C4 concentration as a marker of bile acid synthesis. Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 or Visit 1, excluding unscheduled visits. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and at Week 16

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35[181]	15[182]	21[183]	22[184]
Units: Micrograms per Liter				
arithmetic mean (standard deviation)	4.746 (± 11.5644)	10.703 (± 24.6045)	11.452 (± 16.6371)	29.488 (± 38.7584)

Notes:

[181] - ITT Population

[182] - ITT Population

[183] - ITT Population

[184] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[185]	20[186]		
Units: Micrograms per Liter				
arithmetic mean (standard deviation)	58.674 (± 59.4833)	40.629 (± 36.2769)		

Notes:

[185] - ITT Population

[186] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of GSK2330672 after sparse sampling

End point title	Plasma concentration of GSK2330672 after sparse sampling[187]

End point description:

Blood samples were collected for measurement of plasma GSK2330672 concentration at Week 4 (between [B/W] 1 and 3 hours post-dose) and At Weeks 8, 12 and 16 (between 1 and 3 hours post-dose, and between 5 and 8 hours post-dose. "99999" indicates standard deviation could not be calculated as >30% of samples were below the limit of quantification. Pharmacokinetic (PK) Population consisted of any randomized participant who had at least one PK sample. Only those participants with data available at the specified data points were analyzed (represented by n=X in category titles).

End point type	Secondary

End point timeframe:

At Week 4 (between 1 and 3 hours post-dose) and At Weeks 8, 12 and 16 (between 1 and 3 hours post-dose, and between 5 and 8 hours post-dose)

Notes:

[187] - 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	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD	GSK2330672 40 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16[188]	23[189]	27[190]	23[191]
Units: Picograms per milliliter				
arithmetic mean (standard deviation)				
Week 4, B/W 1 and 3 hours post-dose, n=6, 2,7, 0,4	5.00 (± 99999)	5.00 (± 99999)	32.71 (± 73.325)	99999 (± 99999)
Week8, B/W 1 and 3 hour post-dose,n=16,21,20,22,17	358.04 (± 665.685)	958.81 (± 1563.265)	2327.58 (± 3737.965)	453.45 (± 967.424)
Week8, B/W 5 and 8hour post-dose,n=14, 17,18,21,16	300.04 (± 356.268)	820.87 (± 1143.023)	2234.28 (± 3420.442)	339.74 (± 357.914)
Week12,B/W 1 and 3 hours post-dose,n=14,1917,20,14	447.88 (± 1160.518)	1594.16 (± 3133.370)	2060.51 (± 2888.033)	419.47 (± 774.321)
Week12,B/W 5 and 8 hour post-dose,n=14,16,17,20,13	341.39 (± 638.359)	1084.00 (± 1353.089)	2569.00 (± 3727.883)	303.83 (± 300.716)
Week16,B/W 1 and 3hours post-dose,n=3, 5, 4, 2, 5	394.00 (± 162.151)	864.26 (± 1045.467)	3328.50 (± 3185.646)	338.50 (± 236.881)
Week16,B/W 5 and 8 hour post-dose,n=3, 3, 4, 2, 5	296.33 (± 118.154)	578.00 (± 651.263)	1940.50 (± 1128.203)	364.50 (± 217.082)

Notes:

[188] - PK Population

[189] - PK Population

[190] - PK Population

[191] - PK Population. 99999 indicates data was not available.

End point values	GSK2330672 90 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	22[192]			
Units: Picograms per milliliter				
arithmetic mean (standard deviation)				
Week 4, B/W 1 and 3 hours post-dose, n=6, 2,7, 0,4	5.00 (± 99999)			
Week8, B/W 1 and 3 hour post-dose,n=16,21,20,22,17	2908.06 (± 5106.895)			
Week8, B/W 5 and 8hour post-dose,n=14, 17,18,21,16	1990.89 (± 4061.978)			

Week12,B/W 1 and 3 hours post-dose,n=14,1917,20,14	3531.36 (± 6296.828)			
Week12,B/W 5 and 8 hour post-dose,n=14,16,17,20,13	2197.16 (± 3604.704)			
Week16,B/W 1 and 3hours post-dose,n=3, 5, 4, 2, 5	703.60 (± 756.010)			
Week16,B/W 5 and 8 hour post-dose,n=3, 3, 4, 2, 5	869.40 (± 1148.331)			

Notes:

[192] - PK Population. 99999 indicates data was not available.

Statistical analyses

No statistical analyses for this end point

Post-hoc: Mean change from Baseline in Monthly Itch Score

End point title	Mean change from Baseline in Monthly Itch Score

End point description:

Participants were required to score severity of their itching each morning and evening using a 0-10 NRS where 0(no itching) and 10(worst imaginable itching). The worst of these 2 scores was Worst Daily Itch Score. For each week, mean Worst Daily Itch Score was calculated to form Mean Worst Daily Itch Score. The Monthly Itch Score was defined as worst weekly score (e.g., Mean Worst Daily Itch Score) for that month. The monthly itch score ranges from 0 to 10, higher score indicates worst imaginable itching. Baseline is average of scores in the 7 days prior to Week 4 (Visit 3 [V3]). Change from Baseline was calculated as post-Baseline value minus Baseline value. Analysis was performed on change in Monthly Itch Scores over 12 week treatment period using Mixed model repeated measures (MMRM) with Baseline itch, treatment group, visit and a treatment group*visit interaction as covariates in the model. Only those participants with data available at the specified data points were analyzed.

End point type	Post-hoc

End point timeframe:

Baseline and up to Week 12

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[193]	16[194]	23[195]	24[196]
Units: Scores on a scale				
least squares mean (confidence interval 95%)	-0.46 (-1.01 to 0.08)	-1.17 (-1.99 to -0.35)	-1.08 (-1.77 to -0.39)	-1.36 (-2.03 to -0.69)

Notes:

[193] - ITT Population

[194] - ITT Population

[195] - ITT Population

[196] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[197]	22[198]		
Units: Scores on a scale				
least squares mean (confidence interval 95%)	-1.63 (-2.32 to -0.93)	-1.41 (-2.13 to -0.7)		

Notes:
[197] - ITT Population
[198] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	52
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.69
upper limit	0.28

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	59
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	0.26

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	60
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.76
upper limit	-0.03

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	58
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.05
upper limit	-0.28

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	58
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.85
upper limit	-0.06

Post-hoc: Ratio to Baseline in Total Serum Bile Acid Concentration

End point title	Ratio to Baseline in Total Serum Bile Acid Concentration

End point description:

Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 (Day 1) or Visit 1 (Screening), excluding unscheduled visits. Ratio to Baseline was defined as the geometric mean of post-Baseline visit value divided by the geometric mean of Baseline value. Values were log-transformed and mean change from Baseline on the log-scale was calculated over the 12 week treatment period. Analysis was performed on change in total serum bile acid concentration on the log-scale over the 12 week treatment period using MMRM with log-transformed Baseline total serum bile acid, visit, treatment group, a log-transformed Baseline total serum bile acid*visit interaction, and a treatment group*visit interaction used as covariates in the model. Afterwards, values were back-transformed to the original scale. Ratios of geometric means are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Post-hoc

End point timeframe:

Baseline and up to Week 12

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[199]	16[200]	22[201]	24[202]
Units: Ratio				
least squares mean (confidence interval 95%)	1.01 (0.801 to 1.273)	0.977 (0.688 to 1.386)	1.182 (0.874 to 1.6)	0.918 (0.687 to 1.226)

Notes:

[199] - ITT Population

[200] - ITT Population

[201] - ITT Population

[202] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[203]	22[204]		
Units: Ratio				
least squares mean (confidence interval 95%)	0.697 (0.519 to 0.938)	0.833 (0.616 to 1.127)		

Notes:

[203] - ITT Population

[204] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	52
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	Least Square (LS) mean ratio
Point estimate	0.967
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.635
upper limit	1.471

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD

Number of subjects included in analysis	58
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	LS mean ratio
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.712

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	60
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	LS mean ratio
Point estimate	0.909
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.627
upper limit	1.316

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	58
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	LS mean ratio
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.474
upper limit	1.005

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID

Number of subjects included in analysis	58
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	LS mean ratio
Point estimate	0.825
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.564
upper limit	1.207

Post-hoc: Ratio to Baseline in serum 7-alpha-hydroxy-4-cholesten-3-one (C4) Concentration

End point title	Ratio to Baseline in serum 7-alpha-hydroxy-4-cholesten-3-one (C4) Concentration

End point description:

Baseline is the assessment performed at Week 4 (V3), or if missing then Visit 2 (Day 1) or Visit 1 (Screening), excluding unscheduled visits. Ratio to Baseline was defined as the geometric mean of post-Baseline visit value divided by the geometric mean of Baseline value. Values were log-transformed and mean change from Baseline on the log-scale was calculated over the 12 week treatment period. Analysis was performed on change in C4 on the log-scale over the 12 week treatment period using Mixed model repeated measures (MMRM) with log-transformed Baseline C4, visit, treatment group, a log-transformed Baseline C4*visit interaction, and a treatment group*visit interaction used as covariates in the model. Afterwards, values were back-transformed to the original scale. Ratios of geometric means are presented. Only those participants with data available at the specified data points were analyzed.

End point type	Post-hoc

End point timeframe:

Baseline and up to Week 12

End point values	Placebo	GSK2330672 20 mg QD	GSK2330672 90 mg QD	GSK2330672 180 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36[205]	16[206]	22[207]	24[208]
Units: Ratio				
least squares mean (confidence interval 95%)	1.158 (0.937 to 1.431)	1.579 (1.151 to 2.166)	2.374 (1.812 to 3.109)	2.846 (2.192 to 3.694)

Notes:

[205] - ITT Population

[206] - ITT Population

[207] - ITT Population

[208] - ITT Population

End point values	GSK2330672 40 mg BID	GSK2330672 90 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[209]	22[210]		
Units: Ratio				
least squares mean (confidence interval 95%)	3.622 (2.753 to 4.764)	3.127 (2.385 to 4.101)		

Notes:
[209] - ITT Population
[210] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2330672 20 mg QD
Number of subjects included in analysis	52
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	LS mean ratio
Point estimate	1.363
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.932
upper limit	1.995

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK2330672 90 mg QD
Number of subjects included in analysis	58
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	LS mean ratio
Point estimate	2.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.456
upper limit	2.887

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GSK2330672 180 mg QD
Number of subjects included in analysis	60
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	LS mean ratio
Point estimate	2.457
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.758
upper limit	3.436

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GSK2330672 40 mg BID
Number of subjects included in analysis	58
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	LS mean ratio
Point estimate	3.128
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.206
upper limit	4.435

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v GSK2330672 90 mg BID
Number of subjects included in analysis	58
Analysis specification	Post-hoc
Analysis type	other
Parameter estimate	LS mean ratio
Point estimate	2.701
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.915
upper limit	3.81

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious adverse events (Non-SAEs) and serious adverse events (SAEs) were collected up to 12 weeks during Main study period; up to 4 weeks during Final study period and up to 4 weeks during Follow-up period.

Adverse event reporting additional description:

Safety Population consisted of all randomized participants who received at least 1 dose of study intervention.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Placebo - Main Study Period

Reporting group description:

Placebo - Main Study Period

Reporting group title	GSK2330672 20 mg QD - Main Study Period

Reporting group description:

GSK2330672 20 mg QD - Main Study Period

Reporting group title	GSK2330672 90 mg QD - Main Study Period

Reporting group description:

GSK2330672 90 mg QD - Main Study Period

Reporting group title	GSK2330672 180 mg QD - Main Study Period

Reporting group description:

GSK2330672 180 mg QD - Main Study Period

Reporting group title	GSK2330672 40 mg BID - Main Study Period

Reporting group description:

GSK2330672 40 mg BID - Main Study Period

Reporting group title	GSK2330672 90 mg BID - Main Study Period

Reporting group description:

GSK2330672 90 mg BID - Main Study Period

Reporting group title	Placebo - Final Study Period

Reporting group description:

Placebo - Final Study Period

Reporting group title	GSK2330672 20 mg QD - Final Study Period

Reporting group description:

GSK2330672 20 mg QD - Final Study Period

Reporting group title	GSK2330672 90 mg QD - Final Study Period

Reporting group description:

GSK2330672 90 mg QD - Final Study Period

Reporting group title	GSK2330672 180 mg QD - Final Study Period

Reporting group description:

GSK2330672 180 mg QD - Final Study Period

Reporting group title	GSK2330672 40 mg BID - Final Study Period

Reporting group description:

GSK2330672 40 mg BID - Final Study Period

Reporting group title	GSK2330672 90 mg BID - Final Study Period

Reporting group description:

GSK2330672 90 mg BID - Final Study Period

Reporting group title	Placebo - Follow-up
Reporting group description: Placebo - Follow-up	
Reporting group title	GSK2330672 20 mg QD - Follow-up
Reporting group description: GSK2330672 20 mg QD - Follow-up	
Reporting group title	GSK2330672 90 mg QD - Follow-up
Reporting group description: GSK2330672 90 mg QD - Follow-up	
Reporting group title	GSK2330672 180 mg QD - Follow-up
Reporting group description: GSK2330672 180 mg QD - Follow-up	
Reporting group title	GSK2330672 40 mg BID - Follow-up
Reporting group description: GSK2330672 40 mg BID - Follow-up	
Reporting group title	GSK2330672 90 mg BID - Follow-up
Reporting group description: GSK2330672 90 mg BID - Follow-up	

Serious adverse events	Placebo - Main Study Period	GSK2330672 20 mg QD - Main Study Period	GSK2330672 90 mg QD - Main Study Period
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	1 / 23 (4.35%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (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	GSK2330672 180 mg QD - Main Study Period	GSK2330672 40 mg BID - Main Study Period	GSK2330672 90 mg BID - Main Study Period
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo - Final Study Period	GSK2330672 20 mg QD - Final Study Period	GSK2330672 90 mg QD - Final Study Period
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			

subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (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	GSK2330672 180 mg QD - Final Study Period	GSK2330672 40 mg BID - Final Study Period	GSK2330672 90 mg BID - Final Study Period
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo - Follow-up	GSK2330672 20 mg QD - Follow-up	GSK2330672 90 mg QD - Follow-up
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 35 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 35 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	GSK2330672 180 mg QD - Follow-up	GSK2330672 40 mg BID - Follow-up	GSK2330672 90 mg BID - Follow-up
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 27 (3.70%)	0 / 22 (0.00%)	0 / 22 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 27 (3.70%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			

subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (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

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo - Main Study Period	GSK2330672 20 mg QD - Main Study Period	GSK2330672 90 mg QD - Main Study Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 36 (47.22%)	11 / 16 (68.75%)	19 / 23 (82.61%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	1 / 23 (4.35%)
occurrences (all)	0	1	2
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 16 (12.50%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Fatigue			
subjects affected / exposed	3 / 36 (8.33%)	1 / 16 (6.25%)	2 / 23 (8.70%)
occurrences (all)	3	1	2
Impaired healing			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	1 / 23 (4.35%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Vulvovaginal dryness			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0

Dysmenorrhoea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	1 / 23 (4.35%)
occurrences (all)	1	1	1
Sleep disorder			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	2 / 23 (8.70%)
occurrences (all)	0	1	2
Cardiac murmur			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Bone fissure			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Humerus fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	3 / 23 (13.04%)
occurrences (all)	0	1	5
Memory impairment			

subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	0 / 36 (0.00%)	2 / 16 (12.50%)	1 / 23 (4.35%)
occurrences (all)	0	2	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 36 (8.33%)	3 / 16 (18.75%)	4 / 23 (17.39%)
occurrences (all)	3	3	6
Abdominal pain lower			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	1 / 23 (4.35%)
occurrences (all)	0	1	1
Abdominal pain upper			
subjects affected / exposed	0 / 36 (0.00%)	2 / 16 (12.50%)	0 / 23 (0.00%)
occurrences (all)	0	4	0
Constipation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	4 / 23 (17.39%)
occurrences (all)	0	0	4
Diarrhoea			
subjects affected / exposed	4 / 36 (11.11%)	6 / 16 (37.50%)	15 / 23 (65.22%)
occurrences (all)	5	8	20
Dry mouth			
subjects affected / exposed	0 / 36 (0.00%)	2 / 16 (12.50%)	1 / 23 (4.35%)
occurrences (all)	0	2	1
Dyspepsia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Haemorrhoids			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	1 / 23 (4.35%)
occurrences (all)	1	2	1
Vomiting			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 36 (5.56%)	0 / 16 (0.00%)	2 / 23 (8.70%)
occurrences (all)	2	0	3
Rash			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Arthritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			

subjects affected / exposed	2 / 36 (5.56%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	2 / 23 (8.70%)
occurrences (all)	0	0	3
Myalgia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Back pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Gingivitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	2 / 36 (5.56%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 36 (2.78%)	1 / 16 (6.25%)	1 / 23 (4.35%)
occurrences (all)	1	1	1
Rhinitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	2 / 36 (5.56%)	2 / 16 (12.50%)	0 / 23 (0.00%)
occurrences (all)	2	2	0
Skin bacterial infection			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0

Upper respiratory tract infection			
subjects affected / exposed	2 / 36 (5.56%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	0 / 36 (0.00%)	2 / 16 (12.50%)	0 / 23 (0.00%)
occurrences (all)	0	2	0
Viral pharyngitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Infectious mononucleosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Vitamin A deficiency			
subjects affected / exposed	0 / 36 (0.00%)	1 / 16 (6.25%)	0 / 23 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	GSK2330672 180 mg QD - Main Study Period	GSK2330672 40 mg BID - Main Study Period	GSK2330672 90 mg BID - Main Study Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 27 (88.89%)	16 / 23 (69.57%)	18 / 22 (81.82%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 27 (3.70%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Fatigue			

subjects affected / exposed	2 / 27 (7.41%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	2	1	1
Impaired healing			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 27 (3.70%)	1 / 23 (4.35%)	2 / 22 (9.09%)
occurrences (all)	1	1	2
Reproductive system and breast disorders			
Vulvovaginal dryness			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Sleep disorder			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Bone fissure			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Ligament sprain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 27 (7.41%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	2	1	1
Memory impairment			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 27 (29.63%)	2 / 23 (8.70%)	4 / 22 (18.18%)
occurrences (all)	9	2	5
Abdominal pain lower			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	2 / 27 (7.41%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	2	1	0
Constipation			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	18 / 27 (66.67%)	12 / 23 (52.17%)	15 / 22 (68.18%)
occurrences (all)	22	14	15
Dry mouth			

subjects affected / exposed	0 / 27 (0.00%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	2 / 27 (7.41%)	0 / 23 (0.00%)	1 / 22 (4.55%)
occurrences (all)	2	0	1
Flatulence			
subjects affected / exposed	1 / 27 (3.70%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 27 (14.81%)	0 / 23 (0.00%)	2 / 22 (9.09%)
occurrences (all)	4	0	2
Vomiting			
subjects affected / exposed	3 / 27 (11.11%)	0 / 23 (0.00%)	2 / 22 (9.09%)
occurrences (all)	3	0	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 27 (3.70%)	0 / 23 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Rash			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 27 (0.00%)	2 / 23 (8.70%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 27 (3.70%)	1 / 23 (4.35%)	0 / 22 (0.00%)
occurrences (all)	1	2	0
Gingivitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			

subjects affected / exposed	1 / 27 (3.70%)	0 / 23 (0.00%)	3 / 22 (13.64%)
occurrences (all)	1	0	3
Rhinitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 27 (0.00%)	2 / 23 (8.70%)	0 / 22 (0.00%)
occurrences (all)	0	3	0
Skin bacterial infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	2 / 23 (8.70%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Urinary tract infection			
subjects affected / exposed	0 / 27 (0.00%)	1 / 23 (4.35%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Viral pharyngitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Infectious mononucleosis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Vitamin A deficiency			
subjects affected / exposed	0 / 27 (0.00%)	0 / 23 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo - Final Study Period	GSK2330672 20 mg QD - Final Study Period	GSK2330672 90 mg QD - Final Study Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 35 (5.71%)	6 / 16 (37.50%)	8 / 19 (42.11%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Melanocytic naevus			
subjects affected / exposed	0 / 35 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 35 (0.00%)	2 / 16 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Impaired healing			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Vulvovaginal dryness			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Investigations			

Hepatic enzyme increased			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Bone fissure			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Tooth fracture			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Memory impairment			
subjects affected / exposed	0 / 35 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 35 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Abdominal pain lower			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	1 / 35 (2.86%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Dry mouth			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 35 (2.86%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	0 / 35 (0.00%)	2 / 16 (12.50%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	1 / 35 (2.86%)	1 / 16 (6.25%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Rash			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Rash macular			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Bone pain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Back pain			

subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skin bacterial infection			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Viral pharyngitis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 16 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

Infectious mononucleosis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Vitamin A deficiency			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	GSK2330672 180 mg QD - Final Study Period	GSK2330672 40 mg BID - Final Study Period	GSK2330672 90 mg BID - Final Study Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 19 (10.53%)	2 / 21 (9.52%)	2 / 17 (11.76%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Impaired healing			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Vulvovaginal dryness			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Dysmenorrhoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Bone fissure			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	1 / 19 (5.26%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Memory impairment			

subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 19 (0.00%)	1 / 21 (4.76%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Rash			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			

subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Skin bacterial infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Viral pharyngitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Infectious mononucleosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Vitamin A deficiency			
subjects affected / exposed	0 / 19 (0.00%)	0 / 21 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo - Follow-up	GSK2330672 20 mg QD - Follow-up	GSK2330672 90 mg QD - Follow-up
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Fatigue			

subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Impaired healing			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Vulvovaginal dryness			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Bone fissure			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

Ligament sprain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Dry mouth			

subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			

subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Skin bacterial infection			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Viral pharyngitis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Infectious mononucleosis			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Vitamin A deficiency			
subjects affected / exposed	0 / 35 (0.00%)	0 / 16 (0.00%)	0 / 23 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	GSK2330672 180 mg QD - Follow-up	GSK2330672 40 mg BID - Follow-up	GSK2330672 90 mg BID - Follow-up
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Melanocytic naevus			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Impaired healing			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Vulvovaginal dryness			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Investigations			

Hepatic enzyme increased			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Bone fissure			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Back pain			

subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Skin bacterial infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Viral pharyngitis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 27 (0.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Infectious mononucleosis subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 22 (0.00%) 0	0 / 22 (0.00%) 0
Metabolism and nutrition disorders Vitamin A deficiency subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	0 / 22 (0.00%) 0	0 / 22 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 November 2016	Amendment 1: To clarify requirements for liver safety monitoring and stopping criteria, as well as other administrative changes.
06 December 2017	Amendment 2: To increase access to the trial for participants who will more closely reflect the intended treatment population of primary biliary cholangitis (PBC) participants while maintaining safety, to clarify some existing criteria and information, to make administrative changes, and to correct minor typographical and grammatical errors.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported