Clinical trial results:
A multi-centre, randomized, double-blind (sponsor open), placebo controlled, repeat-dose, proof of mechanism study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and explore efficacy of GSK2330811 in participants with diffuse cutaneous systemic sclerosis

Summary

EudraCT number	2016-003417-95
Trial protocol	GB NL
Global end of trial date	07 July 2020

Results information

Result version number	v1 (current)
This version publication date	15 May 2021
First version publication date	15 May 2021

Trial information

Trial identification

Sponsor protocol code	201247

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 September 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of repeat subcutaneous doses of GSK2330811 in participants with diffuse cutaneous systemic sclerosis (dcSSc)

Protection of trial subjects:

Specific eligibility, monitoring and individual participant/study stopping rules were implemented in the study protocol to mitigate potential risks. Periodic review of safety and PK data by an internal GlaxoSmithKline (GSK) study-specific Data Review Committee, including at dose escalation.
The protocol was amended to ensure safety monitoring during the corona virus disease-19 (COVID-19) pandemic, including the option for study assessments to be conducted remotely during the off-treatment follow up period and local safety laboratory tests to be performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 June 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	Canada: 4
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	35
EEA total number of subjects	4

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	27
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a randomized, double-blind (sponsor open), proof of mechanism study of GSK2330811 in participants with diffuse cutaneous systemic sclerosis. This study was conducted in Canada, Netherlands, United Kingdom and United States.

Pre-assignment

Screening details:

A total of 35 participants were enrolled 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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received subcutaneous injection of placebo on Day 1 and then every other week until the final dose on Day 71 (Week 10).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo contains normal Saline (0.9 percent [%] weight per volume [w/v] Sodium Chloride)

Arm title	GSK2330811 100 mg

Arm description:

Participants received subcutaneous injection of GSK2330811 100 milligrams (mg) on Day 1 and then every other week until the final dose on Day 71 (Week 10).

Arm type	Experimental
Investigational medicinal product name	GSK2330811
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

GSK2330811 was provided in vials each filled with 1 milliliter (mL) extractable volume at 100 milligram (mg) per mL

Arm title	GSK2330811 300 mg

Arm description:

Participants received subcutaneous injection of GSK2330811 300 mg on Day 1 and then every other week until the final dose on Day 71 (Week 10).

Arm type	Experimental

Investigational medicinal product name	GSK2330811
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

GSK2330811 was provided in vials each filled with 1 milliliter (mL) extractable volume at 100 milligram (mg) per mL

Number of subjects in period 1	Placebo	GSK2330811 100 mg	GSK2330811 300 mg
Started	8	3	24
Completed	7	3	22
Not completed	1	0	2
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	-	-	1
Lost to follow-up	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received subcutaneous injection of placebo on Day 1 and then every other week until the final dose on Day 71 (Week 10).	
Reporting group title	GSK2330811 100 mg
Reporting group description:	
Participants received subcutaneous injection of GSK2330811 100 milligrams (mg) on Day 1 and then every other week until the final dose on Day 71 (Week 10).	
Reporting group title	GSK2330811 300 mg
Reporting group description:	
Participants received subcutaneous injection of GSK2330811 300 mg on Day 1 and then every other week until the final dose on Day 71 (Week 10).	

Reporting group values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg
Number of subjects	8	3	24
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	1	20
From 65-84 years	2	2	4
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	50.8	66.7	52.6
standard deviation	± 15.42	± 4.73	± 12.59
Sex: Female, Male Units: Participants			
Female	6	1	19
Male	2	2	5
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	0	0	1
Asian - East Asian Heritage	1	0	0
Black or African American	0	0	3
White - White/Caucasian/European Heritage	7	3	20

Reporting group values	Total		
Number of subjects	35		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	27		
From 65-84 years	8		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	26		
Male	9		
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	1		
Asian - East Asian Heritage	1		
Black or African American	3		
White - White/Caucasian/European Heritage	30		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received subcutaneous injection of placebo on Day 1 and then every other week until the final dose on Day 71 (Week 10).	
Reporting group title	GSK2330811 100 mg
Reporting group description:	
Participants received subcutaneous injection of GSK2330811 100 milligrams (mg) on Day 1 and then every other week until the final dose on Day 71 (Week 10).	
Reporting group title	GSK2330811 300 mg
Reporting group description:	
Participants received subcutaneous injection of GSK2330811 300 mg on Day 1 and then every other week until the final dose on Day 71 (Week 10).	
Subject analysis set title	GSK2330811 100 mg and GSK2330811 300 mg - Overall
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received subcutaneous injection of GSK2330811 100 mg and 300 mg on Day 1 and then every other week until the final dose on Day 71 (Week 10).	

Primary: Number of Participants With Non-serious Adverse Events (Non-SAEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants With Non-serious Adverse Events (Non-SAEs) and Serious Adverse Events (SAEs)[1]
End point description:	
An adverse event (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. An SAE is defined as any untoward medical occurrence that: results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, is a congenital anomaly/birth defect, other situations judged by physician. SAEs were collected up to Day 197, but the protocol also allowed investigators to report SAEs occurring after participants had completed the study. This outcome measure includes two SAEs reported after participants had completed the study, occurring on Day 306 and Day 603 following first dose. Safety Population consisted of all randomized participants who have taken at least 1 dose of study treatment.	
End point type	Primary
End point timeframe:	
Up to Day 197, but protocol allowed for additional events to be collected; up to Day 603 post first dose	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[2]	3[3]	24[4]	
Units: Participants				
Non-SAEs	8	3	24	
SAEs	1	0	2	

Notes:

[2] - Safety Population.

[3] - Safety Population.

[4] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hematology Parameters: Basophils, Eosinophils, Lymphocytes, Monocytes, Total Neutrophils, Platelet Count, White Blood Cell (WBC) count

End point title	Change From Baseline in Hematology Parameters: Basophils, Eosinophils, Lymphocytes, Monocytes, Total Neutrophils, Platelet Count, White Blood Cell (WBC) count[5]

End point description:

Blood samples were collected to analyze the hematology parameters: Basophils, Eosinophils, Lymphocytes, Monocytes, Total Neutrophils, Platelet Count and WBC count. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[6]	3[7]	23[8]	
Units: Giga cells per liter				
arithmetic mean (standard deviation)				
Day 15: Basophils, n=8,3,23	-0.006 (± 0.0262)	0.013 (± 0.0252)	0.007 (± 0.0325)	
Day 29: Basophils, n=8,3,23	-0.005 (± 0.0288)	-0.003 (± 0.0252)	0.003 (± 0.0350)	
Day 43: Basophils, n=8,3,22	-0.005 (± 0.0169)	0.027 (± 0.0635)	-0.005 (± 0.0323)	
Day 57: Basophils, n=6,3,22	-0.010 (± 0.0167)	0.013 (± 0.0404)	-0.004 (± 0.0333)	
Day 71: Basophils, n=8,3,20	-0.010 (± 0.0267)	-0.003 (± 0.0208)	-0.008 (± 0.0341)	
Day 85: Basophils, n=7,2,22	-0.020 (± 0.0294)	0.045 (± 0.0636)	0.000 (± 0.0344)	
Day 113: Basophils, n=7,3,21	-0.006 (± 0.0237)	0.040 (± 0.0693)	-0.002 (± 0.0390)	
Day 155: Basophils, n=7,3,20	0.004 (± 0.0270)	0.060 (± 0.0721)	0.000 (± 0.0400)	
Day 197: Basophils, n=7,3,18	-0.006 (± 0.0399)	0.033 (± 0.0208)	0.015 (± 0.0517)	
Day 15: Eosinophils, n=8,3,23	0.016 (± 0.0616)	0.070 (± 0.0700)	0.084 (± 0.2934)	
Day 29: Eosinophils, n=8,3,23	0.036 (± 0.0901)	0.060 (± 0.2007)	0.001 (± 0.1633)	
Day 43: Eosinophils, n=8,3,22	0.019 (± 0.0500)	0.103 (± 0.1026)	-0.015 (± 0.1954)	
Day 57: Eosinophils, n=6,3,22	0.010 (± 0.0473)	0.113 (± 0.1795)	-0.034 (± 0.1797)	
Day 71: Eosinophils, n=8,3,20	0.018 (± 0.0440)	0.137 (± 0.2344)	0.012 (± 0.1241)	

Day 85: Eosinophils, n=7,2,22	0.001 (± 0.0406)	0.130 (± 0.3111)	-0.035 (± 0.1773)	
Day 113: Eosinophils, n=7,3,21	0.056 (± 0.1005)	0.070 (± 0.0872)	0.087 (± 0.2873)	
Day 155: Eosinophils, n=7,3,20	0.003 (± 0.0403)	0.080 (± 0.0300)	0.005 (± 0.1695)	
Day 197: Eosinophils, n=7,3,18	0.069 (± 0.1426)	0.170 (± 0.1323)	0.056 (± 0.1302)	
Day 15: Lymphocytes, n=8,3,23	-0.116 (± 0.3926)	0.103 (± 0.3955)	-0.125 (± 0.4110)	
Day 29: Lymphocytes, n=8,3,23	-0.064 (± 0.2539)	0.477 (± 0.4177)	-0.102 (± 0.6071)	
Day 43: Lymphocytes, n=8,3,22	0.020 (± 0.2891)	0.530 (± 0.3270)	-0.078 (± 0.6156)	
Day 57: Lymphocytes, n=6,3,22	-0.043 (± 0.3732)	0.563 (± 0.3798)	0.105 (± 0.5853)	
Day 71: Lymphocytes, n=8,3,20	-0.060 (± 0.2384)	0.430 (± 0.3601)	0.155 (± 0.5169)	
Day 85: Lymphocytes, n=7,2,22	-0.109 (± 0.2202)	0.580 (± 0.4667)	0.313 (± 0.5521)	
Day 113: Lymphocytes, n=7,3,21	-0.297 (± 0.5087)	0.383 (± 0.3907)	0.287 (± 0.6783)	
Day 155: Lymphocytes, n=7,3,20	-0.046 (± 0.2327)	0.160 (± 0.2600)	0.202 (± 0.4504)	
Day 197: Lymphocytes, n=7,3,18	-0.066 (± 0.4108)	-0.010 (± 0.4419)	0.039 (± 0.7780)	
Day 15: Monocytes, n=8,3,23	0.096 (± 0.1507)	-0.017 (± 0.1102)	-0.051 (± 0.1659)	
Day 29: Monocytes, n=8,3,23	0.006 (± 0.0578)	-0.030 (± 0.3959)	-0.120 (± 0.2175)	
Day 43: Monocytes, n=8,3,22	0.103 (± 0.2093)	0.047 (± 0.1069)	-0.106 (± 0.2045)	
Day 57: Monocytes, n=6,3,22	-0.037 (± 0.0698)	-0.120 (± 0.1600)	-0.130 (± 0.2216)	
Day 71: Monocytes, n=8,3,20	0.050 (± 0.1414)	-0.003 (± 0.0404)	-0.070 (± 0.1838)	
Day 85: Monocytes, n=7,2,22	-0.007 (± 0.0652)	0.140 (± 0.1697)	-0.127 (± 0.2495)	
Day 113: Monocytes, n=7,3,21	0.070 (± 0.1494)	0.030 (± 0.1735)	-0.028 (± 0.2246)	
Day 155: Monocytes, n=7,3,20	0.064 (± 0.1229)	0.167 (± 0.1250)	-0.022 (± 0.1414)	
Day 197: Monocytes, n=7,3,18	0.051 (± 0.2242)	-0.043 (± 0.1266)	-0.053 (± 0.2234)	
Day 15: Total neutrophils, n=8,3,23	0.228 (± 1.3240)	1.060 (± 3.0143)	-0.917 (± 1.4114)	
Day 29: Total neutrophils, n=8,3,23	0.318 (± 1.4309)	0.323 (± 1.8591)	-1.104 (± 1.4251)	
Day 43: Total neutrophils, n=8,3,22	0.315 (± 1.3403)	-0.350 (± 1.4731)	-1.406 (± 1.4631)	
Day 57: Total neutrophils, n=6,3,22	0.538 (± 0.9156)	-0.517 (± 1.9998)	-1.387 (± 1.4428)	
Day 71: Total neutrophils, n=8,3,20	0.789 (± 2.1739)	-0.223 (± 1.8928)	-1.369 (± 1.6361)	
Day 85: Total neutrophils, n=7,2,22	-0.139 (± 1.1995)	-0.990 (± 2.9698)	-1.424 (± 2.3949)	
Day 113: Total neutrophils, n=7,3,20	0.680 (± 1.2472)	-0.263 (± 1.0384)	-1.002 (± 1.5195)	
Day 155: Total neutrophils, n=7,3,20	0.027 (± 1.2229)	-0.673 (± 2.1324)	-0.183 (± 1.2208)	
Day 197: Total neutrophils, n=7,3,18	0.317 (± 1.3578)	-1.603 (± 4.0868)	-0.001 (± 1.4937)	

Day 15: Platelet count, n=8,3,23	-1.5 (± 24.02)	-42.0 (± 32.70)	-124.6 (± 87.57)	
Day 29: Platelet count, n=7,3,23	-5.9 (± 20.38)	-39.7 (± 29.28)	-145.7 (± 94.01)	
Day 43: Platelet count, n=8,3,23	-16.1 (± 14.56)	-49.0 (± 22.27)	-150.2 (± 90.41)	
Day 57: Platelet count, n=6,3,22	-4.2 (± 20.40)	-66.0 (± 42.04)	-148.6 (± 90.99)	
Day 71: Platelet count, n=7,3,20	-12.3 (± 17.67)	-41.7 (± 45.21)	-129.4 (± 90.54)	
Day 85: Platelet count, n=7,3,22	-18.0 (± 25.89)	-48.0 (± 29.10)	-97.4 (± 73.99)	
Day 113: Platelet count, n=7,3,20	-14.4 (± 25.53)	-20.3 (± 42.52)	-61.2 (± 96.89)	
Day 155: Platelet count, n=6,3,20	-26.7 (± 19.62)	15.0 (± 31.24)	-6.9 (± 60.00)	
Day 197: Platelet count, n=7,3,19	-10.1 (± 30.30)	-20.7 (± 71.53)	-10.3 (± 42.86)	
Day 15: WBC count, n=8,3,23	0.20 (± 1.546)	1.20 (± 2.685)	-1.00 (± 1.487)	
Day 29: WBC count, n=8,3,23	0.28 (± 1.400)	0.80 (± 1.212)	-1.33 (± 1.927)	
Day 43: WBC count, n=8,3,22	0.46 (± 1.418)	0.33 (± 0.950)	-1.60 (± 2.039)	
Day 57: WBC count, n=6,3,22	0.43 (± 0.774)	0.03 (± 1.617)	-1.46 (± 1.947)	
Day 71: WBC count, n=8,3,20	0.76 (± 2.191)	0.33 (± 1.258)	-1.29 (± 1.953)	
Day 85: WBC count, n=7,3,22	-0.29 (± 1.182)	-0.10 (± 1.400)	-1.27 (± 2.509)	
Day 113: WBC count, n=7,3,21	0.47 (± 1.138)	0.27 (± 0.473)	-0.61 (± 1.913)	
Day 155: WBC count, n=7,3,20	0.07 (± 1.228)	-0.20 (± 1.778)	0.01 (± 1.571)	
Day 197: WBC count, n=7,3,19	0.31 (± 1.469)	-1.50 (± 4.444)	-0.01 (± 1.948)	

Notes:

[6] - Safety Population.

[7] - Safety Population.

[8] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hematology Parameters: Hemoglobin, Mean Corpuscle Hemoglobin Concentration (MCHC)

End point title	Change From Baseline in Hematology Parameters: Hemoglobin, Mean Corpuscle Hemoglobin Concentration (MCHC)[9]

End point description:

Blood samples were collected to analyze the hematology parameters: hemoglobin and MCHC. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[10]	3[11]	23[12]	
Units: Grams per liter				
arithmetic mean (standard deviation)				
Day 15: Hemoglobin, n=8,3,23	-2.8 (± 8.89)	2.0 (± 7.00)	-0.2 (± 5.31)	
Day 29: Hemoglobin, n=8,3,23	-2.5 (± 6.55)	-0.7 (± 11.06)	-3.7 (± 7.45)	
Day 43: Hemoglobin, n=8,3,23	-2.5 (± 6.39)	-1.7 (± 8.50)	-7.7 (± 9.06)	
Day 57: Hemoglobin, n=6,3,22	-3.8 (± 8.47)	-2.7 (± 11.15)	-13.7 (± 12.32)	
Day 71: Hemoglobin, n=8,3,20	-4.1 (± 10.38)	-6.3 (± 4.73)	-21.2 (± 11.61)	
Day 85: Hemoglobin, n=7,3,22	-3.9 (± 7.58)	-10.7 (± 6.11)	-22.0 (± 10.05)	
Day 113: Hemoglobin, n=7,3,21	-5.0 (± 8.43)	-9.0 (± 7.55)	-21.3 (± 10.49)	
Day 155: Hemoglobin, n=7,3,20	-6.3 (± 9.41)	-7.3 (± 6.03)	-14.3 (± 8.62)	
Day 197: Hemoglobin, n=7,3,19	-4.1 (± 8.88)	-6.7 (± 2.08)	-5.8 (± 6.58)	
Day 15: MCHC, n=8,3,23	0.9 (± 8.53)	-5.0 (± 3.00)	2.4 (± 7.83)	
Day 29: MCHC, n=8,3,23	-3.6 (± 6.39)	2.0 (± 13.11)	2.0 (± 8.30)	
Day 43: MCHC, n=8,3,22	-1.3 (± 9.27)	1.0 (± 7.55)	2.5 (± 4.86)	
Day 57: MCHC, n=6,3,22	-1.2 (± 10.11)	3.7 (± 4.93)	2.8 (± 8.42)	
Day 71: MCHC, n=8,3,20	2.3 (± 12.87)	2.7 (± 6.81)	0.5 (± 8.62)	
Day 85: MCHC, n=7,3,22	3.3 (± 10.53)	-1.7 (± 9.50)	2.8 (± 6.68)	
Day 113: MCHC, n=7,3,20	-0.4 (± 7.18)	5.0 (± 8.19)	-3.3 (± 8.16)	
Day 155: MCHC, n=7,3,17	-1.4 (± 5.26)	3.7 (± 4.16)	-4.2 (± 9.35)	
Day 197: MCHC, n=7,3,15	-0.4 (± 8.58)	-0.3 (± 7.02)	-3.5 (± 8.18)	

Notes:

[10] - Safety Population.

[11] - Safety Population.

[12] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hematology Parameter: Hematocrit

End point title	Change From Baseline in Hematology Parameter: Hematocrit[13]

End point description:

Blood samples were collected to analyze the hematology parameter: hematocrit. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[14]	3[15]	23[16]	
Units: Proportion of red blood cells in blood				
arithmetic mean (standard deviation)				
Day 15: n=8,3,23	-0.0089 (± 0.02744)	0.0127 (± 0.02203)	-0.0035 (± 0.01771)	
Day 29: n=8,3,23	-0.0023 (± 0.01955)	-0.0027 (± 0.04234)	-0.0141 (± 0.02486)	
Day 43: n=8,3,22	-0.0049 (± 0.01788)	-0.0057 (± 0.03564)	-0.0271 (± 0.03187)	
Day 57: n=6,3,22	-0.0092 (± 0.02500)	-0.0120 (± 0.03274)	-0.0444 (± 0.04224)	
Day 71: n=8,3,20	-0.0146 (± 0.02870)	-0.0217 (± 0.02329)	-0.0637 (± 0.03983)	
Day 85: n=7,3,22	-0.0151 (± 0.02591)	-0.0300 (± 0.01803)	-0.0688 (± 0.03265)	
Day 113: n=7,3,20	-0.0141 (± 0.03007)	-0.0323 (± 0.02822)	-0.0602 (± 0.02839)	
Day 155: n=7,3,17	-0.0164 (± 0.03169)	-0.0263 (± 0.01626)	-0.0349 (± 0.02482)	
Day 197: n=7,3,15	-0.0111 (± 0.02634)	-0.0193 (± 0.00981)	-0.0125 (± 0.02252)	

Notes:

[14] - Safety Population.

[15] - Safety Population.

[16] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hematology Parameter: Mean Corpuscle Hemoglobin (MCH)

End point title	Change From Baseline in Hematology Parameter: Mean Corpuscle Hemoglobin (MCH)[17]

End point description:

Blood samples were collected to analyze the hematology parameter: MCH. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[18]	3[19]	23[20]	
Units: Picogram				
arithmetic mean (standard deviation)				
Day 15: n=8,3,23	-0.08 (± 0.711)	0.03 (± 0.493)	0.04 (± 0.503)	
Day 29: n=8,3,23	-0.24 (± 0.616)	0.37 (± 0.709)	-0.23 (± 0.437)	
Day 43: n=8,3,22	-0.23 (± 0.807)	-0.10 (± 0.173)	-0.41 (± 0.450)	
Day 57: n=6,3,22	-0.25 (± 0.750)	0.10 (± 0.361)	-0.39 (± 0.493)	
Day 71: n=8,3,20	0.18 (± 0.945)	0.17 (± 0.379)	-0.50 (± 0.503)	
Day 85: n=7,3,22	0.07 (± 1.034)	-0.30 (± 0.755)	-0.45 (± 0.709)	
Day 113: n=7,3,20	-0.06 (± 0.808)	0.87 (± 0.513)	-0.27 (± 0.873)	
Day 155: n=7,3,17	-0.16 (± 0.637)	0.90 (± 0.200)	0.04 (± 1.180)	
Day 197: n=7,3,15	-0.44 (± 1.015)	0.33 (± 0.208)	-0.23 (± 1.285)	

Notes:

[18] - Safety Population.

[19] - Safety Population.

[20] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hematology Parameters: Mean Corpuscle Volume (MCV), Mean Platelet Volume (MPV)

End point title	Change From Baseline in Hematology Parameters: Mean Corpuscle Volume (MCV), Mean Platelet Volume (MPV)[21]

End point description:

Blood samples were collected to analyze the hematology parameters: MCV and MPV. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[22]	3[23]	23[24]	
Units: Femtoliter				
arithmetic mean (standard deviation)				
Day 15: MCV, n=8,3,23	-0.63 (± 1.188)	1.33 (± 1.528)	-0.39 (± 1.725)	
Day 29: MCV, n=8,3,23	0.38 (± 1.188)	0.33 (± 1.155)	-1.17 (± 2.188)	
Day 43: MCV, n=8,3,22	-0.38 (± 2.326)	-0.67 (± 1.528)	-1.86 (± 1.583)	
Day 57: MCV, n=6,3,22	-0.17 (± 2.787)	-1.00 (± 0.000)	-1.77 (± 2.308)	
Day 71: MCV, n=8,3,20	-0.13 (± 3.441)	-0.67 (± 1.528)	-1.60 (± 2.722)	
Day 85: MCV, n=7,3,22	-0.71 (± 1.113)	-0.67 (± 0.577)	-2.05 (± 2.478)	
Day 113: MCV, n=7,3,21	-0.29 (± 2.563)	1.00 (± 1.732)	0.00 (± 3.225)	
Day 155: MCV, n=7,3,20	-0.14 (± 1.215)	1.67 (± 0.577)	1.26 (± 4.584)	
Day 197: MCV, n=7,3,18	-1.29 (± 1.799)	0.67 (± 2.082)	-0.02 (± 3.575)	
Day 15: MPV, n=8,3,23	0.04 (± 0.256)	0.20 (± 0.361)	0.45 (± 0.460)	
Day 29: MPV, n=8,3,23	-0.04 (± 0.378)	0.47 (± 0.764)	0.29 (± 0.630)	
Day 43: MPV, n=7,3,22	-0.14 (± 0.276)	0.23 (± 0.737)	0.07 (± 0.594)	
Day 57: MPV, n=6,3,21	0.23 (± 0.446)	0.47 (± 0.416)	0.12 (± 0.599)	
Day 71: MPV, n=7,3,20	-0.21 (± 0.393)	0.23 (± 0.231)	-0.15 (± 0.516)	
Day 85: MPV, n=7,3,22	0.00 (± 0.356)	0.43 (± 0.808)	-0.11 (± 0.462)	
Day 113: MPV, n=7,3,19	-0.04 (± 0.443)	0.30 (± 0.781)	0.03 (± 0.622)	
Day 155: MPV, n=6,3,17	0.17 (± 0.565)	0.10 (± 0.872)	0.01 (± 0.448)	
Day 197: MPV, n=7,3,15	-0.11 (± 0.385)	0.10 (± 0.781)	0.07 (± 0.580)	

Notes:

[22] - Safety Population.

[23] - Safety Population.

[24] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hematology Parameters: Red Blood Cell (RBC) count, Reticulocyte count

End point title	Change From Baseline in Hematology Parameters: Red Blood Cell (RBC) count, Reticulocyte count[25]

End point description:

Blood samples were collected to analyze the hematology parameters: RBC count and reticulocyte count. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[26]	3[27]	23[28]	
Units: Tera cells per liter				
arithmetic mean (standard deviation)				
Day 15: RBC count, n=8,3,23	-0.05 (± 0.321)	0.07 (± 0.208)	-0.01 (± 0.205)	
Day 29: RBC count, n=8,3,23	-0.03 (± 0.225)	-0.07 (± 0.404)	-0.11 (± 0.275)	
Day 43: RBC count, n=8,3,22	-0.03 (± 0.238)	-0.07 (± 0.321)	-0.22 (± 0.331)	
Day 57: RBC count, n=6,3,22	-0.07 (± 0.288)	-0.10 (± 0.361)	-0.42 (± 0.464)	
Day 71: RBC count, n=8,3,20	-0.13 (± 0.396)	-0.23 (± 0.208)	-0.66 (± 0.406)	
Day 85: RBC count, n=7,3,22	-0.10 (± 0.311)	-0.33 (± 0.208)	-0.68 (± 0.343)	
Day 113: RBC count, n=7,3,20	-0.13 (± 0.350)	-0.40 (± 0.265)	-0.68 (± 0.361)	
Day 155: RBC count, n=7,3,17	-0.17 (± 0.330)	-0.37 (± 0.252)	-0.47 (± 0.264)	
Day 197: RBC count, n=7,3,15	-0.04 (± 0.282)	-0.23 (± 0.058)	-0.15 (± 0.160)	
Day 15: Reticulocyte count, n=8,3,23	0.0109 (± 0.02401)	-0.0207 (± 0.02463)	-0.0160 (± 0.00964)	
Day 29: Reticulocyte count, n=8,3,23	-0.0001 (± 0.00543)	-0.0169 (± 0.00911)	-0.0132 (± 0.01784)	
Day 43: Reticulocyte count, n=8,3,22	-0.0032 (± 0.00554)	-0.0228 (± 0.02303)	-0.0109 (± 0.01699)	
Day 57: Reticulocyte count, n=6,3,22	-0.0058 (± 0.00638)	-0.0091 (± 0.02177)	-0.0031 (± 0.01656)	
Day 71: Reticulocyte count, n=8,3,19	0.0026 (± 0.01261)	-0.0125 (± 0.01878)	0.0065 (± 0.01934)	
Day 85: Reticulocyte count, n=7,3,22	-0.0044 (± 0.00539)	-0.0209 (± 0.02471)	0.0152 (± 0.02006)	
Day 113: Reticulocyte count, n=7,3,20	-0.0064 (± 0.01030)	0.0012 (± 0.02944)	0.0356 (± 0.02009)	
Day 155: Reticulocyte count, n=7,3,17	0.0006 (± 0.00623)	-0.0157 (± 0.02263)	0.0158 (± 0.01340)	
Day 197: Reticulocyte count, n=7,3,16	0.0003 (± 0.00550)	-0.0285 (± 0.03458)	0.0017 (± 0.01003)	

Notes:

[26] - Safety Population.

[27] - Safety Population.

[28] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Hematology Parameter: Red Cell Distribution

Width (RDW)

End point title	Change From Baseline in Hematology Parameter: Red Cell Distribution Width (RDW)[29]

End point description:

Blood samples were collected to analyze the hematology parameter: RDW. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[29] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[30]	3[31]	23[32]	
Units: Percentage of width				
arithmetic mean (standard deviation)				
Day 15: n=8,3,23	0.04 (± 0.711)	-0.27 (± 1.050)	-0.26 (± 0.667)	
Day 29: n=8,3,23	0.24 (± 0.417)	-0.53 (± 1.704)	-0.47 (± 1.036)	
Day 43: n=8,3,22	0.25 (± 0.583)	-0.97 (± 1.650)	-0.47 (± 1.049)	
Day 57: n=6,3,22	-0.02 (± 0.578)	-0.83 (± 2.248)	0.15 (± 1.331)	
Day 71: n=8,3,20	0.04 (± 0.725)	-0.23 (± 2.570)	0.96 (± 2.040)	
Day 85: n=7,3,22	-0.04 (± 0.663)	-0.20 (± 2.307)	1.67 (± 1.792)	
Day 113: n=7,3,20	0.26 (± 0.748)	0.73 (± 1.950)	4.24 (± 2.737)	
Day 155: n=7,3,17	-0.09 (± 0.771)	0.10 (± 1.916)	2.86 (± 1.636)	
Day 197: n=7,3,15	-0.16 (± 1.286)	-0.57 (± 1.872)	1.06 (± 1.375)	

Notes:

[30] - Safety Population.

[31] - Safety Population.

[32] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Reticulocyte Production Index

End point title	Change From Baseline in Reticulocyte Production Index[33]

End point description:

Blood samples were collected to analyze the hematology parameter: Reticulocyte Production Index. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Reticulocyte Production Index (RPI) was calculated as 'Reticulocyte Production Index = Reticulocyte Count (percent [%]) multiply by (x) (hematocrit [%] divided by [/] 45) x 1/ reticulocyte maturation time'. Only those participants with data available at the specified time

points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[34]	3[35]	23[36]	
Units: Unitless				
arithmetic mean (standard deviation)				
Day 15: n=8,3,23	0.2009 (± 0.49644)	-0.1787 (± 0.53867)	-0.2757 (± 0.20191)	
Day 29: n=8,3,23	0.0391 (± 0.09687)	-0.2397 (± 0.51850)	-0.2460 (± 0.35460)	
Day 43: n=8,3,22	-0.0691 (± 0.11447)	-0.3437 (± 0.55192)	-0.2342 (± 0.34389)	
Day 57: n=6,3,22	-0.0763 (± 0.13476)	-0.2877 (± 0.48015)	-0.1933 (± 0.32326)	
Day 71: n=8,3,19	0.0154 (± 0.24560)	-0.4643 (± 0.13444)	-0.1344 (± 0.29111)	
Day 85: n=7,3,22	-0.0831 (± 0.14906)	-0.4530 (± 0.48914)	-0.0112 (± 0.32736)	
Day 113: n=7,3,20	-0.1006 (± 0.21168)	-0.2633 (± 0.29016)	0.2826 (± 0.33003)	
Day 155: n=7,3,17	-0.0033 (± 0.24087)	-0.4720 (± 0.24857)	0.1105 (± 0.28718)	
Day 197: n=7,3,15	-0.0296 (± 0.11222)	-0.5693 (± 0.43160)	0.0087 (± 0.16995)	

Notes:

[34] - Safety Population.

[35] - Safety Population.

[36] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline Hematology Parameter: Reticulocytes

End point title	Change from Baseline Hematology Parameter: Reticulocytes[37]

End point description:

Blood samples were collected to analyze the hematology parameter: reticulocytes. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[37] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[38]	3[39]	23[40]	
Units: Percentage of reticulocytes				
arithmetic mean (standard deviation)				
Day 15: n=8,3,23	0.0026 (± 0.00534)	-0.0053 (± 0.00551)	-0.0037 (± 0.00236)	
Day 29: n=8,3,23	0.0001 (± 0.00155)	-0.0040 (± 0.00265)	-0.0030 (± 0.00423)	
Day 43: n=8,3,22	-0.0008 (± 0.00128)	-0.0057 (± 0.00611)	-0.0021 (± 0.00389)	
Day 57: n=6,3,22	-0.0012 (± 0.00214)	-0.0023 (± 0.00551)	0.0004 (± 0.00422)	
Day 71: n=8,3,19	0.0014 (± 0.00325)	-0.0027 (± 0.00551)	0.0037 (± 0.00625)	
Day 85: n=7,3,22	-0.0007 (± 0.00138)	-0.0043 (± 0.00651)	0.0065 (± 0.00647)	
Day 113: n=7,3,20	-0.0011 (± 0.00219)	0.0013 (± 0.00702)	0.0121 (± 0.00704)	
Day 155: n=7,3,17	0.0006 (± 0.00162)	-0.0027 (± 0.00603)	0.0054 (± 0.00405)	
Day 197: n=7,3,15	0.0001 (± 0.00157)	-0.0063 (± 0.00924)	0.0005 (± 0.00233)	

Notes:

[38] - Safety Population.

[39] - Safety Population.

[40] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Worst-Case Chemistry Results Relative to Potential Clinical Importance (PCI) Criteria Post-Baseline Relative to Baseline

End point title	Number of Participants With Worst-Case Chemistry Results Relative to Potential Clinical Importance (PCI) Criteria Post-Baseline Relative to Baseline[41]

End point description:

Blood samples were collected for analysis of clinical chemistry parameters. PCI ranges were low: <30 grams per liter (g/L) (albumin), high: >44.2 micromoles per liter (µmol/L) increase from Baseline (creatinine), low: <3 or high: >9 mmol/L (glucose), low: <3 or high: >5.5 mmol/L (potassium), and low: <130 or high: >150 mmol/L (sodium). Participants were counted in the worst case category that their value changes to (low, within range or no change, or high), unless there was 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 within 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 up to 100%. Only those participants with data available at the specified time points were analyzed.

End point type	Primary

End point timeframe:

Up to Day 197

Notes:

[41] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[42]	3[43]	23[44]	
Units: Participants				
Albumin: To Low	0	0	0	
Albumin: To within Range or No Change	8	3	23	
Albumin: To High	0	0	0	
Creatinine: To Low	0	0	0	
Creatinine: To within Range or No Change	8	3	23	
Creatinine: To High	0	0	0	
Glucose: To Low	0	0	1	
Glucose: To within Range or No Change	8	2	19	
Glucose: To High	0	1	3	
Potassium: To Low	0	0	0	
Potassium: To within Range or No Change	7	3	22	
Potassium: To High	1	0	1	
Sodium: To Low	0	0	0	
Sodium: To within Range or No Change	8	3	23	
Sodium: To High	0	0	0	

Notes:

[42] - Safety Population.

[43] - Safety Population.

[44] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Chemistry Parameter: Total Protein

End point title	Change From Baseline in Chemistry Parameter: Total Protein[45]

End point description:

Blood samples were collected to analyze chemistry parameter: total protein. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[45] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[46]	3[47]	23[48]	
Units: Grams per liter				
arithmetic mean (standard deviation)				
Day 15: n=7,2,23	1.0 (± 3.06)	0.5 (± 4.95)	0.4 (± 3.56)	
Day 29: n=8,2,23	-0.1 (± 3.14)	-1.0 (± 5.66)	0.7 (± 2.86)	

Day 43: n=8,3,22	-0.1 (± 2.36)	-0.3 (± 2.08)	-0.5 (± 3.52)	
Day 57: n=7,3,22	1.3 (± 2.29)	1.3 (± 2.08)	-0.5 (± 3.65)	
Day 71: n=8,3,21	-0.1 (± 3.56)	0.7 (± 1.15)	-1.1 (± 4.44)	
Day 85: n=8,3,22	0.3 (± 1.39)	0.0 (± 2.00)	0.3 (± 3.71)	
Day 113: n=7,3,20	-0.9 (± 2.61)	1.7 (± 0.58)	0.2 (± 4.06)	
Day 155: n=7,3,18	-1.3 (± 1.25)	3.0 (± 7.21)	-0.1 (± 4.59)	
Day 197: n=7,3,19	2.3 (± 3.90)	2.3 (± 3.51)	1.5 (± 5.00)	

Notes:

[46] - Safety Population.

[47] - Safety Population.

[48] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Chemistry Parameters: Alkaline Phosphatase (ALP), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Lactate Dehydrogenase (LDH)

End point title	Change From Baseline in Chemistry Parameters: Alkaline Phosphatase (ALP), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Lactate Dehydrogenase (LDH)[49]

End point description:

Blood samples were collected to analyze chemistry parameters: ALP, ALT, AST and LDH. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[49] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[50]	3[51]	23[52]	
Units: International units per liter				
arithmetic mean (standard deviation)				
Day 15: ALP, n=7,2,23	-1.3 (± 10.53)	-1.0 (± 4.24)	0.6 (± 5.67)	
Day 29: ALP, n=8,2,23	-2.3 (± 7.89)	4.5 (± 6.36)	-1.1 (± 10.94)	
Day 43: ALP, n=8,3,22	-4.4 (± 12.36)	0.7 (± 7.51)	-1.1 (± 9.00)	
Day 57: ALP, n=7,3,22	-5.0 (± 13.23)	3.3 (± 9.07)	1.0 (± 7.55)	
Day 71: ALP, n=8,3,21	-3.5 (± 10.94)	1.3 (± 1.53)	-3.0 (± 11.52)	
Day 85: ALP, n=8,3,22	-2.4 (± 11.96)	-2.3 (± 4.93)	-3.0 (± 11.65)	
Day 113: ALP, n=7,3,20	-1.3 (± 4.99)	-2.3 (± 4.93)	-6.3 (± 8.15)	
Day 155: ALP, n=7,3,19	-8.4 (± 15.88)	-3.3 (± 5.69)	-5.4 (± 9.84)	
Day 197: ALP, n=7,3,19	-3.6 (± 12.16)	-4.0 (± 6.93)	-2.1 (± 11.03)	
Day 15: ALT, n=7,2,23	-0.4 (± 2.70)	0.0 (± 1.41)	1.6 (± 3.85)	
Day 29: ALT, n=8,2,23	0.6 (± 1.85)	-2.0 (± 2.83)	3.3 (± 9.58)	
Day 43: ALT, n=8,3,22	1.3 (± 3.15)	4.0 (± 6.08)	3.1 (± 10.70)	
Day 57: ALT, n=7,3,22	-1.6 (± 1.27)	2.0 (± 4.58)	3.7 (± 10.03)	

Day 71: ALT, n=8,3,21	0.3 (± 2.82)	3.0 (± 6.24)	0.0 (± 2.67)	
Day 85: ALT, n=8,3,22	-1.5 (± 3.89)	-0.3 (± 2.52)	0.4 (± 4.27)	
Day 113: ALT, n=7,3,20	-1.4 (± 5.13)	4.7 (± 8.14)	0.2 (± 3.18)	
Day 155: ALT, n=7,3,18	-2.6 (± 6.65)	1.0 (± 1.00)	0.9 (± 3.95)	
Day 197: ALT, n=7,3,21	3.6 (± 3.87)	-0.3 (± 2.52)	2.4 (± 4.69)	
Day 15: AST, n=7,2,23	-0.1 (± 1.77)	0.5 (± 0.71)	1.7 (± 5.11)	
Day 29: AST, n=8,2,23	1.8 (± 7.11)	1.0 (± 1.41)	2.0 (± 5.42)	
Day 43: AST, n=8,3,22	1.6 (± 6.74)	2.0 (± 3.61)	0.9 (± 4.14)	
Day 57: AST, n=7,3,22	-0.6 (± 2.82)	2.3 (± 3.06)	2.0 (± 5.34)	
Day 71: AST, n=8,3,21	1.9 (± 5.00)	3.3 (± 4.93)	-0.3 (± 1.98)	
Day 85: AST, n=8,3,22	-0.8 (± 4.37)	0.3 (± 2.31)	-0.2 (± 2.20)	
Day 113: AST, n=7,3,20	-2.7 (± 4.39)	1.3 (± 4.04)	-0.9 (± 2.50)	
Day 155: AST, n=7,3,18	-5.0 (± 7.70)	2.3 (± 0.58)	-0.6 (± 2.66)	
Day 197: AST, n=7,3,19	0.1 (± 4.91)	2.7 (± 0.58)	1.2 (± 3.32)	
Day 15: LDH, n=7,2,23	4.1 (± 28.54)	-3.5 (± 51.62)	18.4 (± 32.34)	
Day 29: LDH, n=8,2,23	-7.0 (± 14.95)	11.0 (± 0.00)	20.9 (± 22.90)	
Day 43: LDH, n=8,3,22	12.1 (± 11.54)	2.7 (± 30.62)	27.2 (± 34.69)	
Day 57: LDH, n=7,3,22	-5.1 (± 19.36)	15.3 (± 31.02)	22.4 (± 23.71)	
Day 71: LDH, n=8,3,21	10.5 (± 29.62)	13.3 (± 26.95)	32.7 (± 29.90)	
Day 85: LDH, n=8,3,22	-2.5 (± 26.26)	3.0 (± 11.53)	24.9 (± 28.66)	
Day 113: LDH, n=7,3,20	-17.6 (± 17.89)	6.3 (± 25.50)	14.2 (± 26.43)	
Day 155: LDH, n=7,3,17	-20.4 (± 32.67)	1.0 (± 16.00)	13.4 (± 12.63)	
Day 197: LDH, n=7,3,19	-10.9 (± 27.97)	0.3 (± 20.60)	16.1 (± 21.91)	

Notes:

[50] - Safety Population.

[51] - Safety Population.

[52] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Chemistry Parameters: Total Bilirubin, Direct Bilirubin

End point title	Change From Baseline in Chemistry Parameters: Total Bilirubin, Direct Bilirubin[53]

End point description:

Blood samples were collected to analyze chemistry parameters: total bilirubin and direct bilirubin. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[53] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[54]	3[55]	23[56]	
Units: Micromoles per liter				
arithmetic mean (standard deviation)				
Day 15: Total bilirubin, n=7,2,23	0.571 (± 2.2254)	2.000 (± 2.8284)	-0.957 (± 1.8944)	
Day 29: Total bilirubin, n=8,2,23	-1.000 (± 2.8284)	-3.000 (± 1.4142)	-0.087 (± 1.8565)	
Day 43: Total bilirubin, n=8,3,22	-1.500 (± 1.4142)	-2.000 (± 2.0000)	-0.364 (± 1.4653)	
Day 57: Total bilirubin, n=7,3,22	-0.286 (± 1.3801)	-2.000 (± 0.0000)	-0.636 (± 2.0827)	
Day 71: Total bilirubin, n=8,3,21	0.250 (± 1.9821)	-1.333 (± 1.1547)	-0.095 (± 2.1425)	
Day 85: Total bilirubin, n=8,3,22	0.250 (± 2.7124)	-2.000 (± 0.0000)	-0.364 (± 1.8138)	
Day 113: Total bilirubin, n=7,3,20	0.000 (± 3.2660)	-1.333 (± 1.1547)	0.100 (± 1.5183)	
Day 155: Total bilirubin, n=7,3,18	-1.143 (± 3.0237)	-3.333 (± 1.1547)	-1.604 (± 2.4901)	
Day 197: Total bilirubin, n=7,3,20	0.571 (± 2.7603)	-4.000 (± 0.0000)	-1.416 (± 1.6976)	
Day 15: Direct bilirubin, n=7,2,23	0.0 (± 0.00)	0.0 (± 0.00)	-0.4 (± 1.59)	
Day 29: Direct bilirubin, n=8,2,23	-0.3 (± 0.71)	0.0 (± 0.00)	0.0 (± 1.21)	
Day 43: Direct bilirubin, n=8,3,22	-0.3 (± 0.71)	0.0 (± 0.00)	-0.2 (± 1.05)	
Day 57: Direct bilirubin, n=7,3,22	0.0 (± 0.00)	0.0 (± 0.00)	-0.4 (± 1.18)	
Day 71: Direct bilirubin, n=8,3,21	-0.3 (± 0.71)	0.0 (± 0.00)	-0.1 (± 1.18)	
Day 85: Direct bilirubin, n=8,3,22	-0.3 (± 0.71)	0.0 (± 0.00)	-0.2 (± 1.05)	
Day 113: Direct bilirubin, n=7,3,20	0.0 (± 1.15)	-0.7 (± 1.15)	-0.3 (± 0.98)	
Day 155: Direct bilirubin, n=7,3,17	-0.3 (± 0.76)	0.0 (± 0.00)	-0.2 (± 0.97)	
Day 197: Direct bilirubin, n=7,3,17	0.0 (± 0.00)	0.0 (± 0.00)	-0.1 (± 1.11)	

Notes:

[54] - Safety Population.

[55] - Safety Population.

[56] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Chemistry Parameters: Cholesterol, Direct High-density Lipoprotein (HDL) Cholesterol, Low-density Lipoprotein (LDL) Cholesterol, Triglycerides

End point title	Change From Baseline in Chemistry Parameters: Cholesterol, Direct High-density Lipoprotein (HDL) Cholesterol, Low-density Lipoprotein (LDL) Cholesterol, Triglycerides[57]

End point description:

Blood samples were collected to analyze chemistry parameters: cholesterol, direct HDL cholesterol, LDL cholesterol and triglycerides. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose) and Day 85

Notes:

[57] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[58]	3[59]	22[60]	
Units: Millimoles per liter				
arithmetic mean (standard deviation)				
Cholesterol: n=8,3,22	-0.125 (± 0.7474)	0.067 (± 0.1258)	0.450 (± 0.5780)	
Direct HDL Cholesterol: n=7,3,22	-0.093 (± 0.1718)	-0.033 (± 0.0289)	-0.036 (± 0.2989)	
LDL Cholesterol: n=7,3,21	-0.091 (± 0.7376)	0.110 (± 0.1200)	0.274 (± 0.5011)	
Triglycerides: n=8,3,22	0.025 (± 0.3427)	-0.020 (± 0.0800)	0.535 (± 0.8036)	

Notes:

[58] - Safety Population.

[59] - Safety Population.

[60] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Chemistry Parameter: Corrected Calcium, Urea

End point title	Change From Baseline in Chemistry Parameter: Corrected Calcium, Urea[61]

End point description:

Blood samples were collected to analyze chemistry parameters: corrected calcium and urea. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[61] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[62]	3[63]	23[64]	
Units: Millimoles per liter				
arithmetic mean (standard deviation)				
Day 15: Corrected calcium, n=7,2,23	0.011 (± 0.0540)	-0.020 (± 0.0566)	-0.013 (± 0.0725)	
Day 29: Corrected calcium, n=8,2,23	-0.035 (± 0.0563)	-0.070 (± 0.0424)	-0.036 (± 0.0809)	
Day 43: Corrected calcium, n=8,3,22	-0.003 (± 0.0483)	-0.060 (± 0.0200)	-0.061 (± 0.0737)	

Day 57: Corrected calcium, n=7,3,22	-0.003 (± 0.0509)	-0.060 (± 0.0721)	-0.069 (± 0.0827)	
Day 71: Corrected calcium, n=8,3,21	-0.023 (± 0.0362)	-0.020 (± 0.0000)	-0.066 (± 0.0705)	
Day 85: Corrected calcium, n=8,3,22	-0.043 (± 0.0599)	-0.027 (± 0.0808)	-0.049 (± 0.0689)	
Day 113: Corrected calcium, n=7,3,20	-0.026 (± 0.0746)	0.000 (± 0.0346)	-0.035 (± 0.0550)	
Day 155: Corrected calcium, n=7,3,18	-0.037 (± 0.0678)	0.000 (± 0.0346)	-0.034 (± 0.0508)	
Day 197: Corrected calcium, n=7,3,19	0.014 (± 0.0862)	-0.020 (± 0.0600)	-0.020 (± 0.0629)	
Day 15: Urea, n=7,2,23	0.0714 (± 1.13389)	-2.0000 (± 0.00000)	0.3043 (± 1.56481)	
Day 29: Urea, n=8,2,23	0.0000 (± 1.13389)	-0.7500 (± 0.35355)	0.3043 (± 1.67698)	
Day 43: Urea, n=8,3,22	0.4375 (± 1.08356)	-0.8333 (± 0.28868)	0.3182 (± 1.34116)	
Day 57: Urea, n=7,3,22	-0.1429 (± 1.14434)	-0.8333 (± 0.76376)	0.5682 (± 1.30289)	
Day 71: Urea, n=8,3,21	-0.1875 (± 1.30760)	-0.5000 (± 0.50000)	0.0952 (± 1.50515)	
Day 85: Urea, n=8,3,22	-0.1875 (± 1.25178)	-0.1667 (± 0.76376)	0.4091 (± 1.40269)	
Day 113: Urea, n=7,3,20	0.2857 (± 1.70434)	-0.8333 (± 0.28868)	0.4000 (± 1.47434)	
Day 155: Urea, n=7,3,18	0.2857 (± 1.75255)	-0.8333 (± 1.15470)	0.0912 (± 1.52540)	
Day 197: Urea, n=7,3,19	-0.0714 (± 2.11007)	-1.0000 (± 0.50000)	0.1510 (± 1.76450)	

Notes:

[62] - Safety Population.

[63] - Safety Population.

[64] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Chemistry Parameter: estimated Glomerular Filtration Rate

End point title	Change From Baseline in Chemistry Parameter: estimated Glomerular Filtration Rate[65]

End point description:

Blood samples were collected to analyze chemistry parameter: estimated glomerular filtration rate. Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Change from Baseline was calculated by subtracting the Baseline value from the post-dose visit value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[65] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[66]	3[67]	23[68]	
Units: Milliliter/minute/1.73 square meter				
arithmetic mean (standard deviation)				
Day 15: n=7,2,23	-6.4180 (± 10.28099)	1.7630 (± 1.28693)	-0.7528 (± 9.25789)	
Day 29: n=8,2,23	-4.3085 (± 8.34077)	-2.7765 (± 9.78424)	-1.5543 (± 9.55847)	
Day 43: n=8,3,22	-0.4780 (± 9.34592)	-4.3223 (± 3.88914)	-3.4266 (± 6.99189)	
Day 57: n=7,3,22	1.3446 (± 7.12100)	2.6893 (± 5.61068)	-5.1256 (± 7.41957)	
Day 71: n=8,3,21	-0.4405 (± 12.50899)	-0.9993 (± 5.98467)	-2.5432 (± 7.12712)	
Day 85: n=8,3,22	-1.0010 (± 8.15284)	-7.1513 (± 6.77426)	-5.1038 (± 8.90164)	
Day 113: n=7,3,20	-2.7351 (± 12.23546)	-0.2900 (± 6.19990)	-8.5267 (± 7.71222)	
Day 155: n=7,3,20	-0.9239 (± 13.25672)	-3.9510 (± 5.74000)	-4.2795 (± 9.19612)	
Day 197: n=7,3,21	-4.2733 (± 15.36640)	-7.7100 (± 8.47159)	-2.7185 (± 8.91665)	

Notes:

[66] - Safety Population.

[67] - Safety Population.

[68] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Emergent Worst Case Urinalysis Results by Dipstick

End point title	Number of Participants With Emergent Worst Case Urinalysis Results by Dipstick[69]

End point description:

Urine samples were collected for the assessment of potential of hydrogen, specific gravity, glucose, ketones, occult blood and protein by dipstick method. The dipstick test gave results in a semi-quantitative manner, and results for urinalysis parameters: potential of hydrogen, specific gravity, glucose, ketones, occult blood and protein were categorized as 'any increase from Baseline', which imply any increase in their concentrations in the urine sample. Only participants with emergent worst case any increase from Baseline values are presented. Only those participants with data available at the specified time points were analyzed.

End point type	Primary

End point timeframe:

Up to Day 197

Notes:

[69] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[70]	3[71]	23[72]	
Units: Participants				
Potential of hydrogen, Any increase	0	0	0	
Specific gravity, Any increase	0	0	3	
Glucose, Any increase	0	0	0	
Ketones, Any increase	1	0	4	
Occult blood, Any increase	2	0	3	
Protein, Any increase	1	0	4	

Notes:

[70] - Safety Population.

[71] - Safety Population.

[72] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Vital Signs Relative to Change From Baseline by Potential Clinical Importance (PCI) Criteria

End point title	Number of Participants With Vital Signs Relative to Change From Baseline by Potential Clinical Importance (PCI) Criteria[73]

End point description:

Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) were measured in a seated or semi-supine position after 5 minutes of rest using a completely automated device. PCI ranges were: SBP (increase or decrease from Baseline of >=40 millimeter of mercury [mmHg]), DBP (increase or decrease from Baseline of >=20 mmHg), and HR (increase or decrease from Baseline of >=30 beats per minute). Baseline was defined as the pre-dose Day 1 assessment, unless unavailable, in which case it was the latest pre-dose assessment. Only those participants with data available at the specified time points were analyzed.

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose) and up to Day 197

Notes:

[73] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[74]	3[75]	23[76]	
Units: Participants				
DBP: Decrease >=20	2	0	2	
DBP: Increase >=20	0	0	1	
SBP: Decrease >=40	0	0	0	
SBP: Increase >=40	0	0	2	
HR: Decrease >=30	0	0	0	
HR: Increase >=30	1	0	2	

Notes:

[74] - Safety Population.

[75] - Safety Population.

[76] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Body Temperature

End point title	Change From Baseline in Body Temperature[77]

End point description:

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

End point type	Primary

End point timeframe:

Baseline (Day 1: Pre-dose), Days 15, 29, 43, 57, 71, 85, 113, 155 and 197

Notes:

[77] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[78]	3[79]	23[80]	
Units: Degrees Celsius				
arithmetic mean (standard deviation)				
Day 15: n=8,3,23	0.037 (± 0.4689)	0.400 (± 0.4359)	0.117 (± 0.3833)	
Day 29: n=8,3,23	0.037 (± 0.3889)	0.467 (± 0.6807)	0.130 (± 0.3470)	
Day 43: n=8,3,23	0.012 (± 0.4121)	0.033 (± 0.4163)	0.039 (± 0.4197)	
Day 57: n=7,3,22	0.100 (± 0.2449)	0.133 (± 0.3215)	0.177 (± 0.4253)	
Day 71: n=8,3,21	-0.112 (± 0.5303)	0.267 (± 0.5132)	0.186 (± 0.4328)	
Day 85: n=8,3,22	0.012 (± 0.3563)	0.467 (± 0.5859)	-0.023 (± 0.3854)	
Day 113: n=7,3,20	-0.257 (± 0.3505)	0.400 (± 0.6245)	0.100 (± 0.4952)	
Day 155: n=7,3,17	-0.257 (± 0.3409)	0.167 (± 0.5033)	0.118 (± 0.6054)	
Day 197: n=7,3,17	-0.143 (± 0.4860)	0.267 (± 0.4933)	0.212 (± 0.5122)	

Notes:

[78] - Safety Population.

[79] - Safety Population.

[80] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Worst-case Post-Baseline Abnormal Electrocardiogram (ECG) Findings

End point title	Number of Participants With Worst-case Post-Baseline Abnormal Electrocardiogram (ECG) Findings[81]

End point description:

Twelve lead ECGs were obtained using an ECG machine that automatically calculated the heart rate and measured PR, QRS, QT, and corrected QT intervals. Abnormal findings were categorized as clinically significant and not clinically significant. Clinically significant abnormal findings were those which were not associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition. Data for number of participants with worst case post-Baseline abnormal ECG findings have been presented. Only those participants with data available at the specified time points were analyzed.

End point type	Primary

End point timeframe:

Up to Day 57

Notes:

[81] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.There are no statistical data to report.

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7[82]	3[83]	23[84]	
Units: Participants				
Abnormal- not clinically significant	3	2	10	
Abnormal- clinically significant	0	0	1	

Notes:

[82] - Safety Population.

[83] - Safety Population.

[84] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of GSK2330811

End point title	Plasma Concentrations of GSK2330811[85]

End point description:

Blood samples were collected at the indicated time points for pharmacokinetic analysis of GSK2330811. Pharmacokinetic (PK) Population was defined as participants in the 'Safety' population who received an active dose and for whom a PK sample was obtained and analyzed. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles). 99999 indicates, mean and standard deviation could not be calculated due to high proportion of non-quantifiable (NQ) values (more than [>] 30 percent [%] of values were imputed).

End point type	Secondary

End point timeframe:

Days 1, 15, 29, 57, 85, 113, 155 and 197

Notes:

[85] - 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	GSK2330811 100 mg	GSK2330811 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[86]	24[87]		
Units: Nanogram per milliliter				
arithmetic mean (standard deviation)				
Day 1: n=3,24	99999 (± 99999)	0.0 (± 99999)		
Day 15: n=3,23	5510.7 (± 2455.19)	16197.9 (± 6354.54)		
Day 29: n=3,23	7782.3 (± 1563.04)	23407.0 (± 8830.49)		
Day 57: n=3,22	9868.7 (± 818.51)	32645.7 (± 15225.01)		
Day 85: n=3,22	10993.0 (± 717.89)	29254.4 (± 16911.55)		
Day 113: n=3,20	4123.0 (± 420.29)	11087.1 (± 7661.76)		
Day 155: n=3,16	580.0 (± 408.47)	2892.9 (± 4093.61)		
Day 197: n=3,17	114.0 (± 99999)	729.2 (± 841.17)		

Notes:

[86] - PK Population.

[87] - PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration at the end of the dosing interval (Ctrough) of GSK2330811

End point title	Concentration at the end of the dosing interval (Ctrough) of GSK2330811[88]

End point description:

Blood samples were collected at the indicated time points for PK analysis of GSK2330811. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Days 1, 15, 29, 57, 85, 113, 155 and 197

Notes:

[88] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	GSK2330811 100 mg	GSK2330811 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3[89]	22[90]		
Units: Nanogram per milliliter				
arithmetic mean (standard deviation)	10993.0 (± 717.89)	29254.4 (± 16911.55)		

Notes:

[89] - PK Population.

[90] - PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance (CL/F) of GSK2330811

End point title	Apparent Clearance (CL/F) of GSK2330811

End point description:

Blood samples were collected at the indicated time points for PK analysis of GSK2330811. Data was analyzed by population pharmacokinetic methods using a non-linear mixed-effects modelling approach. Only those participants with data available at the specified time points were analyzed. CL/F was estimated based on population PK modelling on the combination of data of participants dosed with GSK2330811, as it was more appropriate due to limited dose range (100 mg and 300 mg).

End point type	Secondary

End point timeframe:

Days 1, 15, 29, 57, 85, 113, 155 and 197

End point values	GSK2330811 100 mg and GSK2330811 300 mg - Overall			
Subject group type	Subject analysis set			
Number of subjects analysed	26[91]			
Units: Liter per hour				
geometric mean (confidence interval 95%)	0.0147 (0.0132 to 0.0163)			

Notes:

[91] - PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution (Vss/F) of GSK2330811

End point title	Apparent Volume of Distribution (Vss/F) of GSK2330811

End point description:

Blood samples were collected at the indicated time points for PK analysis of GSK2330811. Data was analyzed by population pharmacokinetic methods using a non-linear mixed-effects modelling approach. Only those participants with data available at the specified time points were analyzed. 99999 indicates, PK parameters were calculated by fitting a population PK model using the combined data of participants dosed with 100 mg and 300 mg of GSK2330811. Since a minimal model was utilized, the Vss/F value was fixed to a plasma physiological value obtained from the literature. Hence, a confidence interval cannot be provided for this parameter.

End point type	Secondary

End point timeframe:

Days 1, 15, 29, 57, 85, 113, 155 and 197

End point values	GSK2330811 100 mg and GSK2330811 300 mg - Overall			
Subject group type	Subject analysis set			
Number of subjects analysed	26[92]			
Units: Liter				
geometric mean (confidence interval 95%)	3.25 (-99999 to 99999)			

Notes:

[92] - PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Level of Total Oncostatin M (OSM)

End point title	Serum Level of Total Oncostatin M (OSM)

End point description:

Blood samples were collected at indicated timepoints for analysis of total OSM levels in serum. Per Protocol Population comprised of participants in the 'Safety' population who complied with the protocol. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Secondary

End point timeframe:

Days 1, 15, 29, 57, 85, 113, 155 and 197

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[93]	3[94]	23[95]	
Units: Picogram per milliliter				
median (full range (min-max))				
Day 1: n=8,3,22	22.110 (13.08 to 57.40)	30.590 (6.19 to 38.71)	27.455 (16.93 to 81.71)	
Day 15: n=8,3,23	28.175 (18.07 to 57.48)	576.850 (417.28 to 696.18)	721.020 (496.63 to 1482.91)	
Day 29: n=8,3,23	26.210 (12.84 to 48.82)	499.540 (487.14 to 635.94)	974.220 (398.94 to 2500.01)	
Day 57: n=7,3,22	34.700 (13.40 to 43.94)	651.710 (554.93 to 971.25)	1211.570 (636.83 to 2350.65)	
Day 85: n=8,3,22	17.275 (14.38 to 66.28)	613.290 (555.09 to 1229.71)	1357.645 (542.85 to 2500.01)	

Day 113: n=7,3,20	23.350 (8.42 to 81.11)	687.810 (419.04 to 935.76)	1044.650 (186.06 to 2378.21)	
Day 155: n=7,3,17	23.850 (13.13 to 43.07)	206.900 (143.55 to 363.62)	359.340 (58.13 to 1097.70)	
Day 197: n=7,3,17	28.800 (19.58 to 36.13)	54.290 (40.96 to 137.88)	142.830 (28.82 to 607.09)	

Notes:

[93] - Per Protocol Population.

[94] - Per Protocol Population.

[95] - Per Protocol Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Level of Free OSM

End point title	Serum Level of Free OSM

End point description:

Blood samples were collected at indicated timepoints for analysis of free OSM levels in serum. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Secondary

End point timeframe:

Days 1, 15, 29, 57, 85, 113, 155 and 197

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[96]	3[97]	23[98]	
Units: Picogram per milliliter				
median (full range (min-max))				
Day 1: n=8,3,22	19.72 (8.3 to 45.3)	28.93 (4.5 to 36.8)	20.74 (8.8 to 56.0)	
Day 15: n=8,3,23	23.85 (11.7 to 40.7)	0.73 (0.73 to 0.73)	0.73 (0.73 to 0.73)	
Day 29: n=8,3,23	19.35 (4.5 to 37.1)	0.73 (0.73 to 0.73)	0.73 (0.73 to 0.73)	
Day 57: n=7,3,22	27.62 (6.1 to 35.9)	0.73 (0.73 to 0.73)	0.73 (0.73 to 0.73)	
Day 85: n=8,3,22	12.37 (5.9 to 47.6)	0.73 (0.73 to 0.73)	0.73 (0.73 to 0.73)	
Day 113: n=7,3,20	16.78 (5.7 to 58.5)	0.73 (0.73 to 0.73)	0.73 (0.73 to 0.73)	
Day 155: n=7,3,17	14.54 (7.3 to 32.7)	0.73 (0.73 to 0.73)	0.73 (0.7 to 1.7)	
Day 197: n=7,3,17	18.43 (12.2 to 23.5)	0.73 (0.73 to 0.73)	0.73 (0.7 to 2.7)	

Notes:

[96] - Per Protocol Population.

[97] - Per Protocol Population.

[98] - Per Protocol Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Anti-GSK2330811 Antibodies

End point title	Number of Participants With Positive Anti-GSK2330811 Antibodies

End point description:

Serum samples were collected for the determination of anti-GSK2330811 antibodies (ADA) using a binding antibody detection assay. The assay involved screening, confirmation and titration steps. If serum samples tested positive in the screening assay, they were considered 'potentially positive' and were further analyzed for the specificity using the confirmation assay. Samples that were confirmed positive in the confirmation assay were reported as 'positive'. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Secondary

End point timeframe:

Days 1, 15, 57, 85 and 197

End point values	Placebo	GSK2330811 100 mg	GSK2330811 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[99]	3[100]	23[101]	
Units: Participants				
Day 1: n=8,3,23	0	0	3	
Day 15: n=8,3,23	0	0	1	
Day 57: n=7,3,22	0	0	2	
Day 85: n=8,3,22	0	0	1	
Day 197: n=7,3,17	0	0	0	

Notes:

[99] - Safety Population.

[100] - Safety Population.

[101] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality, SAEs and non-SAEs were collected up to Day 197. The protocol allowed for additional SAEs to be collected after Day 197; collected up to Day 603 post first dose

Adverse event reporting additional description:

Safety Population consisted of all randomized participants who have taken at least 1 dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received subcutaneous injection of placebo on Day 1 and then every other week until the final dose on Day 71 (Week 10).

Reporting group title	GSK2330811 300 mg

Reporting group description:

Participants received subcutaneous injection of GSK2330811 300 mg on Day 1 and then every other week until the final dose on Day 71 (Week 10).

Reporting group title	GSK2330811 100 mg

Reporting group description:

Participants received subcutaneous injection of GSK2330811 100 milligrams (mg) on Day 1 and then every other week until the final dose on Day 71 (Week 10).

Serious adverse events	Placebo	GSK2330811 300 mg	GSK2330811 100 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	2 / 24 (8.33%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal cell carcinoma			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Hypotension			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	0 / 3 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	0 / 3 (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
Pericarditis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	0 / 3 (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
Infections and infestations			
Infected skin ulcer			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (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

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

Non-serious adverse events	Placebo	GSK2330811 300 mg	GSK2330811 100 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	24 / 24 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Raynaud's phenomenon			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Injection site erythema			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Injection site pain			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Nodule			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 8 (25.00%)	3 / 24 (12.50%)	1 / 3 (33.33%)
occurrences (all)	2	4	1
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Dyspnoea exertional			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Oropharyngeal pain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			

Depressed mood			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Cardiac murmur			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram PR prolongation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Haematocrit decreased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Haemoglobin decreased			
subjects affected / exposed	0 / 8 (0.00%)	6 / 24 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Platelet count decreased			
subjects affected / exposed	0 / 8 (0.00%)	3 / 24 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Red blood cell count decreased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Reticulocyte count increased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Reticulocyte percentage increased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Fall			

subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	4 / 24 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Headache			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	4 / 24 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Neutropenia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Thrombocytopenia			
subjects affected / exposed	0 / 8 (0.00%)	3 / 24 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Ear and labyrinth disorders			
Ear pruritus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Angular cheilitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	1 / 8 (12.50%)	4 / 24 (16.67%)	1 / 3 (33.33%)
occurrences (all)	1	5	1
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 8 (0.00%)	3 / 24 (12.50%)	1 / 3 (33.33%)
occurrences (all)	0	4	1
Nausea			
subjects affected / exposed	1 / 8 (12.50%)	3 / 24 (12.50%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Vomiting			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Actinic elastosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Blister			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Hyperkeratosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Lentigo			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lipoatrophy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Rash			
subjects affected / exposed	1 / 8 (12.50%)	3 / 24 (12.50%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Rash maculo-papular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Skin mass			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Skin ulcer			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	1 / 3 (33.33%)
occurrences (all)	0	3	1
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Folliculitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastrointestinal bacterial overgrowth			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Paronychia			

subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Skin bacterial infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	4 / 24 (16.67%)	1 / 3 (33.33%)
occurrences (all)	1	5	4
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	1 / 3 (33.33%)
occurrences (all)	0	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 November 2016	Amendment 1: This amendment was executed in response to the Food and Drug Administration (FDA) request that the participant eligibility criteria be modified to include two forms of contraception for males and females of childbearing potential.
12 December 2016	Amendment 2: This amendment was primarily executed in response to an FDA recommendation for a 30 minute observation period after each dose is administered.
20 July 2017	Amendment 3: This amendment was primarily executed to add the additional exploratory endpoints of change in the Composite Response Index in diffuse cutaneous Systemic Sclerosis (CRISS) and change in Patient Global Assessment.
12 November 2018	Amendment 4: This amendment was executed to provide clarification on the points detailed below: 1. Schedule of Activities, Exclusion Criteria and Clinical Laboratory Tests were updated to reflect use of QuantiFERON-TB Gold PLUS test at central laboratory. 2. Wording clarified in Inclusion Criteria and Permitted medications and Non-Drug Therapies to reflect intent that mycophenolate sodium dose allowed should be equivalent to mycophenolate mofetil dose. 3. Updated text from 'will' to 'may' in Sample Size Determination and Interim Analyses to indicate that it may not be feasible to conduct all interim analyses. 4. Wording updated to clarify circumstances when local laboratory results are acceptable in Clinical Laboratory Tests.
01 April 2020	Amendment 5: This amendment was executed in response to the COVID-19 pandemic to provide clarification on the points detailed below: 1. Schedule of Activities and Study Assessments and Procedures were updated to allow a virtual or telephone visit at Day 113, Day 155, Day 197 and Early Withdrawal (if required) to perform any study assessments that can be conducted remotely in circumstances in which an onsite visit is not possible due to the COVID-19 pandemic. 2. Schedule of Activities updated to extend the visit window on Day 113 to +/- 5 days, and on Day 155 and Day 197 to +/- 10. 3. Schedule of Activities and Clinical Laboratory Tests were updated to allow safety (hematology and chemistry) labs and pregnancy tests to be run locally at the clinical site or within the community at the discretion of the Investigator for the Day 113, Day 155, Day 197 and Early Withdrawal (if required) visits; and updated to allow urine pregnancy test to be performed for the Day 197 and Early Withdrawal (if required) visits if a serum pregnancy test cannot be performed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported