Clinical trial results:
An Open-label, Dose-escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single Doses of GSK2586881 in Participants with Pulmonary Arterial Hypertension

Summary

EudraCT number	2017-000212-41
Trial protocol	ES DE
Global end of trial date	07 May 2019

Results information

Result version number	v1 (current)
This version publication date	23 April 2020
First version publication date	23 April 2020

Trial information

Trial identification

Sponsor protocol code	206246

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	30 August 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate changes in the pulmonary hemodynamics after single IV doses of GSK2586881 administered to participants with PAH receiving background PAH therapy

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 February 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	23
EEA total number of subjects	16

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)	19
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This phase 2a, open-label, dose-escalation study comprised of 4 cohorts. Participants received GSK2586881 by single intravenous (IV) infusion at following doses: 0.1 milligram per kilogram (mg/kg) or 0.2 mg/kg or 0.4 mg/kg or 0.8 mg/kg.

Pre-assignment

Screening details:

A total of 31 participants were screened and of them 7 participants were screen failures and one withdrew consent before dosing. Hence, a total of 23 participants received study treatment. This study was conducted at 4 centers in Germany, 2 centers in Spain, and 2 centers in the United States.

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK2586881 0.1 mg/kg

Arm description:

Participants received a single IV dose of 0.1 mg/kg GSK2586881 and were followed up till 28 days post-dose.

Arm type	Experimental
Investigational medicinal product name	GSK2586881
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

GSK2586881 is a clear colorless liquid for IV infusion. Participants received a single IV dose of 0.1 mg/kg GSK2586881.

Arm title	GSK2586881 0.2 mg/kg

Arm description:

Participants received a single IV dose of 0.2 mg/kg GSK2586881 and were followed up till 28 days post-dose.

Arm type	Experimental
Investigational medicinal product name	GSK2586881
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

GSK2586881 is a clear colorless liquid for IV infusion. Participants received a single IV dose of 0.2 mg/kg GSK2586881.

Arm title	GSK2586881 0.4 mg/kg

Arm description:

Participants received a single IV dose of 0.4 mg/kg GSK2586881 and were followed up till 28 days post-dose.

Arm type	Experimental

Investigational medicinal product name	GSK2586881
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

GSK2586881 is a clear colorless liquid for IV infusion. Participants received a single IV dose of 0.4 mg/kg GSK2586881.

Arm title	GSK2586881 0.8 mg/kg

Arm description:

Participants received a single IV dose of 0.8 mg/kg GSK2586881 and were followed up till 28 days post-dose.

Arm type	Experimental
Investigational medicinal product name	GSK2586881
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

GSK2586881 is a clear colorless liquid for IV infusion. Participants received a single IV dose of 0.8 mg/kg GSK2586881.

Number of subjects in period 1	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg
Started	4	5	6
Completed	4	5	6

Number of subjects in period 1	GSK2586881 0.8 mg/kg
Started	8
Completed	8

Baseline characteristics

Reporting groups	
Reporting group title	GSK2586881 0.1 mg/kg
Reporting group description:	
Participants received a single IV dose of 0.1 mg/kg GSK2586881 and were followed up till 28 days post-dose.	
Reporting group title	GSK2586881 0.2 mg/kg
Reporting group description:	
Participants received a single IV dose of 0.2 mg/kg GSK2586881 and were followed up till 28 days post-dose.	
Reporting group title	GSK2586881 0.4 mg/kg
Reporting group description:	
Participants received a single IV dose of 0.4 mg/kg GSK2586881 and were followed up till 28 days post-dose.	
Reporting group title	GSK2586881 0.8 mg/kg
Reporting group description:	
Participants received a single IV dose of 0.8 mg/kg GSK2586881 and were followed up till 28 days post-dose.	

Reporting group values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg
Number of subjects	4	5	6
Age categorical Units: Subjects			
Total participants	4	5	6
Age Continuous Units: Years			
arithmetic mean	32.0	55.4	52.5
standard deviation	± 4.97	± 14.96	± 8.67
Sex: Female, Male Units: Participants			
Female	3	3	4
Male	1	2	2
Race/Ethnicity, Customized Units: Subjects			
Black or African American	0	1	1
White - White/Caucasian/European Heritage	4	4	5

Reporting group values	GSK2586881 0.8 mg/kg	Total	
Number of subjects	8	23	
Age categorical Units: Subjects			
Total participants	8	23	
Age Continuous Units: Years			
arithmetic mean	50.3		
standard deviation	± 13.35	-	

Sex: Female, Male Units: Participants			
Female	5	15	
Male	3	8	
Race/Ethnicity, Customized Units: Subjects			
Black or African American	1	3	
White - White/Caucasian/European Heritage	7	20	

End points

End points reporting groups

Reporting group title	GSK2586881 0.1 mg/kg
Reporting group description:	
Participants received a single IV dose of 0.1 mg/kg GSK2586881 and were followed up till 28 days post-dose.	
Reporting group title	GSK2586881 0.2 mg/kg
Reporting group description:	
Participants received a single IV dose of 0.2 mg/kg GSK2586881 and were followed up till 28 days post-dose.	
Reporting group title	GSK2586881 0.4 mg/kg
Reporting group description:	
Participants received a single IV dose of 0.4 mg/kg GSK2586881 and were followed up till 28 days post-dose.	
Reporting group title	GSK2586881 0.8 mg/kg
Reporting group description:	
Participants received a single IV dose of 0.8 mg/kg GSK2586881 and were followed up till 28 days post-dose.	

Primary: Change from Baseline in pulmonary vascular resistance (PVR)

End point title	Change from Baseline in pulmonary vascular resistance (PVR)[1]
End point description:	
PVR is the resistance generated by pulmonary circulation. Pulmonary arterial catheters were placed in participants and PVR values were recorded from the right heart catheterization. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was measured as ratio of post-dose visit value to Baseline value. Evaluable Population comprised of all participants who were in the safety population, who completed all Day 1 assessments (including up to 24 hours post dose) and were not deemed to have had major protocol deviations. 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); 1 hour, 2 hours and 4 hours post-dose (Day 1)	

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	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[2]	5[3]	5[4]	8[5]
Units: Ratio				
geometric mean (confidence interval 95%)				
1 hour post-dose (Day 1)	0.936 (0.725 to 1.208)	0.885 (0.686 to 1.141)	0.813 (0.561 to 1.178)	1.017 (0.862 to 1.198)
2 hours post-dose (Day 1)	0.926 (0.671 to 1.279)	1.043 (0.910 to 1.195)	0.945 (0.788 to 1.134)	0.974 (0.823 to 1.153)
4 hours post-dose (Day 1)	0.907 (0.552 to 1.490)	0.895 (0.668 to 1.199)	0.924 (0.589 to 1.448)	1.116 (1.050 to 1.186)

Notes:

[2] - Evaluable Population

[3] - Evaluable Population

[4] - Evaluable Population

[5] - Evaluable Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in cardiac output (CO)

End point title	Change from Baseline in cardiac output (CO)[6]

End point description:

CO is the amount of blood pumped by the heart per minute. Pulmonary arterial catheters were placed in participants and CO values were recorded from the right heart catheterization. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was measured as ratio of post-dose visit value to Baseline value. 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); 1 hour, 2 hours and 4 hours post-dose (Day 1)

Notes:

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

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[7]	5[8]	5[9]	8[10]
Units: Ratio				
geometric mean (confidence interval 95%)				
1 hour post-dose (Day 1)	1.046 (0.881 to 1.240)	1.079 (0.966 to 1.206)	1.076 (0.758 to 1.528)	0.990 (0.948 to 1.033)
2 hours post-dose (Day 1)	1.025 (0.829 to 1.269)	1.029 (0.950 to 1.116)	0.929 (0.712 to 1.210)	1.012 (0.944 to 1.085)
4 hours post-dose (Day 1)	1.114 (0.804 to 1.545)	1.138 (0.949 to 1.365)	0.882 (0.734 to 1.060)	1.002 (0.935 to 1.075)

Notes:

[7] - Evaluable Population

[8] - Evaluable Population

[9] - Evaluable Population

[10] - Evaluable Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in mean pulmonary artery pressure (mPAP)

End point title	Change from Baseline in mean pulmonary artery pressure (mPAP)[11]

End point description:

The pulmonary artery pressure is a measure of the blood pressure found in the main pulmonary artery. Pulmonary arterial catheters were placed in participants and mPAP values were recorded from the right

heart catheterization. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was measured as ratio of post-dose visit value to Baseline value. 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); 1 hour, 2 hours and 4 hours post-dose (Day 1)

Notes:

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

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[12]	5[13]	5[14]	8[15]
Units: Ratio				
geometric mean (confidence interval 95%)				
1 hour post-dose (Day 1)	0.950 (0.781 to 1.154)	0.995 (0.960 to 1.032)	0.939 (0.799 to 1.104)	0.989 (0.879 to 1.114)
2 hours post-dose (Day 1)	0.937 (0.781 to 1.126)	0.994 (0.924 to 1.070)	0.910 (0.766 to 1.081)	0.996 (0.867 to 1.144)
4 hours post-dose (Day 1)	0.991 (0.812 to 1.211)	1.029 (0.881 to 1.202)	0.973 (0.897 to 1.054)	1.062 (0.958 to 1.177)

Notes:

[12] - Evaluable Population

[13] - Evaluable Population

[14] - Evaluable Population

[15] - Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with non-serious adverse events (AEs)

End point title	Number of participants with non-serious adverse events (AEs)

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. Safety Population comprised of all participants who took at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Day 28

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[16]	5[17]	6[18]	8[19]
Units: Participants	1	3	5	2

Notes:

[16] - Safety Population

[17] - Safety Population

[18] - Safety Population

[19] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with serious adverse events (SAEs)

End point title	Number of participants with serious adverse events (SAEs)

End point description:

Any untoward event resulting in death, life threatening, requiring hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention were categorized as SAE.

End point type	Secondary

End point timeframe:

Up to Day 28

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[20]	5[21]	6[22]	8[23]
Units: Participants	0	0	0	0

Notes:

[20] - Safety Population

[21] - Safety Population

[22] - Safety Population

[23] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameters: alkaline phosphatase, alanine amino transferase and aspartate amino transferase

End point title	Change from Baseline in clinical chemistry parameters: alkaline phosphatase, alanine amino transferase and aspartate amino transferase

End point description:

Blood samples were collected for the assessment of clinical chemistry parameters: alkaline phosphatase, alanine amino transferase (ALT) and aspartate amino transferase (AST). Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), 24 hours post-dose (Day 1) and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[24]	5[25]	6[26]	8[27]
Units: International units per liter				
arithmetic mean (standard deviation)				
Alkaline phosphatase, 24 hours post-dose (Day 1)	4.8 (± 8.42)	-1.4 (± 7.44)	5.3 (± 3.08)	3.1 (± 3.48)
Alkaline phosphatase, Day 7 to Day 14	6.5 (± 5.00)	3.2 (± 4.21)	3.0 (± 3.52)	2.6 (± 4.31)
ALT, 24 hours post-dose (Day 1)	-2.0 (± 2.16)	0.0 (± 1.58)	-1.8 (± 3.76)	-0.1 (± 2.17)
ALT, Day 7 to Day 14	1.3 (± 0.96)	1.8 (± 3.27)	-4.3 (± 12.94)	0.9 (± 4.85)
AST, 24 hours post-dose (Day 1)	0.0 (± 1.63)	-0.4 (± 0.55)	0.5 (± 1.76)	-1.8 (± 3.77)
AST, Day 7 to Day 14	2.8 (± 2.50)	1.4 (± 1.67)	-0.3 (± 3.67)	-0.9 (± 6.71)

Notes:

[24] - Safety Population

[25] - Safety Population

[26] - Safety Population

[27] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameters: direct bilirubin, total bilirubin and creatinine

End point title	Change from Baseline in clinical chemistry parameters: direct bilirubin, total bilirubin and creatinine

End point description:

Blood samples were collected for the assessment of clinical chemistry parameters: direct bilirubin, total bilirubin and creatinine. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), 24 hours post-dose (Day 1) and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[28]	5[29]	6[30]	8[31]
Units: Micromoles per liter				
arithmetic mean (standard deviation)				
Direct bilirubin, 24 hours post-dose (Day 1)	2.0 (± 1.63)	0.4 (± 0.89)	0.3 (± 1.97)	1.0 (± 2.14)
Direct bilirubin, Day 7 to Day 14	1.0 (± 1.15)	0.0 (± 0.00)	0.0 (± 1.26)	0.5 (± 2.56)
Total bilirubin, 24 hours post-dose (Day 1)	3.0 (± 4.16)	0.8 (± 1.79)	0.7 (± 4.84)	4.8 (± 6.76)

Total bilirubin, Day 7 to Day 14	1.5 (± 3.42)	0.4 (± 2.61)	-1.7 (± 3.44)	0.0 (± 4.14)
Creatinine, 24 hours post-dose (Day 1)	5.08 (± 4.102)	10.80 (± 6.110)	12.22 (± 20.214)	1.76 (± 2.759)
Creatinine, Day 7 to Day 14	-1.12 (± 6.530)	8.68 (± 13.353)	4.57 (± 9.638)	3.20 (± 4.885)

Notes:

[28] - Safety Population

[29] - Safety Population

[30] - Safety Population

[31] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameters: calcium, glucose, potassium, sodium and blood urea nitrogen (BUN)

End point title	Change from Baseline in clinical chemistry parameters: calcium, glucose, potassium, sodium and blood urea nitrogen (BUN)

End point description:

Blood samples were collected for the assessment of clinical chemistry parameters: calcium, glucose, potassium, sodium and BUN. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), 24 hours post-dose (Day 1) and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[32]	5[33]	6[34]	8[35]
Units: Millimoles per liter				
arithmetic mean (standard deviation)				
Calcium, 24 hours post-dose (Day 1)	0.035 (± 0.1427)	0.012 (± 0.0867)	0.047 (± 0.1033)	0.060 (± 0.0466)
Calcium, Day 7 to Day 14	0.025 (± 0.1399)	0.064 (± 0.0888)	0.047 (± 0.1250)	0.115 (± 0.0583)
Glucose, 24 hours post-dose (Day 1)	0.85 (± 0.957)	1.10 (± 1.398)	0.50 (± 1.752)	0.89 (± 2.039)
Glucose, Day 7 to Day 14	0.95 (± 1.760)	-0.32 (± 0.646)	-0.57 (± 0.635)	-0.20 (± 1.995)
Potassium, 24 hours post-dose (Day 1)	0.28 (± 0.377)	0.18 (± 0.179)	0.08 (± 0.306)	-0.05 (± 0.239)
Potassium, Day 7 to Day 14	0.10 (± 0.356)	0.22 (± 0.148)	0.25 (± 0.207)	0.18 (± 0.301)
Sodium, 24 hours post-dose (Day 1)	-1.3 (± 1.26)	-0.6 (± 2.30)	-0.2 (± 1.47)	-1.0 (± 1.85)
Sodium, Day 7 to Day 14	-0.3 (± 4.19)	0.0 (± 1.87)	0.5 (± 1.64)	0.0 (± 1.60)
BUN, 24 hours post-dose (Day 1)	0.00 (± 1.080)	-0.20 (± 0.758)	0.83 (± 1.033)	-0.25 (± 0.463)
BUN, Day 7 to Day 14	-0.25 (± 1.258)	1.50 (± 1.541)	0.00 (± 1.000)	0.31 (± 1.067)

Notes:

[32] - Safety Population

[33] - Safety Population

[34] - Safety Population

[35] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in clinical chemistry parameter: total protein

End point title	Change from Baseline in clinical chemistry parameter: total protein

End point description:

Blood samples were collected for the assessment of clinical chemistry parameter, total protein. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), 24 hours post-dose (Day 1) and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[36]	5[37]	6[38]	8[39]
Units: Grams per liter				
arithmetic mean (standard deviation)				
24 hours post-dose (Day 1)	1.3 (± 6.13)	0.6 (± 3.78)	1.8 (± 2.93)	2.6 (± 3.66)
Day 7 to Day 14	1.5 (± 2.38)	6.2 (± 4.55)	2.0 (± 4.73)	4.9 (± 3.31)

Notes:

[36] - Safety Population

[37] - Safety Population

[38] - Safety Population

[39] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameters: basophils, eosinophils, lymphocytes, monocytes, total neutrophils, platelet count and white blood cell (WBC) count

End point title	Change from Baseline in hematology parameters: basophils, eosinophils, lymphocytes, monocytes, total neutrophils, platelet count and white blood cell (WBC) count

End point description:

Blood samples were collected for the assessment of hematology parameters: basophils, eosinophils, lymphocytes, monocytes, total neutrophils (T.neutrophils), platelet count and WBC count. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-

dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), 24 hours post-dose (Day 1) and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[40]	5[41]	6[42]	8[43]
Units: Giga cells per liter				
arithmetic mean (standard deviation)				
Basophils, 24 hours post-dose (Day 1), n=4,4,6,3	-0.008 (± 0.0359)	0.013 (± 0.0206)	-0.005 (± 0.0302)	0.003 (± 0.0115)
Basophils, Day 7 to Day 14, n=4,5,6,8	0.000 (± 0.0327)	0.002 (± 0.0192)	0.008 (± 0.0306)	0.003 (± 0.0238)
Eosinophils, 24 hours post-dose (Day 1), n=4,4,6,3	0.007 (± 0.0695)	0.018 (± 0.0222)	0.012 (± 0.0662)	-0.007 (± 0.0503)
Eosinophils, Day 7 to Day 14, n=4,5,6,8	-0.035 (± 0.0835)	0.004 (± 0.0230)	-0.025 (± 0.0807)	0.023 (± 0.1004)
Lymphocytes, 24 hours post-dose (Day 1), n=4,4,6,3	0.000 (± 0.5509)	-0.070 (± 0.1612)	-0.157 (± 0.1558)	0.190 (± 0.4553)
Lymphocytes, Day 7 to Day 14, n=4,5,6,8	-0.025 (± 0.4277)	-0.054 (± 0.1422)	-0.250 (± 0.2001)	0.130 (± 0.4032)
Monocytes, 24 hours post-dose (Day 1), n=4,4,6,3	0.050 (± 0.0673)	-0.028 (± 0.0914)	0.098 (± 0.1125)	0.140 (± 0.0700)
Monocytes, Day 7 to Day 14, n=4,5,6,8	0.038 (± 0.1066)	0.038 (± 0.0998)	0.047 (± 0.1263)	0.091 (± 0.1654)
T.neutrophils, 24 hours post-dose(Day1),n=4,4,6,3	0.643 (± 1.0052)	0.415 (± 0.3924)	0.738 (± 0.5615)	0.727 (± 0.7298)
T.neutrophils, Day 7 to Day 14, n=4,5,6,8	0.185 (± 0.9008)	0.504 (± 0.4884)	0.397 (± 1.3173)	0.366 (± 0.7204)
Platelets, 24 hours post-dose (Day 1), n=4,4,6,5	11.8 (± 36.28)	-33.0 (± 73.51)	7.8 (± 16.65)	12.6 (± 27.74)
Platelets, Day 7 to Day 14, n=4,5,6,8	35.3 (± 17.40)	19.8 (± 45.03)	14.3 (± 52.89)	23.4 (± 24.44)
WBC count, 24 hours post-dose (Day 1), n=4,4,6,5	0.35 (± 1.330)	0.30 (± 0.183)	0.68 (± 0.542)	2.16 (± 2.492)
WBC count, Day 7 to Day 14, n=4,5,6,8	-0.20 (± 1.334)	0.46 (± 0.498)	0.20 (± 1.355)	0.64 (± 0.588)

Notes:

[40] - Safety Population

[41] - Safety Population

[42] - Safety Population

[43] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter: hemoglobin

End point title	Change from Baseline in hematology parameter: hemoglobin

End point description:

Blood samples were collected for the assessment of hematology parameter, hemoglobin. Baseline was

defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), 24 hours post-dose (Day 1) and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[44]	5[45]	6[46]	8[47]
Units: Grams per liter				
arithmetic mean (standard deviation)				
24 hours post-dose (Day 1), n=4,4,6,5	1.8 (± 11.09)	2.0 (± 5.72)	5.0 (± 4.77)	3.0 (± 5.61)
Day 7 to Day 14, n=4,5,6,8	-4.3 (± 6.55)	3.4 (± 5.98)	-1.5 (± 7.09)	4.0 (± 5.15)

Notes:

[44] - Safety Population

[45] - Safety Population

[46] - Safety Population

[47] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter: hematocrit

End point title	Change from Baseline in hematology parameter: hematocrit

End point description:

Blood samples were collected for the assessment of hematology parameter, hematocrit. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), 24 hours post-dose (Day 1) and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[48]	5[49]	6[50]	8[51]
Units: Proportion of red blood cells in blood				
arithmetic mean (standard deviation)				
24 hours post-dose (Day 1), n=4,4,6,5	0.0030 (± 0.02858)	0.0053 (± 0.02156)	0.0098 (± 0.01546)	0.0140 (± 0.02448)

Day 7 to Day 14, n=4,5,6,8	-0.0225 (± 0.00929)	0.0104 (± 0.02173)	0.0030 (± 0.02391)	0.0135 (± 0.01891)

Notes:

[48] - Safety Population

[49] - Safety Population

[50] - Safety Population

[51] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter: Mean corpuscle hemoglobin

End point title	Change from Baseline in hematology parameter: Mean corpuscle hemoglobin

End point description:

Blood samples were collected for the assessment of hematology parameter, mean corpuscle hemoglobin. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), 24 hours post-dose (Day 1) and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[52]	5[53]	6[54]	8[55]
Units: Picograms				
arithmetic mean (standard deviation)				
24 hours post-dose (Day 1), n=4,4,6,5	-0.08 (± 0.150)	0.05 (± 0.507)	0.25 (± 0.302)	-0.10 (± 0.235)
Day 7 to Day 14, n=4,5,6,8	0.10 (± 0.483)	0.04 (± 0.182)	-0.33 (± 0.314)	0.15 (± 0.177)

Notes:

[52] - Safety Population

[53] - Safety Population

[54] - Safety Population

[55] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter: Mean corpuscle volume

End point title	Change from Baseline in hematology parameter: Mean corpuscle volume

End point description:

Blood samples were collected for the assessment of hematology parameter, mean corpuscle volume.

Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), 24 hours post-dose (Day 1) and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[56]	5[57]	6[58]	8[59]
Units: Femtoliters				
arithmetic mean (standard deviation)				
24 hours post-dose (Day 1), n=4,4,6,5	-0.5 (± 2.52)	0.0 (± 0.82)	-0.5 (± 0.84)	0.6 (± 1.95)
Day 7 to Day 14, n=4,5,6,8	-1.5 (± 2.08)	-0.2 (± 0.84)	0.7 (± 1.03)	0.8 (± 1.04)

Notes:

[56] - Safety Population

[57] - Safety Population

[58] - Safety Population

[59] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter: Red blood cell (RBC) count

End point title	Change from Baseline in hematology parameter: Red blood cell (RBC) count

End point description:

Blood samples were collected for the assessment of hematology parameter: RBC count. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), 24 hours post-dose (Day 1) and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[60]	5[61]	6[62]	8[63]
Units: Trillion cells per liter				
arithmetic mean (standard deviation)				
24 hours post-dose (Day 1), n=4,4,6,5	0.03 (± 0.435)	0.03 (± 0.287)	0.13 (± 0.163)	0.12 (± 0.192)
Day 7 to Day 14, n=4,5,6,8	-0.20 (± 0.183)	0.14 (± 0.261)	0.00 (± 0.310)	0.11 (± 0.203)

Notes:

[60] - Safety Population

[61] - Safety Population

[62] - Safety Population

[63] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematology parameter: Reticulocytes

End point title	Change from Baseline in hematology parameter: Reticulocytes

End point description:

Blood samples were collected for the assessment of hematology parameter: reticulocytes. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose), 24 hours post-dose (Day 1) and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[64]	5[65]	6[66]	8[67]
Units: Percentage of reticulocytes in blood				
arithmetic mean (standard deviation)				
24 hours post-dose (Day 1), n=4,4,6,5	0.0012 (± 0.00330)	0.0017 (± 0.00310)	0.0017 (± 0.00216)	0.0000 (± 0.00100)
Day 7 to Day 14, n=4,5,6,8	0.0058 (± 0.00411)	0.0014 (± 0.00358)	0.0025 (± 0.00333)	0.0040 (± 0.00325)

Notes:

[64] - Safety Population

[65] - Safety Population

[66] - Safety Population

[67] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Urinalysis Results by Dipstick Method

End point title	Number of Participants With Urinalysis Results by Dipstick Method

End point description:

Urine samples were collected to assess urine bilirubin, urine occult blood, urine glucose, urine ketones, and urine protein by dipstick test. The dipstick test gives results in a semi-quantitative manner, and results for urinalysis parameter of urine bilirubin, urine occult blood, urine glucose, urine ketones and urine protein can be read as negative, trace, 1+, 2+ and 3+ indicating proportional concentrations in the urine sample.

End point type	Secondary

End point timeframe:

24 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[68]	5[69]	6[70]	8[71]
Units: Participants				
Bilirubin, 24 hours post-dose (Day 1), negative	4	5	6	8
Bilirubin, 24 hours post-dose (Day 1), trace	0	0	0	0
Bilirubin, 24 hours post-dose (Day 1), 1+	0	0	0	0
Bilirubin, 24 hours post-dose (Day 1), 2+	0	0	0	0
Bilirubin, 24 hours post-dose (Day 1), 3+	0	0	0	0
Occult Blood, 24 hours post-dose (Day 1), negative	2	5	4	7
Occult Blood, 24 hours post-dose (Day 1), trace	0	0	2	1
Occult Blood, 24 hours post-dose (Day 1), 1+	1	0	0	0
Occult Blood, 24 hours post-dose (Day 1), 2+	1	0	0	0
Occult Blood, 24 hours post-dose (Day 1), 3+	0	0	0	0
Glucose, 24 hours post-dose (Day 1), negative	4	5	5	8
Glucose, 24 hours post-dose (Day 1), trace	0	0	0	0
Glucose, 24 hours post-dose (Day 1), 1+	0	0	0	0
Glucose, 24 hours post-dose (Day 1), 2+	0	0	0	0
Glucose, 24 hours post-dose (Day 1), 3+	0	0	1	0
Ketones, 24 hours post-dose (Day 1), negative	4	4	3	8
Ketones, 24 hours post-dose (Day 1), trace	0	1	3	0
Ketones, 24 hours post-dose (Day 1), 1+	0	0	0	0

Ketones, 24 hours post-dose (Day 1), 2+	0	0	0	0
Ketones, 24 hours post-dose (Day 1), 3+	0	0	0	0
Protein, 24 hours post-dose (Day 1), negative	4	4	6	8
Protein, 24 hours post-dose (Day 1), trace	0	1	0	0
Protein, 24 hours post-dose (Day 1), 1+	0	0	0	0
Protein, 24 hours post-dose (Day 1), 2+	0	0	0	0
Protein, 24 hours post-dose (Day 1), 3+	0	0	0	0

Notes:

[68] - Safety Population

[69] - Safety Population

[70] - Safety Population

[71] - 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 supine position after at least a 5-minute rest. Change from Baseline in pulse rate was evaluated. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose); 0.5 hour, 1 hour, 2 hours, 4 hours, 8 hours, 24 hours post-dose (Day 1); and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[72]	5[73]	6[74]	8[75]
Units: Beats per minute				
arithmetic mean (standard deviation)				
0.5 hour post-dose (Day 1), n=4,5,6,8	-1.3 (± 5.85)	-0.8 (± 3.42)	3.5 (± 8.64)	3.6 (± 6.00)
1 hour post-dose (Day 1), n=4,5,6,8	-3.0 (± 6.98)	0.8 (± 6.69)	-0.7 (± 3.67)	-1.0 (± 3.93)
2 hours post-dose (Day 1), n=4,5,6,8	-5.0 (± 7.62)	-0.4 (± 1.95)	-1.8 (± 6.65)	1.0 (± 5.93)
4 hours post-dose (Day 1), n=4,5,6,8	-1.8 (± 6.80)	11.6 (± 13.67)	-1.2 (± 6.40)	-0.8 (± 7.42)
8 hours post-dose (Day 1), n=4,4,6,8	2.8 (± 6.90)	1.8 (± 5.19)	5.7 (± 5.85)	8.6 (± 9.83)
24 hours post-dose (Day 1), n=4,5,6,8	4.3 (± 11.27)	3.6 (± 6.50)	7.5 (± 7.12)	13.0 (± 9.20)
Day 7 to Day 14, n=4,5,6,8	10.0 (± 14.31)	4.4 (± 5.86)	5.3 (± 6.25)	9.8 (± 8.36)

Notes:

[72] - Safety Population

[73] - Safety Population

[74] - Safety Population

[75] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in respiratory rate

End point title	Change From Baseline in respiratory rate

End point description:

Respiratory rate was measured in supine position after at least a 5-minute rest. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose); 0.5 hour, 1 hour, 2 hours, 4 hours, 8 hours and 24 hours post-dose (Day 1); and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[76]	5[77]	6[78]	8[79]
Units: Breaths per minute				
arithmetic mean (standard deviation)				
0.5 hour post-dose (Day 1), n=4,5,6,8	-2.5 (± 3.11)	-3.4 (± 4.39)	-2.2 (± 4.92)	0.1 (± 1.13)
1 hour post-dose (Day 1), n=4,5,6,8	-2.8 (± 1.71)	-3.2 (± 5.67)	1.8 (± 9.22)	0.0 (± 0.76)
2 hours post-dose (Day 1), n=4,5,6,8	-2.0 (± 2.16)	-2.6 (± 2.97)	-3.0 (± 4.52)	-1.0 (± 4.50)
4 hours post-dose (Day 1), n=4,5,6,8	-2.5 (± 2.08)	-2.2 (± 5.63)	-2.2 (± 3.54)	0.1 (± 0.64)
8 hours post-dose (Day 1), n=4,4,6,8	-2.0 (± 1.63)	-0.3 (± 3.50)	0.2 (± 2.56)	1.1 (± 2.59)
24 hours post-dose (Day 1), n=4,5,6,8	-1.8 (± 0.96)	0.8 (± 2.28)	0.3 (± 2.58)	-0.1 (± 1.81)
Day 7 to Day 14, n=4,5,6,8	-0.5 (± 1.73)	-0.4 (± 3.58)	2.0 (± 2.28)	0.3 (± 1.16)

Notes:

[76] - Safety Population

[77] - Safety Population

[78] - Safety Population

[79] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in diastolic blood pressure (DBP) and systolic blood pressure (SBP)

End point title	Change From Baseline in diastolic blood pressure (DBP) and systolic blood pressure (SBP)

End point description:

DBP and SBP were measured in supine position after at least a 5-minute rest. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose); 0.5 hour, 1 hour, 2 hours, 4 hours, 8 hours and 24 hours post-dose (Day 1); and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[80]	5[81]	6[82]	8[83]
Units: Millimeters of mercury				
arithmetic mean (standard deviation)				
DBP, 0.5 hour post-dose (Day 1), n=4,5,6,8	-3.5 (± 8.58)	-1.0 (± 10.42)	-5.0 (± 14.67)	-3.3 (± 4.53)
DBP, 1 hour post-dose (Day 1), n=4,5,6,8	-2.0 (± 6.22)	0.6 (± 8.56)	-4.3 (± 9.73)	-2.3 (± 3.73)
DBP, 2 hours post-dose (Day 1), n=4,5,6,8	0.5 (± 12.40)	1.2 (± 10.55)	-5.8 (± 8.80)	3.3 (± 5.87)
DBP, 4 hours post-dose (Day 1), n=4,5,6,8	-1.5 (± 2.65)	3.0 (± 8.37)	-2.7 (± 13.22)	1.6 (± 6.07)
DBP, 8 hours post-dose (Day 1), n=4,4,6,8	-12.3 (± 6.65)	-6.3 (± 8.66)	-10.2 (± 9.15)	-1.0 (± 9.32)
DBP, 24 hours post-dose (Day 1), n=4,5,6,8	-7.5 (± 7.94)	-8.6 (± 9.61)	-2.8 (± 10.61)	-3.1 (± 8.46)
DBP, Day 7 to Day 14, n=4,5,6,8	-4.5 (± 7.19)	-2.2 (± 6.91)	-2.5 (± 11.78)	2.8 (± 12.83)
SBP, 0.5 hour post-dose (Day 1), n=4,5,6,8	-2.3 (± 12.28)	-0.2 (± 12.60)	-5.2 (± 6.11)	-0.1 (± 5.03)
SBP, 1 hour post-dose (Day 1), n=4,5,6,8	-1.8 (± 9.91)	3.4 (± 12.68)	-2.7 (± 9.37)	3.0 (± 8.07)
SBP, 2 hours post-dose (Day 1), n=4,5,6,8	1.0 (± 15.12)	2.0 (± 10.20)	-0.7 (± 18.84)	2.0 (± 11.80)
SBP, 4 hours post-dose (Day 1), n=4,5,6,8	5.5 (± 19.69)	4.2 (± 9.34)	6.3 (± 13.03)	6.1 (± 13.53)
SBP, 8 hours post-dose (Day 1), n=4,4,6,8	-4.5 (± 10.38)	3.0 (± 16.57)	-5.2 (± 7.63)	-4.8 (± 9.65)
SBP, 24 hours post-dose (Day 1), n=4,5,6,8	-2.5 (± 4.51)	-0.2 (± 14.72)	-4.7 (± 11.41)	-3.8 (± 14.85)
SBP, Day 7 to Day 14, n=4,5,6,8	2.0 (± 21.37)	6.0 (± 6.78)	-5.8 (± 15.07)	-2.1 (± 9.63)

Notes:

[80] - Safety Population

[81] - Safety Population

[82] - Safety Population

[83] - Safety Population

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

12-lead ECGs were obtained at each time point using an ECG machine that automatically calculates the heart rate and measures PR, QRS, QT, and Corrected QT (QTc) intervals. Only those participants who had any abnormal ECG findings are presented. Abnormal ECG findings were categorized as clinically significant (CS) and not clinically significant (NCS) abnormal ECG findings. 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. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

4 hours and 24 hours post-dose (Day 1) and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[84]	5[85]	6[86]	8[87]
Units: Participants				
Abnormal NCS, 4 hours post-dose (Day 1), n=4,5,6,8	1	3	3	7
Abnormal CS, 4 hours post-dose (Day 1), n=4,5,6,8	0	0	0	0
Abnormal NCS, 24 hours post-dose(Day 1), n=3,5,6,8	1	3	4	5
Abnormal CS, 24 hours post-dose (Day 1), n=3,5,6,8	0	0	0	0
Abnormal NCS, Day 7 to Day 14, n=4,5,6,8	1	3	3	3
Abnormal CS, Day 7 to Day 14, n=4,5,6,8	0	0	0	0

Notes:

[84] - Safety Population

[85] - Safety Population

[86] - Safety Population

[87] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in pulse oximetry parameter: Percent oxygen in blood

End point title	Change from Baseline in pulse oximetry parameter: Percent oxygen in blood

End point description:

Percent oxygen in blood was measured using pulse oximetry after the participant had rested for at least 5 minutes. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose); 0.5 hour, 1 hour, 2 hours, 4 hours, 8 hours and 24 hours post-dose (Day 1); and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[88]	5[89]	6[90]	8[91]
Units: Percentage of oxygen in blood				
arithmetic mean (standard deviation)				
0.5 hour post-dose (Day 1), n=4,5,6,8	-1.0 (± 2.30)	-1.7 (± 2.77)	0.8 (± 2.31)	-0.5 (± 2.03)
1 hour post-dose (Day 1), n=4,5,6,8	-0.7 (± 2.87)	-2.1 (± 2.79)	-0.3 (± 1.03)	-0.9 (± 2.48)
2 hours post-dose (Day 1), n=4,5,6,8	-1.5 (± 1.91)	-0.7 (± 1.99)	0.6 (± 1.21)	0.9 (± 1.37)
4 hours post-dose (Day 1), n=4,5,6,8	-0.7 (± 2.21)	-1.0 (± 1.87)	-0.3 (± 1.96)	0.5 (± 2.13)
8 hours post-dose (Day 1), n=4,4,6,8	-0.7 (± 2.50)	-0.2 (± 3.58)	0.8 (± 2.31)	0.4 (± 2.98)
24 hours post-dose (Day 1), n=4,5,6,8	-1.0 (± 2.00)	-2.3 (± 3.06)	2.1 (± 1.60)	1.0 (± 3.28)
Day 7 to Day 14, n=4,5,6,8	-0.2 (± 0.95)	-2.9 (± 2.37)	0.5 (± 3.33)	0.8 (± 2.49)

Notes:

[88] - Safety Population

[89] - Safety Population

[90] - Safety Population

[91] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with positive immunogenicity results

End point title	Number of participants with positive immunogenicity results

End point description:

Immunogenicity samples were collected into a serum-separating tube, mixed by gentle inversion 5 times and left to coagulate at room temperature for a minimum of 30 minutes and a maximum of 60 minutes. All samples were first tested for anti-angiotensin converting enzyme type 2 (ACE2) binding antibodies by screening and confirmation assay steps. If post-dose samples were found to be positive for anti-ACE2 binding antibodies, they would have been further characterized for anti-ACE2 neutralizing antibodies. Number of participants with positive immunogenicity results post-dosing are presented.

End point type	Secondary

End point timeframe:

Up to Day 28

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[92]	5[93]	6[94]	8[95]
Units: Participants	0	0	0	0

Notes:

[92] - Safety Population

[93] - Safety Population

[94] - Safety Population

[95] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in systemic Renin-Angiotensin System (RAS) peptides: Angiotensin II, Angiotensin (1-5) and Angiotensin (1-7)

End point title	Change from Baseline in systemic Renin-Angiotensin System (RAS) peptides: Angiotensin II, Angiotensin (1-5) and Angiotensin (1-7)

End point description:

Blood samples were collected to evaluate systemic RAS peptides: Angiotensin (Ang) II, Ang (1-5) and Ang (1-7). Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was measured as ratio of post-dose visit value to Baseline value. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles). 99999 indicates confidence interval could not be estimated as more than 75 percentage (%) of the values were below lower limit of quantification.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose); 0.08 hour, 0.5 hour, 1 hour, 2 hours, 4 hours, 8 hours and 24 hours post-dose (Day 1); and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[96]	5[97]	5[98]	8[99]
Units: Ratio				
geometric mean (confidence interval 95%)				
Ang II, 0.08 hour post-dose (Day 1), n=4,5,5,8	0.143 (0.028 to 0.723)	0.185 (-99999 to 99999)	1.020 (0.063 to 16.661)	0.254 (0.078 to 0.831)
Ang II, 0.5 hour post-dose (Day 1), n=4,5,5,8	0.179 (0.040 to 0.792)	0.210 (-99999 to 99999)	0.500 (0.065 to 3.825)	0.211 (-99999 to 99999)
Ang II, 1 hour post-dose (Day 1), n=4,5,5,8	0.238 (0.097 to 0.582)	0.162 (-99999 to 99999)	0.420 (0.086 to 2.062)	0.235 (-99999 to 99999)
Ang II, 2 hours post-dose (Day 1), n=4,5,5,8	0.230 (0.041 to 1.280)	0.166 (-99999 to 99999)	0.393 (0.159 to 0.970)	0.211 (-99999 to 99999)
Ang II, 4 hours post-dose (Day 1), n=4,5,5,8	0.372 (0.159 to 0.872)	0.187 (-99999 to 99999)	0.398 (0.161 to 0.980)	0.387 (0.160 to 0.933)
Ang II, 8 hours post-dose (Day 1), n=4,5,5,8	0.889 (0.148 to 5.327)	0.669 (0.249 to 1.798)	0.503 (0.311 to 0.813)	0.277 (0.080 to 0.963)
Ang II, 24 hours post-dose (Day 1), n=4,5,5,8	2.329 (0.692 to 7.836)	1.372 (0.462 to 4.070)	0.763 (0.267 to 2.184)	0.939 (0.186 to 4.751)
Ang II, Day 7 to Day 14, n=4,5,5,7	1.625 (0.084 to 31.300)	2.380 (0.703 to 8.063)	0.616 (0.115 to 3.307)	1.826 (0.399 to 8.354)
Ang (1-5), 0.08 hour post-dose (Day 1), n=4,5,4,6	1.884 (0.505 to 7.026)	4.696 (1.303 to 16.923)	2.222 (0.774 to 6.373)	2.982 (1.360 to 6.535)
Ang (1-5), 0.5 hour post-dose (Day 1), n=4,5,4,6	2.342 (0.435 to 12.622)	5.325 (1.427 to 19.873)	2.895 (1.206 to 6.950)	3.187 (1.303 to 7.797)

Ang (1-5), 1 hour post-dose (Day 1), n=4,5,4,6	2.427 (0.414 to 14.225)	4.263 (1.463 to 12.418)	2.572 (0.775 to 8.539)	3.264 (1.134 to 9.396)
Ang (1-5), 2 hours post-dose (Day 1), n=4,5,4,6	2.269 (0.344 to 14.945)	3.499 (1.377 to 8.890)	3.423 (0.698 to 16.789)	2.463 (0.982 to 6.174)
Ang (1-5), 4 hours post-dose (Day 1), n=4,5,4,6	2.442 (0.344 to 17.340)	2.740 (1.245 to 6.033)	3.513 (0.750 to 16.459)	2.717 (1.033 to 7.146)
Ang (1-5), 8 hours post-dose (Day 1), n=4,5,4,6	4.365 (1.094 to 17.420)	4.125 (0.716 to 23.775)	6.691 (0.812 to 55.117)	4.882 (1.581 to 15.072)
Ang (1-5), 24 hours post-dose (Day 1), n=4,5,4,6	2.397 (0.879 to 6.536)	3.701 (1.413 to 9.690)	2.573 (0.403 to 16.426)	5.117 (1.910 to 13.712)
Ang (1-5), Day 7 to Day 14, n=4,5,3,6	1.469 (0.714 to 3.020)	2.110 (0.775 to 5.744)	0.548 (-99999 to 99999)	1.642 (0.781 to 3.450)
Ang (1-7), 0.08 hour post-dose (Day 1), n=4,5,5,7	2.252 (0.366 to 13.855)	4.392 (1.405 to 13.732)	3.465 (1.025 to 11.719)	1.817 (0.969 to 3.405)
Ang (1-7), 0.5 hour post-dose (Day 1), n=4,5,5,7	2.943 (0.335 to 25.843)	4.935 (1.383 to 17.617)	2.242 (0.639 to 7.865)	2.205 (1.260 to 3.859)
Ang (1-7), 1 hour post-dose (Day 1), n=4,5,5,7	3.002 (0.318 to 28.319)	3.494 (1.438 to 8.490)	2.362 (0.542 to 10.291)	1.780 (0.783 to 4.047)
Ang (1-7), 2 hours post-dose (Day 1), n=4,5,5,7	2.311 (0.161 to 33.222)	4.025 (1.393 to 11.630)	3.471 (0.651 to 18.500)	1.949 (1.012 to 3.756)
Ang (1-7), 4 hours post-dose (Day 1), n=4,5,5,7	3.350 (0.230 to 48.748)	3.115 (1.349 to 7.190)	3.623 (0.679 to 19.331)	1.818 (0.715 to 4.623)
Ang (1-7), 8 hours post-dose (Day 1), n=4,5,5,7	4.910 (0.654 to 36.845)	3.517 (0.635 to 19.477)	6.002 (0.762 to 47.289)	4.229 (1.433 to 12.477)
Ang (1-7), 24 hours post-dose (Day 1), n=4,5,5,7	3.423 (0.618 to 18.944)	4.096 (1.430 to 11.730)	2.812 (0.503 to 15.732)	7.095 (2.426 to 20.752)
Ang (1-7), Day 7 to Day 14, n=4,5,5,6	1.190 (0.684 to 2.073)	1.904 (0.596 to 6.089)	0.925 (-99999 to 99999)	1.932 (1.111 to 3.362)

Notes:

[96] - Evaluable Population

[97] - Evaluable Population

[98] - Evaluable Population

[99] - Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in pulmonary wedge RAS peptides: Angiotensin II, Angiotensin (1-5) and Angiotensin (1-7)

End point title	Change from Baseline in pulmonary wedge RAS peptides: Angiotensin II, Angiotensin (1-5) and Angiotensin (1-7)

End point description:

Blood samples were collected to evaluate pulmonary wedge RAS peptides: Ang II, Ang (1-7) and Ang (1-5). Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was measured as ratio of post-dose visit value to Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles). 99999 indicates confidence interval could not be estimated as more than 75% of the values were below lower limit of quantification.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose); 1 hour, 2 hours and 4 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[100]	4[101]	4[102]	8[103]
Units: Ratio				
geometric mean (confidence interval 95%)				
Ang II, 1 hour post-dose (Day 1), n=4,4,4,8	0.270 (0.059 to 1.244)	0.190 (0.025 to 1.475)	0.394 (0.046 to 3.414)	0.369 (-99999 to 99999)
Ang II, 2 hours post-dose (Day 1), n=4,4,4,8	0.310 (0.068 to 1.419)	0.193 (0.025 to 1.476)	0.505 (0.147 to 1.738)	0.369 (-99999 to 99999)
Ang II, 4 hours post-dose (Day 1), n=4,4,3,8	0.332 (0.089 to 1.240)	0.191 (0.025 to 1.475)	0.183 (0.038 to 0.879)	0.420 (-99999 to 99999)
Ang (1-5), 1 hour post-dose (Day 1), n=4,4,4,7	2.985 (0.279 to 31.931)	3.313 (0.892 to 12.310)	2.709 (0.792 to 9.269)	1.834 (0.743 to 4.528)
Ang (1-5), 2 hours post-dose (Day 1), n=4,4,3,7	3.443 (0.282 to 42.025)	4.621 (0.803 to 26.600)	5.246 (1.386 to 19.859)	1.562 (0.566 to 4.312)
Ang (1-5), 4 hours post-dose (Day 1), n=4,4,3,7	2.373 (0.401 to 14.050)	3.213 (0.757 to 13.646)	5.239 (1.565 to 17.541)	1.472 (0.575 to 3.768)
Ang (1-7), 1 hour post-dose (Day 1), n=4,4,4,8	2.840 (0.353 to 22.846)	4.150 (0.912 to 18.880)	2.993 (0.356 to 25.136)	1.558 (0.969 to 2.504)
Ang (1-7), 2 hours post-dose (Day 1), n=4,4,4,8	3.376 (0.279 to 40.910)	3.792 (0.878 to 16.368)	4.476 (0.612 to 32.754)	1.589 (0.830 to 3.043)
Ang (1-7), 4 hours post-dose (Day 1), n=4,4,3,8	2.857 (0.362 to 22.550)	3.151 (0.849 to 11.693)	8.521 (0.733 to 99.048)	1.693 (0.818 to 3.504)

Notes:

[100] - Evaluable Population

[101] - Evaluable Population

[102] - Evaluable Population

[103] - Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Systemic RAS peptide: Angiotensin II/Angiotensin (1-7) ratio at indicated time points

End point title	Systemic RAS peptide: Angiotensin II/Angiotensin (1-7) ratio at indicated time points

End point description:

Blood samples were collected to assess systemic RAS peptides: Angiotensin II and Angiotensin (1-7). Data for angiotensin II/angiotensin (1-7) ratio is presented. Assessment of follow up visit was conducted between any day of Days 7 to 14. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles). 99999 indicates confidence interval could not be estimated as more than 75% of the values were below lower limit of quantification.

End point type	Secondary

End point timeframe:

0.08 hour, 0.5 hour, 1 hour, 2 hours, 4 hours, 8 hours and 24 hours post-dose (Day 1) and one sample between Day 7 to Day 14 (follow up visit)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[104]	5[105]	5[106]	8[107]
Units: Ratio				
geometric mean (confidence interval 95%)				
0.08 hour post-dose (Day 1), n=4,5,5,8	0.752 (0.175 to 3.239)	0.463 (-99999 to 99999)	1.450 (0.313 to 6.711)	0.843 (0.491 to 1.447)
0.5 hour post-dose (Day 1), n=4,5,5,8	0.718 (0.186 to 2.779)	0.468 (-99999 to 99999)	1.097 (-99999 to 99999)	0.590 (-99999 to 99999)
1 hour post-dose (Day 1), n=4,5,5,8	0.937 (0.351 to 2.504)	0.509 (-99999 to 99999)	0.875 (-99999 to 99999)	0.794 (-99999 to 99999)
2 hours post-dose (Day 1), n=4,5,5,8	1.174 (0.539 to 2.559)	0.455 (-99999 to 99999)	0.558 (0.150 to 2.077)	0.657 (-99999 to 99999)
4 hours post-dose (Day 1), n=4,5,5,8	1.312 (0.571 to 3.011)	0.659 (-99999 to 99999)	0.540 (0.136 to 2.144)	1.283 (0.530 to 3.102)
8 hours post-dose (Day 1), n=4,5,5,8	2.139 (0.623 to 7.339)	2.093 (0.778 to 5.625)	0.412 (0.083 to 2.055)	0.439 (0.181 to 1.062)
24 hours post-dose (Day 1), n=4,5,5,8	8.041 (2.416 to 26.757)	3.682 (1.929 to 7.030)	1.335 (0.908 to 1.965)	0.946 (0.435 to 2.054)
Day 7 to Day 14, n=4,5,5,7	16.132 (1.204 to 216.087)	13.742 (3.829 to 49.326)	3.278 (-99999 to 99999)	6.156 (2.618 to 14.479)

Notes:

[104] - Evaluable Population

[105] - Evaluable Population

[106] - Evaluable Population

[107] - Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Pulmonary Wedge RAS peptide: Angiotensin II/Angiotensin (1-7) ratio at indicated time points

End point title	Pulmonary Wedge RAS peptide: Angiotensin II/Angiotensin (1-7) ratio at indicated time points

End point description:

Blood samples were collected to assess pulmonary wedge RAS peptides: Angiotensin II and Angiotensin (1-7). Data for angiotensin II/angiotensin (1-7) ratio is presented. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles). 99999 indicates confidence interval could not be estimated as more than 75% of the values were below lower limit of quantification.

End point type	Secondary

End point timeframe:

1 hour, 2 hours and 4 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[108]	4[109]	4[110]	8[111]
Units: Ratio				
geometric mean (confidence interval 95%)				

1 hour post-dose (Day 1), n=4,4,4,8	0.888 (0.275 to 2.866)	0.443 (0.108 to 1.821)	0.620 (0.058 to 6.650)	0.789 (-99999 to 99999)
2 hours post-dose (Day 1), n=4,4,4,8	0.858 (0.253 to 2.908)	0.493 (0.116 to 2.096)	0.531 (0.117 to 2.403)	0.774 (-99999 to 99999)
4 hours post-dose (Day 1), n=4,4,3,8	1.085 (0.478 to 2.462)	0.587 (0.172 to 2.003)	0.148 (0.012 to 1.759)	0.826 (-99999 to 99999)

Notes:

[108] - Evaluable Population

[109] - Evaluable Population

[110] - Evaluable Population

[111] - Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in disease biomarkers: N-terminal pro B-type natriuretic peptide (NT pro-BNP)

End point title	Change from Baseline in disease biomarkers: N-terminal pro B-type natriuretic peptide (NT pro-BNP)

End point description:

Blood samples were collected at specific time points to evaluate NT pro-BNP, a biomarker of disease activity. NT-pro-BNP is a biomarker of cardiac stress or ventricular workload and decreases as a result of reduced force of contraction if pulmonary blood pressure is reduced. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was measured as ratio of post-dose visit value to Baseline value. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose); 2 hours, 4 hours and 24 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[112]	5[113]	4[114]	8[115]
Units: Ratio				
geometric mean (confidence interval 95%)				
2 hours post-dose (Day 1)	1.034 (0.955 to 1.119)	1.005 (0.842 to 1.199)	0.923 (0.795 to 1.071)	1.015 (0.841 to 1.224)
4 hours post-dose (Day 1)	1.025 (0.924 to 1.138)	1.042 (0.852 to 1.276)	0.944 (0.795 to 1.120)	1.074 (0.840 to 1.373)
24 hours post-dose (Day 1)	0.606 (0.253 to 1.453)	0.896 (0.481 to 1.670)	0.703 (0.430 to 1.151)	0.810 (0.539 to 1.217)

Notes:

[112] - Evaluable Population

[113] - Evaluable Population

[114] - Evaluable Population

[115] - Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in nitrite, nitrate and endogenous nitrite (biomarkers of nitric oxide [NO])

End point title	Change from Baseline in nitrite, nitrate and endogenous nitrite (biomarkers of nitric oxide [NO])

End point description:

Blood samples were collected at specific time points to evaluate levels of nitrite, nitrate and endogenous nitrite (En. nitrite) (biomarkers of NO). Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was measured as ratio of post-dose visit value to Baseline 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	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose); 2 hours, 4 hours and 24 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[116]	4[117]	5[118]	8[119]
Units: Ratio				
geometric mean (confidence interval 95%)				
Nitrite, 2 hours post-dose (Day 1), n=4,4,5,8	1.246 (0.440 to 3.533)	1.029 (0.870 to 1.216)	0.530 (0.145 to 1.931)	0.858 (0.797 to 0.923)
Nitrite, 4 hours post-dose (Day 1), n=4,4,5,8	0.760 (0.635 to 0.910)	0.992 (0.749 to 1.312)	0.679 (0.420 to 1.096)	0.770 (0.654 to 0.907)
Nitrite, 24 hours post-dose (Day 1), n=4,4,4,7	1.038 (0.898 to 1.199)	1.146 (1.044 to 1.259)	0.667 (0.245 to 1.814)	0.914 (0.605 to 1.381)
Nitrate, 2 hours post-dose (Day 1), n=4,4,5,8	1.251 (0.432 to 3.623)	1.025 (0.862 to 1.218)	0.485 (0.108 to 2.177)	0.836 (0.768 to 0.910)
Nitrate, 4 hours post-dose (Day 1), n=4,4,5,8	0.739 (0.595 to 0.917)	0.977 (0.700 to 1.362)	0.655 (0.395 to 1.086)	0.762 (0.649 to 0.895)
Nitrate, 24 hours post-dose (Day 1), n=4,4,4,7	1.017 (0.853 to 1.212)	1.149 (1.049 to 1.259)	0.641 (0.222 to 1.854)	0.911 (0.597 to 1.390)
En. nitrite, 2 hours post-dose (Day 1), n=4,4,5,8	1.099 (0.798 to 1.512)	2.036 (0.309 to 13.411)	1.171 (0.878 to 1.563)	0.975 (0.647 to 1.469)
En. nitrite, 4 hours post-dose (Day 1), n=4,4,5,8	1.245 (0.665 to 2.330)	2.819 (0.079 to 100.021)	1.329 (0.643 to 2.747)	0.820 (0.466 to 1.443)
En. nitrite, 24 hours post-dose (Day 1), n=4,4,4,7	1.290 (0.543 to 3.063)	1.399 (0.503 to 3.894)	1.289 (0.501 to 3.316)	1.271 (0.614 to 2.634)

Notes:

[116] - Evaluable Population

[117] - Evaluable Population

[118] - Evaluable Population

[119] - Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in disease biomarker: cardiac troponin-I

End point title	Change from Baseline in disease biomarker: cardiac troponin-I

End point description:

Blood samples were collected at specific time points to assess cardiac troponin I. Cardiac troponin I is a biomarker of cardiac stress. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was measured as ratio of

post-dose visit value to Baseline value. Only those participants with data available at the specified time points were analyzed. 99999 indicates confidence interval could not be estimated as more than 75% of the values were below lower limit of quantification.

End point type	Secondary

End point timeframe:

Baseline (Day 1, Pre-dose); 2 hours, 4 hours and 24 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[120]	5[121]	5[122]	8[123]
Units: Ratio				
geometric mean (confidence interval 95%)				
2 hours post-dose (Day 1)	1.565 (0.660 to 3.714)	1.320 (0.824 to 2.114)	1.585 (0.657 to 3.822)	1.414 (0.761 to 2.628)
4 hours post-dose (Day 1)	1.968 (0.543 to 7.131)	1.149 (0.782 to 1.688)	1.695 (0.592 to 4.856)	2.030 (1.064 to 3.873)
24 hours post-dose (Day 1)	1.316 (0.549 to 3.154)	1.000 (-99999 to 99999)	1.000 (-99999 to 99999)	1.000 (-99999 to 99999)

Notes:

[120] - Evaluable Population

[121] - Evaluable Population

[122] - Evaluable Population

[123] - Evaluable Population

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed plasma concentration (Cmax) of GSK2586881

End point title	Maximum observed plasma concentration (Cmax) of GSK2586881

End point description:

Blood samples were collected at indicated time points for evaluation of Cmax. Pharmacokinetic parameters were calculated by standard non-compartmental analysis. Pharmacokinetic population comprised of participants in the Safety Population for whom a pharmacokinetic sample was obtained and analyzed.

End point type	Secondary

End point timeframe:

Pre-dose (Day 1) and 0.08, 0.5, 1, 2, 4, 8 and 24 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[124]	5[125]	6[126]	8[127]
Units: Micrograms per milliliter				
geometric mean (geometric coefficient of variation)	1.5159 (± 37.0)	4.0229 (± 37.4)	8.9701 (± 26.1)	14.8042 (± 33.1)

Notes:

[124] - Pharmacokinetic Population

[125] - Pharmacokinetic Population

[126] - Pharmacokinetic Population

[127] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Cmax (tmax) of GSK2586881

End point title	Time to Cmax (tmax) of GSK2586881

End point description:

Blood samples were collected at indicated time points for evaluation of tmax. Pharmacokinetic parameters were calculated by standard non-compartmental analysis.

End point type	Secondary

End point timeframe:

Pre-dose (Day 1) and 0.08, 0.5, 1, 2, 4, 8 and 24 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[128]	5[129]	6[130]	8[131]
Units: Hours				
median (full range (min-max))	0.08333 (0.0833 to 0.1333)	0.16667 (0.0667 to 0.5000)	0.10000 (0.0667 to 0.5500)	0.13333 (0.0833 to 0.6333)

Notes:

[128] - Pharmacokinetic Population

[129] - Pharmacokinetic Population

[130] - Pharmacokinetic Population

[131] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUC[0-t]) of GSK2586881

End point title	Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUC[0-t]) of GSK2586881

End point description:

Blood samples were collected at indicated time points for evaluation of AUC(0-t). Pharmacokinetic parameters were calculated by standard non-compartmental analysis.

End point type	Secondary

End point timeframe:

Pre-dose (Day 1) and 0.08, 0.5, 1, 2, 4, 8 and 24 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[132]	5[133]	6[134]	8[135]
Units: Hours*micrograms per milliliter				
geometric mean (geometric coefficient of variation)	3.941 (± 53.6)	17.874 (± 30.9)	46.789 (± 16.3)	68.042 (± 37.0)

Notes:

[132] - Pharmacokinetic Population

[133] - Pharmacokinetic Population

[134] - Pharmacokinetic Population

[135] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the concentration-time curve from time zero (pre-dose) extrapolated to infinite time (AUC[0-inf]) of GSK2586881

End point title	Area under the concentration-time curve from time zero (pre-dose) extrapolated to infinite time (AUC[0-inf]) of GSK2586881

End point description:

Blood samples were collected at indicated time points for evaluation of AUC(0-inf). Pharmacokinetic parameters were calculated by standard non-compartmental analysis. Only those participants with data available at the specified time points were analyzed. 99999 indicates terminal elimination phase could not be identified from the concentration-time profile for any participants in the 0.1 mg/kg treatment group over the study period; hence, AUC(0-inf) could not be estimated.

End point type	Secondary

End point timeframe:

Pre-dose (Day 1) and 0.08, 0.5, 1, 2, 4, 8 and 24 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[136]	2[137]	6[138]	7[139]
Units: Hours*micrograms per milliliter				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	25.26 (± 7.7)	52.46 (± 20.0)	76.87 (± 42.1)

Notes:

[136] - Pharmacokinetic Population

[137] - Pharmacokinetic Population

[138] - Pharmacokinetic Population

[139] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Last observed quantifiable concentration (Ct) of GSK2586881

End point title	Last observed quantifiable concentration (Ct) of GSK2586881

End point description:

Blood samples were collected at indicated time points for evaluation of Ct. Pharmacokinetic parameters were calculated by standard non-compartmental analysis.

End point type	Secondary

End point timeframe:

Pre-dose (Day 1) and 0.08, 0.5, 1, 2, 4, 8 and 24 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[140]	5[141]	6[142]	8[143]
Units: Micrograms per milliliter				
geometric mean (geometric coefficient of variation)	0.2563 (± 22.8)	0.3327 (± 54.4)	0.4800 (± 44.9)	0.6380 (± 54.9)

Notes:

[140] - Pharmacokinetic Population

[141] - Pharmacokinetic Population

[142] - Pharmacokinetic Population

[143] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time of the last quantifiable concentration (tlast) of GSK2586881

End point title	Time of the last quantifiable concentration (tlast) of GSK2586881

End point description:

Blood samples were collected at indicated time points for evaluation of tlast. Pharmacokinetic parameters were calculated by standard non-compartmental analysis.

End point type	Secondary

End point timeframe:

Pre-dose (Day 1) and 0.08, 0.5, 1, 2, 4, 8 and 24 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[144]	5[145]	6[146]	8[147]
Units: Hours				
median (full range (min-max))	8.000 (4.20 to 8.47)	24.000 (8.18 to 24.25)	24.017 (23.73 to 24.15)	24.117 (23.97 to 24.28)

Notes:

[144] - Pharmacokinetic Population

[145] - Pharmacokinetic Population

[146] - Pharmacokinetic Population

[147] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma clearance (CL) of GSK2586881

End point title	Plasma clearance (CL) of GSK2586881

End point description:

Blood samples were collected at indicated time points for evaluation of CL. Pharmacokinetic parameters were calculated by standard non-compartmental analysis. Only those participants with data available at the specified time points were analyzed. 99999 indicates terminal elimination phase could not be identified from the concentration-time profile for any participants in the 0.1 mg/kg treatment group over the study period; hence, CL could not be estimated.

End point type	Secondary

End point timeframe:

Pre-dose (Day 1) and 0.08, 0.5, 1, 2, 4, 8 and 24 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[148]	2[149]	6[150]	7[151]
Units: Liters per hour				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	0.5838 (± 10.1)	0.6207 (± 16.8)	0.8170 (± 30.8)

Notes:

[148] - Pharmacokinetic Population

[149] - Pharmacokinetic Population

[150] - Pharmacokinetic Population

[151] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent volume of distribution of GSK2586881

End point title	Apparent volume of distribution of GSK2586881

End point description:

Blood samples were collected at indicated time points for evaluation of apparent volume of distribution. Pharmacokinetic parameters were calculated by standard non-compartmental analysis. Only those participants with data available at the specified time points were analyzed. 99999 indicates terminal elimination phase could not be identified from the concentration-time profile for any participants in the 0.1 mg/kg treatment group over the study period; hence, apparent volume of distribution could not be estimated.

End point type	Secondary

End point timeframe:

Pre-dose (Day 1) and 0.08, 0.5, 1, 2, 4, 8 and 24 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[152]	2[153]	6[154]	7[155]
Units: Liters				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	6.443 (± 2.4)	6.593 (± 20.5)	8.084 (± 20.6)

Notes:

[152] - Pharmacokinetic Population

[153] - Pharmacokinetic Population

[154] - Pharmacokinetic Population

[155] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent terminal phase half-life (t1/2) of GSK2586881

End point title	Apparent terminal phase half-life (t1/2) of GSK2586881

End point description:

Blood samples were collected at indicated time points for evaluation of t1/2. Pharmacokinetic parameters were calculated by standard non-compartmental analysis. Only those participants with data available at the specified time points were analyzed. 99999 indicates terminal elimination phase could not be identified from the concentration-time profile for any participants in the 0.1 mg/kg treatment group over the study period; hence, t1/2 could not be estimated.

End point type	Secondary

End point timeframe:

Pre-dose (Day 1) and 0.08, 0.5, 1, 2, 4, 8 and 24 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[156]	2[157]	6[158]	7[159]
Units: Hours				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	7.651 (± 7.7)	7.362 (± 23.2)	6.858 (± 19.6)

Notes:

[156] - Pharmacokinetic Population

[157] - Pharmacokinetic Population

[158] - Pharmacokinetic Population

[159] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in cardiac index (CI)

End point title	Change from Baseline in cardiac index (CI)

End point description:

Cardiac index (CI) was measured using thermodilution. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including those from unscheduled visits. Change from Baseline was measured as ratio of post-dose visit value to Baseline value. Only those participants with data available at the specified time points were analyzed.

End point type	Other pre-specified

End point timeframe:

Baseline (Day 1, Pre-dose); 1 hour, 2 hours and 4 hours post-dose (Day 1)

End point values	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg	GSK2586881 0.8 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[160]	5[161]	5[162]	8[163]
Units: Ratio				
geometric mean (confidence interval 95%)				
1 hour post-dose (Day 1)	1.045 (0.874 to 1.248)	1.076 (0.947 to 1.223)	1.084 (0.766 to 1.533)	0.990 (0.948 to 1.034)
2 hours post-dose (Day 1)	1.021 (0.816 to 1.278)	1.029 (0.951 to 1.113)	0.926 (0.719 to 1.193)	1.020 (0.948 to 1.097)
4 hours post-dose (Day 1)	1.107 (0.801 to 1.530)	1.128 (0.941 to 1.352)	0.889 (0.740 to 1.068)	1.000 (0.933 to 1.072)

Notes:

[160] - Evaluable Population

[161] - Evaluable Population

[162] - Evaluable Population

[163] - Evaluable Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Non-SAEs and SAEs were reported from start of study treatment and up to Day 28	
Adverse event reporting additional description:	
Non-SAEs and SAEs were reported for Safety Population. Adverse events were presented treatment-wise.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	GSK2586881 0.1 mg/kg
Reporting group description:	
Participants received a single IV dose of 0.1 mg/kg GSK2586881 and were followed up till 28 days post-dose.	
Reporting group title	GSK2586881 0.2 mg/kg
Reporting group description:	
Participants received a single IV dose of 0.2 mg/kg GSK2586881 and were followed up till 28 days post-dose.	
Reporting group title	GSK2586881 0.4 mg/kg
Reporting group description:	
Participants received a single IV dose of 0.4 mg/kg GSK2586881 and were followed up till 28 days post-dose.	
Reporting group title	GSK2586881 0.8 mg/kg
Reporting group description:	
Participants received a single IV dose of 0.8 mg/kg GSK2586881 and were followed up till 28 days post-dose.	

Serious adverse events	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	GSK2586881 0.8 mg/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	GSK2586881 0.1 mg/kg	GSK2586881 0.2 mg/kg	GSK2586881 0.4 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	3 / 5 (60.00%)	5 / 6 (83.33%)
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 5 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 5 (20.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			

subjects affected / exposed	0 / 4 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Non-serious adverse events	GSK2586881 0.8 mg/kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 May 2017	Amendment 1: Protocol was amended to include risk of exposure to ionizing radiating which was previously omitted as well as for updating information around participants re-screening numbers.
07 November 2017	Amendment 2: This was a non-substantial amendment to clarify the target population to be enrolled, the changes made to the inclusion and exclusion criteria. In addition, an upper limit for the six minute walk (6MW) was added, the evaluable population was changed, and the proposed linear regression analysis was expanded.
01 December 2017	Amendment 3: This was a substantial amendment to enable characterization of the response at a lower starting level of 0.1 mg/kg GSK2586881.
10 July 2018	Amendment 4: This was a substantial amendment with changes to the inclusion and exclusion criteria to more accurately reflect the participant population.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported