Clinical trial results:
A placebo-controlled, double-blind (sponsor open), randomised, crossover study to assess the efficacy, safety, and tolerability of GSK2798745 in participants with chronic cough

Summary

EudraCT number	2017-002265-21
Trial protocol	GB
Global end of trial date	08 October 2018

Results information

Result version number	v1 (current)
This version publication date	22 September 2019
First version publication date	22 September 2019

Trial information

Trial identification

Sponsor protocol code	207702

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	22 March 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 October 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of 7 days dosing of GSK2798745 with placebo in participants with idiopathic or treatment-resistant chronic cough.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 April 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	United Kingdom: 17
Worldwide total number of subjects	17
EEA total number of subjects	17

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)	10
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 4 centers in the United Kingdom. Participants who met eligibility criteria entered a 2-period crossover study. Participants were randomized to either placebo or GSK2798745 in each Treatment Period (each 7 days, with a 14-21 day washout). Total duration of participation was 10.5 weeks. Study terminated on grounds of futility

Pre-assignment

Screening details:

A total of 34 participants were screened of which 17 failed screening and 17 participants were included in the study.

Period 1

Period 1 title	Treatment Period 1 (Up to 7 days)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/GSK2798745

Arm description:

Participants were administered two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of 2.4 milligrams (mg) GSK2798745 each on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

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

Dosage and administration details:

Participants were randomized to receive two tablets of placebo on Day 1 and one tablet on Days 2 to 7, via the oral route with a glass of water.

Investigational medicinal product name	2.4 mg GSK2798745
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were randomized to receive two tablets of 2.4 mg GSK2798748 on Day 1 and one tablet on Days 2 to 7, via the oral
route with a glass of water.

Arm title	GSK2798745/Placebo

Arm description:

Participants were administered two tablets of 2.4 mg GSK2798745 on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Arm type	Experimental

Investigational medicinal product name	2.4 mg GSK2798745
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were randomized to receive two tablets of 2.4 mg GSK2798748 on Day 1 and one tablet on Days 2 to 7, via the oral route with a glass of water.

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

Dosage and administration details:

Participants were randomized to receive two tablets of placebo on Day 1 and one tablet on Days 2 to 7, via the oral route with a glass of water.

Number of subjects in period 1	Placebo/GSK2798745	GSK2798745/Placebo
Started	9	8
Completed	9	8

Period 2

Period 2 title	Wash-out period (14-21 days)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/GSK2798745

Arm description:

Participants were administered two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of 2.4 milligrams (mg) GSK2798745 each on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

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

Dosage and administration details:

Participants were randomized to receive two tablets of placebo on Day 1 and one tablet on Days 2 to 7,

via the oral route with a glass of water.

Investigational medicinal product name	2.4 mg GSK2798745
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were randomized to receive two tablets of 2.4 mg GSK2798748 on Day 1 and one tablet on Days 2 to 7, via the oral route with a glass of water.

Arm title	GSK2798745/Placebo

Arm description:

Participants were administered two tablets of 2.4 mg GSK2798745 on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

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

Dosage and administration details:

Participants were randomized to receive two tablets of placebo on Day 1 and one tablet on Days 2 to 7, via the oral route with a glass of water.

Investigational medicinal product name	2.4 mg GSK2798745
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were randomized to receive two tablets of 2.4 mg GSK2798748 on Day 1 and one tablet on Days 2 to 7, via the oral route with a glass of water.

Number of subjects in period 2	Placebo/GSK2798745	GSK2798745/Placebo
Started	9	8
Completed	8	8
Not completed	1	0
Sponsor terminated study treatment	1	-

Period 3

Period 3 title	Treatment Period 2 (Up to 7 days)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/GSK2798745

Arm description:

Participants were administered two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of 2.4 milligrams (mg) GSK2798745 each on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

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

Dosage and administration details:

Participants were randomized to receive two tablets of placebo on Day 1 and one tablet on Days 2 to 7, via the oral route with a glass of water.

Investigational medicinal product name	2.4 mg GSK2798745
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were randomized to receive two tablets of 2.4 mg GSK2798748 on Day 1 and one tablet on Days 2 to 7, via the oral route with a glass of water.

Arm title	GSK2798745/Placebo

Arm description:

Participants were administered two tablets of 2.4 mg GSK2798745 on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Arm type	Experimental
Investigational medicinal product name	2.4 mg GSK2798745
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were randomized to receive two tablets of 2.4 mg GSK2798748 on Day 1 and one tablet on Days 2 to 7, via the oral route with a glass of water.

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

Dosage and administration details:

Participants were randomized to receive two tablets of placebo on Day 1 and one tablet on Days 2 to 7, via the oral route with a glass of water.

Number of subjects in period 3	Placebo/GSK2798745	GSK2798745/Placebo
Started	8	8
Completed	7	8
Not completed	1	0
Study closed/Terminated	1	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo/GSK2798745

Reporting group description:

Participants were administered two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of 2.4 milligrams (mg) GSK2798745 each on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Reporting group title	GSK2798745/Placebo

Reporting group description:

Participants were administered two tablets of 2.4 mg GSK2798745 on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Reporting group values	Placebo/GSK2798745	GSK2798745/Placebo	Total
Number of subjects	9	8	17
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)	5	5	10
From 65-84 years	4	3	7
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	0	0	
standard deviation	± 0	± 0	-
Sex: Female, Male Units: Subjects			
Female	8	7	15
Male	1	1	2
Race/Ethnicity, Customized Units: Subjects			
Asian-Japanese/East Asian (EA) /South EA Heritage	1	0	1
White	8	8	16

Subject analysis sets

Subject analysis set title	All study participants
Subject analysis set type	Full analysis

Subject analysis set description:

All participants who were randomized to either of the two treatment sequences Placebo/GSK2798745 and GSK2798745/Placebo and received GSK2798745 and placebo in either Treatment period 1 or 2 were included. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

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

Subject analysis set description:

Participants were administered two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7 in either treatment period 1 or 2. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Subject analysis set title	GSK2798745
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants were administered two tablets of 2.4 mg GSK2798745 on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7 in either treatment period 1 or 2. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Reporting group values	All study participants	Placebo	GSK2798745
Number of subjects	17	17	16
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous Units: Years			
arithmetic mean	61.0		
standard deviation	± 9.85	±	±
Sex: Female, Male Units: Subjects			
Female	15		
Male	2		
Race/Ethnicity, Customized Units: Subjects			
Asian-Japanese/East Asian (EA) /South EA Heritage	1		
White	16		

End points

End points reporting groups

Reporting group title	Placebo/GSK2798745

Reporting group description:

Participants were administered two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of 2.4 milligrams (mg) GSK2798745 each on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Reporting group title	GSK2798745/Placebo

Reporting group description:

Participants were administered two tablets of 2.4 mg GSK2798745 on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Reporting group title	Placebo/GSK2798745

Reporting group description:

Participants were administered two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of 2.4 milligrams (mg) GSK2798745 each on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Reporting group title	GSK2798745/Placebo

Reporting group description:

Participants were administered two tablets of 2.4 mg GSK2798745 on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Reporting group title	Placebo/GSK2798745

Reporting group description:

Participants were administered two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of 2.4 milligrams (mg) GSK2798745 each on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Reporting group title	GSK2798745/Placebo

Reporting group description:

Participants were administered two tablets of 2.4 mg GSK2798745 on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Subject analysis set title	All study participants
Subject analysis set type	Full analysis

Subject analysis set description:

All participants who were randomized to either of the two treatment sequences Placebo/GSK2798745 and GSK2798745/Placebo and received GSK2798745 and placebo in either Treatment period 1 or 2 were included. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

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

Subject analysis set description:

Participants were administered two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7 in either treatment period 1 or 2. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Subject analysis set title	GSK2798745

Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants were administered two tablets of 2.4 mg GSK2798745 on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7 in either treatment period 1 or 2. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Primary: Total cough counts during day time hours following 7-days of dosing

End point title	Total cough counts during day time hours following 7-days of dosing

End point description:

Coughs were monitored using the VitaloJAK cough monitor. Total cough counts during day-time (10 hours) was calculated from the time of monitor being attached i.e. immediately after dosing on Day 7 to 10 hours past the time of monitoring. Total cough counts were log-transformed prior to analysis. A non-informative prior was used. Analysis was performed using a Bayesian mixed model adjusting for subject-level and period-adjusted baselines, treatment and period. Subject-level baseline is defined as the mean of two period-specific baselines. Period-adjusted baseline is defined as difference between the period-specific baseline and subject-level baseline for each period. Posterior median and 95% credible interval is reported. All Subjects Population included all randomized participants who took at least 1 dose of study treatment. Participants were analyzed according to treatment they actually received. Only those participants with data available at specified data points were analyzed.

End point type	Primary

End point timeframe:

Up to 10 hours post-dose on Day 7 of each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	15		
Units: Cough counts				
median (confidence interval 95%)	180.570 (137.852 to 235.446)	241.105 (181.383 to 320.600)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK2798745
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Ratio
Point estimate	1.336
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.965
upper limit	1.847

Notes:

[1] - Treatment comparison ratio of GSK2798745 and placebo using posterior median ratio and 90% credible interval is presented.

Secondary: Number of participants reporting adverse events (AEs) and serious adverse events (SAEs)

End point title	Number of participants reporting adverse events (AEs) and serious adverse events (SAEs)

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. An SAE is defined as any untoward medical occurrence that, at any dose 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, associated with liver injury and impaired liver function or any other situations as per medical or scientific judgment.

End point type	Secondary

End point timeframe:

Up to 45 days

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	16		
Units: Participants				
Any AE	9	11		
Any SAE	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline values for clinical chemistry parameters: alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate amino transferase (AST) and creatinine kinase (CK)

End point title	Change from Baseline values for clinical chemistry parameters: alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate amino transferase (AST) and creatinine kinase (CK)

End point description:

Blood samples were collected for the analysis of clinical chemistry parameters including ALP, ALT, AST and CK. Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Day 8 of each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	14		
Units: International units per liter				
arithmetic mean (standard deviation)				
ALP	1.8 (± 9.28)	-3.1 (± 6.75)		
ALT	0.2 (± 2.31)	-0.2 (± 5.32)		
AST	-0.6 (± 3.69)	-0.5 (± 2.65)		
CK	-3.0 (± 21.71)	-12.1 (± 52.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline values for clinical chemistry parameter: direct bilirubin, total bilirubin and creatinine

End point title	Change from Baseline values for clinical chemistry parameter: direct bilirubin, total bilirubin and creatinine

End point description:

Blood samples were collected for the analysis of clinical chemistry parameters including direct bilirubin, total bilirubin and creatinine. Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Day 8 for each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	14		
Units: Micromoles per liter				
arithmetic mean (standard deviation)				
Direct bilirubin	0.1 (± 1.11)	0.0 (± 0.78)		
Total bilirubin	-0.4 (± 3.41)	-0.4 (± 3.25)		
Creatinine	0.31 (± 6.458)	1.70 (± 4.031)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline values for clinical chemistry parameters: calcium, glucose, potassium, sodium and urea

End point title	Change from Baseline values for clinical chemistry parameters: calcium, glucose, potassium, sodium and urea

End point description:

Blood samples were collected for the analysis of clinical chemistry parameters including calcium, glucose, potassium, sodium and urea/blood urea nitrogen (BUN). Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Day 8 of each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	14		
Units: Millimoles per liter				
arithmetic mean (standard deviation)				
Calcium	0.011 (± 0.0588)	0.019 (± 0.0782)		
Glucose	-0.22 (± 1.234)	-0.06 (± 0.956)		
Potassium	0.09 (± 0.299)	0.09 (± 0.270)		
Sodium	0.2 (± 1.44)	-0.1 (± 1.46)		
Urea	0.18 (± 0.683)	-0.36 (± 0.908)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline values for clinical chemistry parameter: Total protein

End point title	Change from Baseline values for clinical chemistry parameter: Total protein

End point description:

Blood samples were collected for the analysis of clinical chemistry parameter total protein. Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Day 8 of each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	14		
Units: Grams per liter				
arithmetic mean (standard deviation)	1.2 (± 2.65)	0.9 (± 2.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal values of cardiac troponin

End point title	Number of participants with abnormal values of cardiac troponin

End point description:

Cardiac troponin values was measured in participants.

End point type	Secondary

End point timeframe:

Up to 45 days

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	16		
Units: Participants	99999	99999		

Statistical analyses

No statistical analyses for this end point

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

End point title	Change from Baseline values for 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 analysis of hematology parameters including basophils, eosinophils, lymphocytes, monocytes, total neutrophils, platelet count and WBC count. Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Day 8 of each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	15		
Units: Giga units per liter				
arithmetic mean (standard deviation)				
Basophils	0.005 (± 0.0250)	-0.005 (± 0.0316)		
Eosinophils	-0.005 (± 0.0400)	-0.007 (± 0.0758)		
Lymphocytes	0.019 (± 0.3065)	-0.002 (± 0.2608)		
Monocytes	-0.012 (± 0.1110)	0.027 (± 0.1012)		
Total neutrophils	0.186 (± 0.5817)	0.064 (± 1.0102)		
Platelet count	6.8 (± 13.57)	6.9 (± 19.76)		
WBC count	0.20 (± 0.614)	0.09 (± 1.276)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline values for hematology parameter: hemoglobin

End point title	Change from Baseline values for hematology parameter: hemoglobin

End point description:

Blood samples were collected for the analysis of hematology parameter: hemoglobin. Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Day 8 for each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	15		
Units: Grams per liter				
arithmetic mean (standard deviation)	0.5 (± 2.29)	0.5 (± 3.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline values for hematology parameter: hematocrit

End point title	Change from Baseline values for hematology parameter: hematocrit

End point description:

Blood samples were collected for the analysis of hematology parameter: hematocrit. Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Day 8 of each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	15		
Units: Percentage of red blood cells in blood				
arithmetic mean (standard deviation)	0.0020 (± 0.01009)	0.0029 (± 0.00979)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline values for hematology parameter: Mean corpuscular hemoglobin (MCH)

End point title	Change from Baseline values for hematology parameter: Mean corpuscular hemoglobin (MCH)

End point description:

Blood samples were collected for the analysis of hematology parameter: MCH. Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Day 8 for each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	15		
Units: Picograms				
arithmetic mean (standard deviation)	-0.07 (± 0.377)	-0.09 (± 0.442)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline values for hematology parameter: Mean corpuscular volume (MCV)

End point title	Change from Baseline values for hematology parameter: Mean corpuscular volume (MCV)

End point description:

Blood samples were collected for the analysis of hematology parameter: MCV. Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Day 8 of each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	15		
Units: Femtoliters				
arithmetic mean (standard deviation)	-0.1 (± 2.01)	-0.1 (± 1.53)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Blood samples were collected for the analysis of hematology parameter: RBC count. Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Day 8 for each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	15		
Units: Tera units per liter				
arithmetic mean (standard deviation)	0.04 (± 0.112)	0.03 (± 0.103)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline values for hematology parameter: reticulocytes

End point title	Change from Baseline values for hematology parameter: reticulocytes

End point description:

Blood samples were collected for the analysis of hematology parameter: reticulocytes. Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Day 8 for each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	15		
Units: Percentage of reticulocytes in blood				
arithmetic mean (standard deviation)	-0.0002 (± 0.00300)	-0.0002 (± 0.00260)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal urinalysis data

End point title	Number of participants with abnormal urinalysis data

End point description:

Urine samples were collected for analysis of urinalysis data by dipstick method. Number of participants with abnormal urinalysis data has been presented. Abnormality was defined as value of potential clinical importance (PCI). PCI was flagged when a result changed from negative on Day 1 (pre-dose) to positive on Day 8. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Up to Day 8

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	15		
Units: Participants				
number (not applicable)	4	2		

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:

Blood pressure was measured at indicated time points in supine position after 5 minutes rest for the participant. Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (pre-dose on Day 1) and Day 8 of each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	15		
Units: Millimeters of mercury				
arithmetic mean (standard deviation)				
DBP	-0.2 (± 8.59)	-0.5 (± 13.07)		
SBP	1.6 (± 12.65)	0.9 (± 20.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in temperature

End point title	Change from Baseline in temperature

End point description:

Temperature was measured at indicated time points in supine position after 5 minutes rest for the

participant. Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (pre-dose on Day 1) and Day 8 of each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	15		
Units: Degrees Celsius				
arithmetic mean (standard deviation)	0.02 (± 0.635)	-0.05 (± 0.331)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in heart rate

End point title	Change from Baseline in heart rate

End point description:

Heart rate was measured at indicated time points in supine position after 5 minutes rest for the participant. Baseline was defined as latest pre-dose assessment with a non-missing value in each treatment period. Change from Baseline was calculated as the value at the post-dose visit minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (pre-dose on Day 1) and Day 8 of each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	15		
Units: Beats per minute				
arithmetic mean (standard deviation)	0.6 (± 8.65)	-1.3 (± 12.09)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Twelve-lead ECG was obtained using an ECG machine that automatically calculated the heart rate and measured PR, QRS, QT, and corrected QT (QTc) intervals. Number of participants with abnormal-clinically significant and abnormal-not clinically significant values has been presented. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category title).

End point type	Secondary

End point timeframe:

Baseline (pre-dose on Day 1) and Day 8 of each treatment period

End point values	Placebo	GSK2798745		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	16		
Units: Participants				
Day 1 pre-dose, not clinically significant,n=17,16	2	1		
Day 1 pre-dose, clinically significant, n=17,16	0	0		
Day 8, not clinically significant, n=17,15	2	1		
Day 8, clinically significant, n=17,15	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected from the start of the treatment up to 45 days

Adverse event reporting additional description:

AEs and SAEs were collected for All Subjects population

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants were administered two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of 2.4 milligrams (mg) GSK2798745 each on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Reporting group title	GSK2798745

Reporting group description:

Participants were administered two tablets of 2.4 mg GSK2798745 on Day 1 followed by one tablet of 2.4 mg GSK2798745 on Days 2 to 7 of treatment period 1. In treatment period 2, participants received two tablets of placebo on Day 1 followed by one tablet of placebo on Days 2 to 7. All doses were administered once daily via the oral route with a glass of water. The treatment periods were separated by a wash-out period of 14 to 21 days.

Serious adverse events	Placebo	GSK2798745	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Placebo	GSK2798745	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 17 (52.94%)	11 / 16 (68.75%)	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	

Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 17 (17.65%)	7 / 16 (43.75%)	
occurrences (all)	3	7	
Lethargy			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Migraine			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 17 (5.88%)	2 / 16 (12.50%)	
occurrences (all)	1	2	
Feeling cold			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Suprapubic pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Ear pruritus			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Hypoacusis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Tinnitus			

subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Eye pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 17 (11.76%)	1 / 16 (6.25%)	
occurrences (all)	2	1	
Vomiting			
subjects affected / exposed	1 / 17 (5.88%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Irritable bowel syndrome			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 17 (11.76%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Nasal pruritus			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Productive cough			

subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Sneezing			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Infections and infestations			
Oral herpes			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 16 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 October 2017	Amendment No.01: The primary reason for amending the protocol was the removal of the Simplified Nutritional Appetite Questionnaire (SNAQ).
22 November 2017	Amendment No.02: Medicines and Healthcare Products Regulatory Agency (MHRA) requested: • Addition of the Columbia Suicidality Severity Rating Scale (CSSRS) at Follow-up. • That in case of an emergency, the investigator has the sole responsibility for determining if unblinding of a participant's treatment assignment is warranted. • Addition of adverse event stopping criteria.
25 June 2018	Amendment No.03: A non-substantial protocol amendment was made to clarify the inclusion criteria and make administrative corrections.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported