Clinical trial results:
A Randomized Double-Blind, Double-Dummy, Placebo-Controlled, Parallel-Group, Multicenter, Dose Ranging Study to Evaluate the Efficacy and Safety of GW685698X Inhalation Powder Once Daily and Fluticasone Propionate Inhalation Powder 100mcg Twice Daily compared with Placebo for 8 Weeks in Adolescent and Adult Subjects with Persistent Asthma Symptomatic on Non Steroidal Asthma Therapy

Summary

EudraCT number	2007-004442-32
Trial protocol	FR SE EE PL SK BG DE
Global end of trial date	02 October 2008

Results information

Result version number	v1 (current)
This version publication date	13 April 2016
First version publication date	23 May 2015

Trial information

Trial identification

Sponsor protocol code	FFA109687

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00603382
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000431-PIP01-08
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 December 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 October 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this 8-week study is to evaluate the dose response, efficacy and safety of four dosage regimens of GW685698X (25mcg, 50mcg, 100mcg and 200mcg) administered once daily in the evening in adolescent and adult subjects 12 years of age and older with persistent uncontrolled asthma to effectively select the appropriate dose of GW685698X to be evaluated in further clinical studies.

Protection of trial subjects:

The following steps were taken to protect trial subjects:
1). Only subjects meeting all of the inclusion criteria and none of the exclusion criteria were randomized to investigational medication.
2). All subjects enrolled into the study were provided rescue medication for use as necessary.
3). Subject lung function, as measured by morning and evening peak expiratory flow (PEF), use of rescue medication and symptoms were monitored through the use of a daily electronic diary.
4) Both safety and efficacy parameters were also assessed by the investigator regularly in the clinic to minimise any potential risks to the patients.
5). The investigator or treating physician may unblind a subject's treatment assignment in the case of an emergency, when knowledge of the study treatment is essential for the appropriate clinical management or welfare of the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 December 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 74
Country: Number of subjects enrolled	Korea, Republic of: 37
Country: Number of subjects enrolled	Mexico: 69
Country: Number of subjects enrolled	Peru: 67
Country: Number of subjects enrolled	Philippines: 177
Country: Number of subjects enrolled	Russian Federation: 25
Country: Number of subjects enrolled	United States: 659
Country: Number of subjects enrolled	Poland: 100
Country: Number of subjects enrolled	Slovakia: 24
Country: Number of subjects enrolled	Sweden: 35
Country: Number of subjects enrolled	Bulgaria: 75
Country: Number of subjects enrolled	Estonia: 12
Country: Number of subjects enrolled	France: 86

Country: Number of subjects enrolled	Germany: 19
Worldwide total number of subjects	1459
EEA total number of subjects	351

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)	177
Adults (18-64 years)	1230
From 65 to 84 years	52
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants (par.) meeting eligibility criteria at the Screening visit completed a 28-day Run-in Period for Baseline, safety evaluations and measures of asthma status. Par. were then randomized to an 8-week Treatment Period. Total 1459 par. were screened, 601 were randomized of which 598 par. received at least one dose of study treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo once daily (OD) in the evening from the dry powder inhaler (DPI) and placebo twice daily (BID) from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

twice daily via dry powder inhaler

Arm title	GW685698X 25 µg OD

Arm description:

Participants received GW685698X 25 micrograms (µg) OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Arm type	Experimental
Investigational medicinal product name	GW685698X
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

25 mcg once daily via dry powder inhaler

Arm title	GW685698X 50 µg OD

Arm description:

Participants received GW685698X 50 µg OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Arm type	Experimental
Investigational medicinal product name	GW685698X
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

50 mcg once daily via dry powder inhaler

Arm title	GW685698X 100 µg OD

Arm description:

Participants received GW685698X 100 µg OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Arm type	Experimental
Investigational medicinal product name	GW685698X
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

100 mcg once daily via dry powder inhaler

Arm title	GW685698X 200 µg OD

Arm description:

Participants received GW685698X 200 µg OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Arm type	Experimental
Investigational medicinal product name	GW685698X
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

200 mcg once daily via dry powder inhaler

Arm title	FP 100 µg BID

Arm description:

Participants received fluticasone propionate (FP) 100 µg BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) plus placebo OD in the evening from the DPI for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Arm type	Active comparator
Investigational medicinal product name	FP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

100 mcg twice daily via dry powder inhaler

Number of subjects in period 1[1]	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD
Started	94	97	100
Completed	76	83	91
Not completed	18	14	9
Consent withdrawn by subject	3	3	1
Physician decision	-	-	2
Adverse event, non-fatal	-	1	1
Lost to follow-up	-	1	1
Lack of efficacy	14	9	3
Protocol deviation	1	-	1

Number of subjects in period 1[1]	GW685698X 100 µg OD	GW685698X 200 µg OD	FP 100 µg BID
Started	110	95	102
Completed	98	86	84
Not completed	12	9	18
Consent withdrawn by subject	1	-	1
Physician decision	-	1	3
Adverse event, non-fatal	2	1	2
Lost to follow-up	1	-	1
Lack of efficacy	6	6	11
Protocol deviation	2	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Only those enrolled participants who received >=1 dose of study treatment are reported to be in the baseline period.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo once daily (OD) in the evening from the dry powder inhaler (DPI) and placebo twice daily (BID) from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study.	
Reporting group title	GW685698X 25 µg OD
Reporting group description:	
Participants received GW685698X 25 micrograms (µg) OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.	
Reporting group title	GW685698X 50 µg OD
Reporting group description:	
Participants received GW685698X 50 µg OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.	
Reporting group title	GW685698X 100 µg OD
Reporting group description:	
Participants received GW685698X 100 µg OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.	
Reporting group title	GW685698X 200 µg OD
Reporting group description:	
Participants received GW685698X 200 µg OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.	
Reporting group title	FP 100 µg BID
Reporting group description:	
Participants received fluticasone propionate (FP) 100 µg BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) plus placebo OD in the evening from the DPI for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.	

Reporting group values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD
Number of subjects	94	97	100
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	39.2	37.7	38.3
standard deviation	± 15.82	± 15.4	± 14.49
Gender categorical Units: Subjects			
Female	47	57	59
Male	47	40	41

Race, Customized Units: Subjects			
African American/African Heritage (AA/AHER)	5	4	4
American Indian or Alaska Native	5	7	5
Asian	7	13	9
White	69	64	72
AA/AHER & American Indian or Alaska Native	0	0	0
American Indian or Alaska Native & White	8	8	9
Native Hawaiian or other Pacific Islander & White	0	1	1

Reporting group values	GW685698X 100 µg OD	GW685698X 200 µg OD	FP 100 µg BID
Number of subjects	110	95	102
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	36.8	40.7	39.9
standard deviation	± 15.56	± 15.96	± 15.03
Gender categorical Units: Subjects			
Female	60	60	56
Male	50	35	46
Race, Customized Units: Subjects			
African American/African Heritage (AA/AHER)	8	6	5
American Indian or Alaska Native	6	6	5
Asian	10	10	10
White	76	64	74
AA/AHER & American Indian or Alaska Native	0	1	0
American Indian or Alaska Native & White	10	8	8
Native Hawaiian or other Pacific Islander & White	0	0	0

Reporting group values	Total		
Number of subjects	598		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	339		

Male	259		

Race, Customized Units: Subjects			
African American/African Heritage (AA/AHER)	32		
American Indian or Alaska Native	34		
Asian	59		
White	419		
AA/AHER & American Indian or Alaska Native	1		
American Indian or Alaska Native & White	51		
Native Hawaiian or other Pacific Islander & White	2		

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo once daily (OD) in the evening from the dry powder inhaler (DPI) and placebo twice daily (BID) from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study.

Reporting group title	GW685698X 25 µg OD

Reporting group description:

Participants received GW685698X 25 micrograms (µg) OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Reporting group title	GW685698X 50 µg OD

Reporting group description:

Participants received GW685698X 50 µg OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Reporting group title	GW685698X 100 µg OD

Reporting group description:

Participants received GW685698X 100 µg OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Reporting group title	GW685698X 200 µg OD

Reporting group description:

Participants received GW685698X 200 µg OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Reporting group title	FP 100 µg BID

Reporting group description:

Participants received fluticasone propionate (FP) 100 µg BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) plus placebo OD in the evening from the DPI for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Primary: Mean change from Baseline in trough (evening pre-dose and pre- rescue bronchodilator) FEV1 at Week 8

End point title	Mean change from Baseline in trough (evening pre-dose and pre- rescue bronchodilator) FEV1 at Week 8

End point description:

Pulmonary function was measured by forced expiratory volume in one second (FEV1), defined as the maximal amount of air that can be forcefully exhaled from the lungs in one second. Pre-dose and pre-rescue bronchodilator (albuterol/salbutamol) trough FEV1(the measurement of FEV1 performed at the end of the dosing interval) was measured electronically by spirometry in the evening at the Baseline through Week 8 clinic visits. Trough FEV1 is the FEV1 measured approximately 24 hours after the last administration of study drug. The highest of 3 technically acceptable measurements was recorded. The Visit 3 FEV1 assessment was used as the Baseline value. Change from Baseline in trough FEV1 was calculated as the value at Week 8 minus the value at Baseline. The analysis was performed using an Analysis of Covariance (ANCOVA) model with covariates of Baseline trough FEV1, country, sex, age, and treatment group. ITT=Intent-to-Treat. The Last Observation Carried Forward (LOCF) method was used.

End point type	Primary

End point timeframe:
Baseline and Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93[1]	94[2]	97[3]	109[4]
Units: Liters				
least squares mean (standard error)	0.137 (± 0.0428)	0.239 (± 0.0428)	0.266 (± 0.042)	0.341 (± 0.0396)

Notes:
[1] - ITT Population: all participants randomized to treatment who received >=1 dose of study medication.
[2] - ITT Population: all participants randomized to treatment who received >=1 dose of study medication.
[3] - ITT Population: all participants randomized to treatment who received >=1 dose of study medication.
[4] - ITT Population: all participants randomized to treatment who received >=1 dose of study medication.

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94[5]	101[6]		
Units: Liters				
least squares mean (standard error)	0.367 (± 0.0428)	0.243 (± 0.0411)		

Notes:
[5] - ITT Population: all participants randomized to treatment who received >=1 dose of study medication.
[6] - ITT Population: all participants randomized to treatment who received >=1 dose of study medication.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GW685698X 25 µg OD
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.095
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.101
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.018
upper limit	0.221

Statistical analysis title	Statistical Analysis 2

Comparison groups	Placebo v GW685698X 50 µg OD
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.033
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.129
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.011
upper limit	0.247

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v GW685698X 100 µg OD
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.204
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.089
upper limit	0.319

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v GW685698X 200 µg OD
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Median difference (final values)
Point estimate	0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.111
upper limit	0.349

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v FP 100 µg BID
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.074
Method	ANCOVA
Parameter estimate	Median difference (final values)
Point estimate	0.106
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.223

Secondary: Mean change from Baseline in daily trough (pre-dose and pre-rescue bronchodilator) evening peak expiratory flow (PEF) averaged over the 8-week Treatment Period

End point title	Mean change from Baseline in daily trough (pre-dose and pre-rescue bronchodilator) evening peak expiratory flow (PEF) averaged over the 8-week Treatment Period

End point description:

PEF is defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. Trough PEF is defined as the PEF measurement performed at the end of the dosing interval. PEF was measured by the participants using a hand-held electronic peak flow meter each evening prior to the dose of study medication and any rescue albuterol/salbutamol inhalation aerosol use. The best of three attempts was recorded by the participants in a daily diary. The Baseline value was derived from the last 7 days of the daily diary prior to the randomization of the participant. Change from Baseline was calculated as the value of the averaged daily evening PEF over the 8-week treatment period minus the value at Baseline. The analysis was performed using an ANCOVA model with covariates of Baseline trough evening PEF, country, sex, age, and treatment group.

End point type	Secondary

End point timeframe:

From Baseline up to Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[7]	96[8]	98[9]	110[10]
Units: Liters per minute				
least squares mean (standard error)	9.6 (± 4.21)	23.6 (± 4.17)	30.3 (± 4.12)	25.7 (± 3.9)

Notes:

[7] - ITT Population. Only those participants available at the specified time points were analyzed.

[8] - ITT Population. Only those participants available at the specified time points were analyzed.

[9] - ITT Population. Only those participants available at the specified time points were analyzed.

[10] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	GW685698X 200 µg OD	FP 100 µg BID		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[11]	102[12]		
Units: Liters per minute				
least squares mean (standard error)	31.3 (± 4.2)	24.4 (± 4.04)		

Notes:

[11] - ITT Population. Only those participants available at the specified time points were analyzed.

[12] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in daily morning PEF averaged over the 8-week Treatment Period

End point title	Mean change from Baseline in daily morning PEF averaged over the 8-week Treatment Period

End point description:

PEF is defined as the maximum airflow during a forced expiration beginning with the lungs fully inflated. Trough PEF is defined as the PEF measurement performed at the end of the dosing interval. PEF was measured by the participants using a hand-held electronic peak flow meter each morning prior to the dose of study medication and any rescue albuterol/salbutamol inhalation aerosol use. The best of three attempts was recorded by the participants in a daily diary. The Baseline value was derived from the last 7 days of the daily diary prior to the randomization of the participant. Change from Baseline was calculated as the value of the averaged daily morning PEF over the 8-week treatment period minus the value at Baseline. The analysis was performed using an ANCOVA model with covariates of Baseline trough morning PEF, country, sex, age, and treatment group.

End point type	Secondary

End point timeframe:

From Baseline up to Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[13]	96[14]	98[15]	110[16]
Units: Liters per minute				
least squares mean (standard error)	13.6 (± 4.27)	27.2 (± 4.23)	33.5 (± 4.17)	29.5 (± 3.95)

Notes:

[13] - ITT Population. Only those participants available at the specified time points were analyzed.

[14] - ITT Population. Only those participants available at the specified time points were analyzed.

[15] - ITT Population. Only those participants available at the specified time points were analyzed.

[16] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[17]	102[18]		
Units: Liters per minute				
least squares mean (standard error)	35.6 (± 4.26)	25.6 (± 4.09)		

Notes:

[17] - ITT Population. Only those participants available at the specified time points were analyzed.

[18] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in the percentage of symptom-free 24 hour (hr) periods during the 8-week Treatment Period

End point title	Mean change from Baseline in the percentage of symptom-free 24 hour (hr) periods during the 8-week Treatment Period

End point description:

Asthma symptoms were recorded in a daily dairy by the participants every day in the morning and evening before taking any rescue or study medication and before PEF measurement. A 24-hour period in which a participant's responses to both the morning and evening assessments indicated no symptoms was considered as symptom-free. The Baseline value was derived from the last 7 days of the daily diary prior to the randomization of the participant. Change from Baseline was calculated as the averaged value during the 8-week Treatment Period minus the value at Baseline. The analysis was performed using an ANCOVA model with covariates of Baseline, country, sex, age, and treatment group.

End point type	Secondary

End point timeframe:

From Baseline up to Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[19]	96[20]	98[21]	110[22]
Units: Percentage of symptom-free 24-hr periods				
least squares mean (standard error)	18.4 (± 3.21)	25.3 (± 3.17)	31.1 (± 3.14)	38.7 (± 2.97)

Notes:

[19] - ITT Population. Only those participants available at the specified time points were analyzed.

[20] - ITT Population. Only those participants available at the specified time points were analyzed.

[21] - ITT Population. Only those participants available at the specified time points were analyzed.

[22] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[23]	102[24]		
Units: Percentage of symptom-free 24-hr periods				
least squares mean (standard error)	31.7 (± 3.2)	33.3 (± 3.08)		

Notes:

[23] - ITT Population. Only those participants available at the specified time points were analyzed.

[24] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in the percentage of rescue free 24-hour (hr) periods during the 8-week Treatment Period

End point title	Mean change from Baseline in the percentage of rescue free 24-hour (hr) periods during the 8-week Treatment Period

End point description:

The number of inhalations of rescue albuterol/salbutamol inhalation aerosol used during the day and night was recorded by the participants in a daily diary. A 24-hour period in which a participant's responses to both the morning and evening assessments indicated no use of rescue medication was considered as rescue-free. The Baseline value was derived from the last 7 days of the daily diary prior to the randomization of the participant. Change from Baseline was calculated as the averaged value during the 8-week Treatment Period minus the value at Baseline. The analysis was performed using an ANCOVA model with covariates of Baseline, country, sex, age, and treatment group.

End point type	Secondary

End point timeframe:

From Baseline up to Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[25]	96[26]	98[27]	110[28]
Units: Percentage of rescue-free 24-hr periods				
least squares mean (standard error)	21.9 (± 3.32)	29.3 (± 3.28)	34.5 (± 3.24)	40.8 (± 3.08)

Notes:

[25] - ITT Population. Only those participants available at the specified time points were analyzed.

[26] - ITT Population. Only those participants available at the specified time points were analyzed.

[27] - ITT Population. Only those participants available at the specified time points were analyzed.

[28] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[29]	102[30]		
Units: Percentage of rescue-free 24-hr periods				
least squares mean (standard error)	32 (± 3.31)	35.5 (± 3.18)		

Notes:

[29] - ITT Population. Only those participants available at the specified time points were analyzed.

[30] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who withdrew due to lack of efficacy during the 8-Week Treatment Period

End point title	Number of participants who withdrew due to lack of efficacy during the 8-Week Treatment Period

End point description:

The number of participants whose primary reason for withdrawal was lack of efficacy was analyzed.

End point type	Secondary

End point timeframe:

From the first dose of study medication up to Week 8/Early Withdrawal

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[31]	97[32]	100[33]	110[34]
Units: Participants	14	9	3	6

Notes:

[31] - ITT Population

[32] - ITT Population

[33] - ITT Population

[34] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[35]	102[36]		
Units: Participants	6	11		

Notes:

[35] - ITT Population

[36] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any on-treatment adverse events or serious adverse events throughout the 8-week Treatment Period

End point title	Number of participants with any on-treatment adverse events or serious adverse events throughout the 8-week Treatment Period

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. A serious adverse event (SAE) is defined as any untoward medical occurrence that, at any dose: results in death; is life-threatening; requires hospitalization or prolongation of existing hospitalization; results in disability/incapacity; or is a congenital anomaly/birth defect. Medical or scientific judgement should have been exercised in other situations. Refer to the general AE/SAE module for a list of AEs (occurring at a frequency threshold >=3%) and SAEs.

End point type	Secondary

End point timeframe:

From the first dose of study medication up to Week 8/Early Withdrawal

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[37]	97[38]	100[39]	110[40]
Units: Particpants				
Any AE	24	19	28	35
Any SAE	0	1	0	1

Notes:

[37] - ITT Population

[38] - ITT Population

[39] - ITT Population

[40] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[41]	102[42]		
Units: Particpants				
Any AE	27	35		
Any SAE	0	2		

Notes:

[41] - ITT Population

[42] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinical/visual evidence of oropharyngeal candidiasis

End point title	Number of participants with clinical/visual evidence of oropharyngeal candidiasis

End point description:

A detailed oropharyngeal examination for visual evidence of oral candidiasis was performed.

End point type	Secondary

End point timeframe:

From Baseline up to Week 8/Early Withdrawal

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[43]	97[44]	100[45]	110[46]
Units: Participants				
Clinical evidence	0	0	4	4
No clinical evidence	94	97	96	106

Notes:

[43] - ITT Population

[44] - ITT Population

[45] - ITT Population

[46] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[47]	102[48]		
Units: Participants				
Clinical evidence	2	2		
No clinical evidence	93	100		

Notes:

[47] - ITT Population

[48] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of basophils, eosinophils, lymphocytes, monocytes, and total neutrophils in the blood at Baseline and Week 8

End point title	Percentage of basophils, eosinophils, lymphocytes, monocytes, and total neutrophils in the blood at Baseline and Week 8

End point description:

Blood samples were collected for the measurement of basophils, eosinophils, lymphocytes, monocytes, and total neutrophils at Baseline (BL) and Week 8 (W8). The Baseline value was the measurement taken at screening (Visit 1). Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Different participants may have been analyzed for different parameters, so the overall number of participants analyzed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[49]	97[50]	100[51]	110[52]
Units: Percentage				
arithmetic mean (standard deviation)				
Basophils, BL, n=92, 94, 95, 106, 92, 97	0.31 (± 0.199)	0.32 (± 0.2)	0.31 (± 0.194)	0.32 (± 0.19)
Basophils, W8, n=72, 80, 83, 94, 82, 79	0.3 (± 0.186)	0.26 (± 0.153)	0.31 (± 0.169)	0.35 (± 0.236)
Eosinophils, BL, n=92, 94, 95, 106, 92, 97	3.87 (± 3.022)	3.38 (± 2.693)	3.95 (± 2.503)	4.4 (± 3.286)
Eosinophils, W8, n=72, 80, 83, 94, 82, 79	4.31 (± 3.544)	3.38 (± 3.3)	3.76 (± 2.608)	3.77 (± 3.066)
Lymphocytes, BL, n=92, 94, 95, 106, 92, 97	33.96 (± 8.378)	31.57 (± 8.821)	33.33 (± 7.768)	33.69 (± 8.682)
Lymphocytes, W8, n=72, 80, 83, 94, 82, 79	32.88 (± 8.063)	29.82 (± 10.12)	30.36 (± 8.322)	30.39 (± 7.326)
Monocytes, BL, n=92, 94, 95, 106, 92, 97	5.09 (± 2.379)	4.41 (± 1.851)	4.7 (± 2.056)	5.2 (± 2.113)
Monocytes, W8, n=72, 80, 83, 94, 82, 79	5.41 (± 3.042)	4.32 (± 2.098)	4.6 (± 2.486)	4.6 (± 2.178)
Total Neutrophils, BL, n=92, 94, 95, 106, 92, 97	56.74 (± 9.22)	60.24 (± 9.62)	57.68 (± 8.309)	56.34 (± 9.832)
Total Neutrophils, W8, n=72, 80, 83, 94, 82, 79	57.08 (± 9.543)	62.19 (± 11.58)	60.95 (± 9.008)	60.86 (± 8.054)

Notes:

[49] - ITT Population

[50] - ITT Population

[51] - ITT Population

[52] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[53]	102[54]		
Units: Percentage				
arithmetic mean (standard deviation)				
Basophils, BL, n=92, 94, 95, 106, 92, 97	0.33 (± 0.205)	0.33 (± 0.234)		
Basophils, W8, n=72, 80, 83, 94, 82, 79	0.35 (± 0.22)	0.34 (± 0.264)		
Eosinophils, BL, n=92, 94, 95, 106, 92, 97	4.75 (± 3.358)	3.88 (± 3.073)		
Eosinophils, W8, n=72, 80, 83, 94, 82, 79	3.96 (± 2.867)	3.34 (± 2.364)		
Lymphocytes, BL, n=92, 94, 95, 106, 92, 97	34.32 (± 8.806)	34.25 (± 8.514)		
Lymphocytes, W8, n=72, 80, 83, 94, 82, 79	31.97 (± 7.44)	32.22 (± 7.877)		
Monocytes, BL, n=92, 94, 95, 106, 92, 97	4.78 (± 2.301)	4.92 (± 2.093)		
Monocytes, W8, n=72, 80, 83, 94, 82, 79	4.5 (± 2.174)	4.87 (± 2.38)		
Total Neutrophils, BL, n=92, 94, 95, 106, 92, 97	55.8 (± 10.281)	56.6 (± 9.226)		
Total Neutrophils, W8, n=72, 80, 83, 94, 82, 79	59.2 (± 8.881)	59.19 (± 8.672)		

Notes:

[53] - ITT Population

[54] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hematocrit at Baseline and Week 8

End point title	Hematocrit at Baseline and Week 8

End point description:

Blood samples were collected for the measurement of Hematocrit at Baseline (BL) and Week 8 (W8). The Baseline value was the measurement taken at screening (Visit 1). Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[55]	97[56]	100[57]	110[58]
Units: Proportion of 1				
arithmetic mean (standard deviation)				
Hematocrit, BL, n=92, 94, 95, 106, 92, 97	0.43 (± 0.041)	0.42 (± 0.039)	0.42 (± 0.04)	0.43 (± 0.043)
Hematocrit, W8, n=72, 79, 83, 94, 82, 79	0.43 (± 0.038)	0.42 (± 0.038)	0.42 (± 0.037)	0.43 (± 0.04)

Notes:

[55] - ITT Population

[56] - ITT Population

[57] - ITT Population

[58] - ITT Popultion

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[59]	102[60]		
Units: Proportion of 1				
arithmetic mean (standard deviation)				
Hematocrit, BL, n=92, 94, 95, 106, 92, 97	0.42 (± 0.039)	0.43 (± 0.034)		
Hematocrit, W8, n=72, 79, 83, 94, 82, 79	0.42 (± 0.033)	0.43 (± 0.039)		

Notes:

[59] - ITT Population

[60] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Hemoglobin at Baseline and Week 8

End point title	Hemoglobin at Baseline and Week 8

End point description:

Blood samples were collected for the measurement of hemoglobin at Baseline (BL)and Week 8 (W8). The Baseline value was the measurement taken at screening (Visit 1). Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[61]	97[62]	100[63]	110[64]
Units: Grams per liter (G/L)				
arithmetic mean (standard deviation)				

Hemoglobin, BL, n=92, 94, 95, 106, 92, 96	141.54 (± 14.116)	138.05 (± 13.178)	140.7 (± 13.769)	141.14 (± 14.625)
Hemoglobin, W8, n=72, 79, 83, 94, 82, 79	140.81 (± 12.973)	137.86 (± 12.862)	138.95 (± 12.785)	140.16 (± 13.647)

Notes:

[61] - ITT Population

[62] - ITT Population

[63] - ITT Population

[64] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[65]	102[66]		
Units: Grams per liter (G/L)				
arithmetic mean (standard deviation)				
Hemoglobin, BL, n=92, 94, 95, 106, 92, 96	139.5 (± 12.978)	141.9 (± 11.632)		
Hemoglobin, W8, n=72, 79, 83, 94, 82, 79	136.32 (± 11.594)	139.81 (± 13.009)		

Notes:

[65] - ITT Population

[66] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet count and white blood cell (WBC) count at Baseline and Week 8

End point title	Platelet count and white blood cell (WBC) count at Baseline and Week 8

End point description:

Blood samples were collected for the measurement of platelet count and WBC count at Baseline (BL) and Week 8 (W8). The Baseline value was the measurement taken at screening (Visit 1). Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Different participants may have been analyzed for different parameters, so the overall number of participants analyzed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[67]	97[68]	100[69]	110[70]
Units: 10^9 cells per liter (GI/L)				
arithmetic mean (standard deviation)				
Platelet count, BL, n=91, 91, 95, 106, 92, 95	271.68 (± 62.861)	265.75 (± 51.446)	279.38 (± 57.658)	272.2 (± 61.111)
Platelet count, W8, n=72, 76, 83, 93, 81, 78	265.47 (± 49.978)	262.07 (± 45.837)	271.03 (± 47.156)	278.57 (± 58.302)
WBC, BL, n=92, 94, 95, 106, 92, 97	7.82 (± 2.018)	7.96 (± 1.892)	8.01 (± 2.095)	7.62 (± 1.878)
WBC, W8, n=72, 79, 83, 94, 82, 79	7.56 (± 1.679)	8.26 (± 2.169)	8.34 (± 2.211)	7.94 (± 2.046)

Notes:

[67] - ITT Population

[68] - ITT Population

[69] - ITT Population

[70] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[71]	102[72]		
Units: 10^9 cells per liter (GI/L)				
arithmetic mean (standard deviation)				
Platelet count, BL, n=91, 91, 95, 106, 92, 95	268.37 (± 60.442)	281.26 (± 66.492)		
Platelet count, W8, n=72, 76, 83, 93, 81, 78	272.53 (± 68.404)	274.46 (± 61.819)		
WBC, BL, n=92, 94, 95, 106, 92, 97	7.79 (± 2.055)	7.94 (± 1.982)		
WBC, W8, n=72, 79, 83, 94, 82, 79	7.94 (± 1.769)	8 (± 2.292)		

Notes:

[71] - ITT Population

[72] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Red blood cells (RBC) count at Baseline and Week 8

End point title	Red blood cells (RBC) count at Baseline and Week 8

End point description:

Blood samples were collected for the measurement of RBC count at Baseline (BL) and Week 8 (W8). The Baseline value was the measurement taken at screening (Visit 1). Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[73]	97[74]	100[75]	110[76]
Units: 10^12 cells per liter (TI/L)				
arithmetic mean (standard deviation)				
RBC, BL, n=92, 94, 95, 106, 92, 97	4.71 (± 0.429)	4.65 (± 0.438)	4.68 (± 0.425)	4.71 (± 0.46)
RBC, W8, n=72, 79, 83, 94, 82, 79	4.65 (± 0.41)	4.61 (± 0.445)	4.63 (± 0.435)	4.67 (± 0.45)

Notes:

[73] - ITT Population

[74] - ITT Population

[75] - ITT Population

[76] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[77]	102[78]		
Units: 10^12 cells per liter (TI/L)				
arithmetic mean (standard deviation)				
RBC, BL, n=92, 94, 95, 106, 92, 97	4.68 (± 0.422)	4.71 (± 0.416)		
RBC, W8, n=72, 79, 83, 94, 82, 79	4.6 (± 0.369)	4.65 (± 0.462)		

Notes:

[77] - ITT Population

[78] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical chemistry parameters of alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LD), and gamma glutamyltransferase (GGT) at Baseline and Week 8

End point title	Clinical chemistry parameters of alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LD), and gamma glutamyltransferase (GGT) at Baseline and Week 8

End point description:

Blood samples were collected for the measurement of ALP, ALT, AST, LD and GGT at Baseline (BL) and Week 8 (W8). The Baseline value was the measurement taken at Screening (Visit 1). Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Different participants may have been analyzed for different parameters, so the overall number of participants analyzed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[79]	97[80]	100[81]	110[82]
Units: International units per liter (IU/L)				
arithmetic mean (standard deviation)				
ALP, BL, n=94, 97, 99, 106, 94, 101	82.7 (± 36.11)	79.7 (± 32.21)	83.5 (± 40.07)	90.3 (± 56.43)
ALP, W8, n=78, 84, 90, 97, 85, 83	83 (± 40.83)	74.8 (± 27.91)	82.9 (± 41.61)	87 (± 49.65)
ALT, BL, n=94, 97, 99, 106, 94, 101	21.8 (± 15.91)	21.5 (± 14.57)	23.6 (± 19.4)	22.3 (± 16.61)
ALT, W8, n=78, 84, 90, 97, 86, 83	22.3 (± 22.79)	20.3 (± 11.92)	20.7 (± 10.39)	20.8 (± 14.01)
AST, BL, n=94, 96, 99, 105, 93, 101	21 (± 7.64)	22.8 (± 11.39)	22.8 (± 13.35)	21.9 (± 9.68)
AST, W8, n=78, 83, 90, 97, 86, 82	22.2 (± 10.76)	20.8 (± 6.48)	21.1 (± 7.52)	20.5 (± 8.07)
LD, BL, n=94, 96, 99, 105, 93, 101	157.9 (± 47.78)	170.7 (± 59.82)	169.3 (± 64.08)	165.6 (± 70.56)
LD, W8, n=78, 83, 90, 97, 86, 82	151.8 (± 32.37)	159.1 (± 31.46)	159.9 (± 32.14)	153.8 (± 26.9)
GGT, BL, n=94, 97, 99, 106, 94, 101	27.6 (± 20)	33 (± 30.67)	33.1 (± 31.42)	30.1 (± 22.29)
GGT, W8, n=78, 84, 90, 97, 86, 83	29.7 (± 27.53)	31.1 (± 24.61)	32.4 (± 30.84)	31.9 (± 24.96)

Notes:

[79] - ITT Population

[80] - ITT Population

[81] - ITT Population

[82] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[83]	102[84]		
Units: International units per liter (IU/L)				
arithmetic mean (standard deviation)				
ALP, BL, n=94, 97, 99, 106, 94, 101	94.4 (± 71.94)	84.7 (± 62.31)		
ALP, W8, n=78, 84, 90, 97, 85, 83	90.8 (± 76.22)	84 (± 59.81)		
ALT, BL, n=94, 97, 99, 106, 94, 101	20.7 (± 11.38)	20.1 (± 9.84)		
ALT, W8, n=78, 84, 90, 97, 86, 83	19.5 (± 12.03)	19.9 (± 10.04)		
AST, BL, n=94, 96, 99, 105, 93, 101	21.3 (± 7.2)	20.3 (± 5.1)		
AST, W8, n=78, 83, 90, 97, 86, 82	20.2 (± 5.91)	20.5 (± 5.38)		
LD, BL, n=94, 96, 99, 105, 93, 101	172.9 (± 62.38)	164.2 (± 57.04)		
LD, W8, n=78, 83, 90, 97, 86, 82	161.9 (± 36.79)	157.3 (± 27.36)		
GGT, BL, n=94, 97, 99, 106, 94, 101	29.9 (± 26.3)	28.2 (± 21.4)		
GGT, W8, n=78, 84, 90, 97, 86, 83	29.3 (± 32.75)	27.9 (± 21.24)		

Notes:

[83] - ITT Population

[84] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical chemistry parameters of albumin and total protein at Baseline and Week 8

End point title	Clinical chemistry parameters of albumin and total protein at Baseline and Week 8

End point description:

Blood samples were collected for the measurement of albumin and total protein at Baseline (BL) and Week 8 (W8). The Baseline value was the measurement taken at Screening (Visit 1). Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Different participants may have been analyzed for different parameters, so the overall number of participants analyzed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[85]	97[86]	100[87]	110[88]
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
Albumin,BL, n=94, 97, 99, 106, 94, 101	45.2 (± 3.18)	45.6 (± 3.08)	45.1 (± 2.86)	45.9 (± 3)
Albumin, W8, n= 78, 84, 90, 97, 86, 83	44.9 (± 3.12)	44.8 (± 3.3)	44.9 (± 2.97)	45.6 (± 2.91)
Total protein, BL, n=94, 97, 99, 106, 94, 101	73.2 (± 4.04)	74 (± 4.46)	73.1 (± 4.6)	74.1 (± 4.63)
Total protein, W8, n= 78, 84, 90, 97, 86, 83	71.7 (± 3.65)	72.6 (± 4.21)	72.6 (± 4.62)	73.4 (± 4.58)

Notes:

[85] - ITT Population

[86] - ITT Population

[87] - ITT Population

[88] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[89]	102[90]		
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
Albumin,BL, n=94, 97, 99, 106, 94, 101	45.3 (± 2.96)	45.2 (± 3.01)		
Albumin, W8, n= 78, 84, 90, 97, 86, 83	44.5 (± 3.22)	44.9 (± 2.62)		
Total protein, BL, n=94, 97, 99, 106, 94, 101	73.4 (± 4.5)	73.2 (± 4.23)		
Total protein, W8, n= 78, 84, 90, 97, 86, 83	72 (± 4.66)	72.5 (± 4.05)		

Notes:

[89] - ITT Population

[90] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical chemistry parameters of chloride, calcium, carbon dioxide content/bicarbonate (CO2/BI), cholesterol, glucose, phosphorus inorganic(PI), potassium, sodium, and urea/blood urea nitrogen (BUN) at Baseline and Week 8

End point title	Clinical chemistry parameters of chloride, calcium, carbon dioxide content/bicarbonate (CO2/BI), cholesterol, glucose, phosphorus inorganic(PI), potassium, sodium, and urea/blood urea nitrogen (BUN) at Baseline and Week 8

End point description:

Blood samples were collected for the measurement of chloride, calcium, CO2/BI, cholesterol, glucose, PI, potassium, sodium, and urea/blood urea nitrogen at Baseline (BL) and Week 8 (W8). The Baseline value was the measurement taken at screening (Visit 1). Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Different participants may have been analyzed for different parameters, so the overall number of participants analyzed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[91]	97[92]	100[93]	110[94]
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
Chloride, BL, n=94, 97, 99, 106, 94, 101	104.4 (± 2.25)	104.7 (± 2.38)	104.5 (± 2.5)	104.4 (± 2.41)
Chloride, W8, n=78, 84, 90, 97, 86, 83	104.8 (± 2.24)	104.8 (± 2.36)	104.7 (± 2.55)	104.2 (± 2.15)
Calcium, BL, n=94, 96, 99, 105, 93, 101	2.4 (± 0.1)	2.4 (± 0.1)	2.3 (± 0.09)	2.4 (± 0.11)
Calcium, W8, n=78, 83, 90, 97, 85, 82	2.4 (± 0.1)	2.3 (± 0.1)	2.3 (± 0.1)	2.4 (± 0.1)
CO2/BI, BL, n=94, 96, 99, 105, 93, 101	23.2 (± 2.58)	22.8 (± 2.71)	23 (± 2.31)	23.4 (± 2.49)
CO2/BI, W8, n=78, 83, 90, 97, 86, 82	23.1 (± 2.57)	22.8 (± 2.62)	22.7 (± 2.61)	23.3 (± 2.55)
Cholesterol, BL, n=94, 97, 99, 106, 94, 101	4.9 (± 1.02)	5 (± 1.04)	5.2 (± 1.14)	5 (± 0.97)
Cholesterol, W8, n=78, 84, 90, 97, 86, 83	5 (± 1.24)	4.9 (± 1.05)	5.1 (± 1.05)	5.2 (± 1.16)
Glucose, BL, n=94, 97, 99, 106, 94, 101	5.2 (± 0.99)	5.5 (± 2.05)	5.2 (± 1.18)	5.1 (± 0.89)
Glucose, W8, n=78, 84, 90, 97, 86, 83	5.2 (± 1.07)	5.4 (± 1.96)	5.2 (± 1.2)	5 (± 0.88)
PI, BL, n=94, 97, 99, 106, 94, 101	1.2 (± 0.22)	1.1 (± 0.2)	1.2 (± 0.17)	1.2 (± 0.22)
PI, W8, n=78, 84, 90, 97, 86, 83	1.3 (± 0.21)	1.2 (± 0.17)	1.2 (± 0.18)	1.3 (± 0.2)
Potassium, BL, n=94, 96, 99, 105, 93, 101	4.1 (± 0.39)	4.2 (± 0.44)	4.1 (± 0.38)	4.2 (± 0.4)
Potassium, W8, n=78, 83, 90, 97, 85, 82	4.2 (± 0.34)	4.2 (± 0.41)	4.2 (± 0.32)	4.2 (± 0.38)
Sodium, BL, n=94, 97, 99, 106, 94, 101	140.8 (± 1.82)	140.5 (± 2.05)	140.6 (± 1.92)	140.8 (± 2.16)
Sodium, W8, n=78, 84, 90, 97, 86, 83	140.7 (± 2.09)	140.5 (± 2.01)	140.7 (± 2.02)	140.6 (± 1.63)
BUN, BL, n=94, 97, 99, 106, 94, 101	5.4 (± 1.75)	5.3 (± 1.66)	5.3 (± 1.92)	5.7 (± 1.94)
BUN, W8, n=78, 84, 90, 97, 86, 83	5.5 (± 1.68)	5.2 (± 1.97)	5 (± 1.3)	5.5 (± 1.44)

Notes:

[91] - ITT Population

[92] - ITT Population

[93] - ITT Population

[94] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[95]	102[96]		
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
Chloride, BL, n=94, 97, 99, 106, 94, 101	104.8 (± 2.17)	104.4 (± 2.49)		
Chloride, W8, n=78, 84, 90, 97, 86, 83	104.7 (± 2.11)	104.6 (± 2.67)		
Calcium, BL, n=94, 96, 99, 105, 93, 101	2.4 (± 0.13)	2.3 (± 0.09)		
Calcium, W8, n=78, 83, 90, 97, 85, 82	2.4 (± 0.11)	2.4 (± 0.09)		
CO2/BI, BL, n=94, 96, 99, 105, 93, 101	23.5 (± 2.45)	23.5 (± 2.74)		
CO2/BI, W8, n=78, 83, 90, 97, 86, 82	22.7 (± 2.42)	22.8 (± 2.6)		
Cholesterol, BL, n=94, 97, 99, 106, 94, 101	5 (± 1.08)	5 (± 1.1)		

Cholesterol, W8, n=78, 84, 90, 97, 86, 83	5 (± 1.03)	5 (± 1.07)		
Glucose, BL, n=94, 97, 99, 106, 94, 101	5.1 (± 0.83)	5.3 (± 1.54)		
Glucose, W8, n=78, 84, 90, 97, 86, 83	5.2 (± 1.21)	5.1 (± 1.18)		
PI, BL, n=94, 97, 99, 106, 94, 101	1.2 (± 0.21)	1.2 (± 0.18)		
PI, W8, n=78, 84, 90, 97, 86, 83	1.2 (± 0.21)	1.2 (± 0.2)		
Potassium, BL, n=94, 96, 99, 105, 93, 101	4.2 (± 0.45)	4.2 (± 0.4)		
Potassium, W8, n=78, 83, 90, 97, 85, 82	4.2 (± 0.38)	4.2 (± 0.36)		
Sodium, BL, n=94, 97, 99, 106, 94, 101	141.1 (± 1.91)	140.8 (± 2.04)		
Sodium, W8, n=78, 84, 90, 97, 86, 83	140.9 (± 2.36)	140.8 (± 1.97)		
BUN, BL, n=94, 97, 99, 106, 94, 101	5.7 (± 2.09)	5.4 (± 1.72)		
BUN, W8, n=78, 84, 90, 97, 86, 83	5.2 (± 1.54)	5 (± 1.43)		

Notes:

[95] - ITT Population

[96] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical chemistry parameters of creatinine, direct bilirubin, total bilirubin, and uric acid at Baseline and Week 8

End point title	Clinical chemistry parameters of creatinine, direct bilirubin, total bilirubin, and uric acid at Baseline and Week 8

End point description:

Blood samples were collected for the measurement of creatinine, direct bilirubin (DBIL), total bilirubin (TBIL), and uric acid at Baseline and Week 8. The Baseline value was the measurement taken at screening (Visit 1). Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Different participants may have been analyzed for different parameters, so the overall number of participants analyzed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[97]	97[98]	100[99]	110[100]
Units: Micromoles per liter (µmol/L)				
arithmetic mean (standard deviation)				
DBIL, BL, n=94, 97, 99, 106, 94, 101	2.1 (± 1.26)	2.1 (± 1.29)	2 (± 1.04)	2 (± 1.13)
DBIL, W8, n=77, 84, 89, 97, 86, 83	2 (± 1.03)	2 (± 0.94)	1.9 (± 0.98)	1.9 (± 1.02)
TBIL, BL, n=94, 97, 99, 106, 94, 101	9.6 (± 6.1)	9.7 (± 6.08)	9 (± 4.39)	9.3 (± 4.35)
TBIL, W8, n=78, 84, 90, 97, 86, 83	10.3 (± 5.57)	9.1 (± 4.14)	8.7 (± 3.99)	9.1 (± 3.88)
Uric acid, BL, n=94, 97, 99, 105, 94, 101	337.8 (± 88.15)	327.2 (± 85.64)	325.6 (± 85.82)	334.1 (± 90.63)
Uric acid, W8, n=78, 84, 90, 96, 86, 83	353.6 (± 86.64)	327.5 (± 84.69)	321.9 (± 91.9)	340.9 (± 89.48)
Creatinine, BL, n=94, 97, 99, 106, 94, 101	83.2 (± 19.89)	79.8 (± 14.72)	77.7 (± 14.52)	81.9 (± 16.68)

Creatinine, W8, n=78, 84, 90, 97, 86, 83	84.5 (± 19.21)	79.7 (± 15.67)	79 (± 13.45)	81.7 (± 14.9)

Notes:

[97] - ITT Population

[98] - ITT Population

[99] - ITT Population

[100] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[101]	102[102]		
Units: Micromoles per liter (µmol/L)				
arithmetic mean (standard deviation)				
DBIL, BL, n=94, 97, 99, 106, 94, 101	1.8 (± 1.17)	2 (± 1.04)		
DBIL, W8, n=77, 84, 89, 97, 86, 83	1.7 (± 0.93)	1.9 (± 1.05)		
TBIL, BL, n=94, 97, 99, 106, 94, 101	8.7 (± 4.11)	9 (± 3.93)		
TBIL, W8, n=78, 84, 90, 97, 86, 83	8.5 (± 3.46)	9.4 (± 4.39)		
Uric acid, BL, n=94, 97, 99, 105, 94, 101	326.6 (± 85.37)	324.5 (± 78.64)		
Uric acid, W8, n=78, 84, 90, 96, 86, 83	316.5 (± 81.29)	325.4 (± 80.48)		
Creatinine, BL, n=94, 97, 99, 106, 94, 101	78.3 (± 15.21)	79.3 (± 15.08)		
Creatinine, W8, n=78, 84, 90, 97, 86, 83	77.7 (± 14.32)	80.4 (± 15.97)		

Notes:

[101] - ITT Population

[102] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated result for the indicated urinalysis parameters tested by dipstick at Baseline and Week 8/Early Withdrawal

End point title	Number of participants with the indicated result for the indicated urinalysis parameters tested by dipstick at Baseline and Week 8/Early Withdrawal

End point description:

Urinalysis parameters included: Urine Occult Blood (UOB), Urine Glucose (UG), Urine Ketones (UK), Urine Protein (UP), and Urine Leukocyte Esterase test for detecting White Blood Cell (UWBC). The dipstick was a strip used to detect the presence or absence of these parameters in the urine sample. The dipstick test gives results in a semi-quantitative manner, and results for urinalysis parameters can be read as large, moderate (Mod), negative (Neg), small, Trace, 1+, 2+, 3+ and 4+, and for UG the result can be read as Neg, Trace, Trace or 1/10 G/dL, 1+ or 1/4 G/dL, 3+ or 1 G/dL, indicating proportional concentrations in the urine sample. Data are reported as the number of participants who had neg, Trace, 1+, 2+, 3+ and 4+ levels at Baseline (BL) and Week 8 (W8)/Early Withdrawal (EW). The Baseline value was the measurement taken at screening (Visit 1). Only those participants available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and Week 8/Early Withdrawal

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[103]	97[104]	100[105]	110[106]
Units: Participants				
UOB, 1+, BL, n=92, 94, 95, 106, 93, 96	2	1	3	4
UOB, 2+, BL, n=92, 94, 95, 106, 93, 96	3	1	2	0
UOB, 3+, BL, n=92, 94, 95, 106, 93, 96	2	0	0	2
UOB, 4+, BL, n=92, 94, 95, 106, 93, 96	0	0	0	1
UOB, Mod, BL, n=92, 94, 95, 106, 93, 96	1	0	0	0
UOB, Neg, BL, n=92, 94, 95, 106, 93, 96	79	91	83	97
UOB, Small, BL, n=92, 94, 95, 106, 93, 96	0	0	3	0
UOB, Trace, BL, n=92, 94, 95, 106, 93, 96	5	1	4	2
UOB, 1+, W8, n=71, 81, 82, 93, 82, 77	1	1	1	0
UOB, 2+, W8, n=71, 81, 82, 93, 82, 77	4	2	2	2
UOB, 3+, W8, n=71, 81, 82, 93, 82, 77	0	3	0	0
UOB, Large, W8, n=71, 81, 82, 93, 82, 77	0	0	0	0
UOB, Mod, W8, n=71, 81, 82, 93, 82, 77	0	0	0	0
UOB, Neg, W8, n=71, 81, 82, 93, 82, 77	62	71	73	83
UOB, Trace, W8, n=71, 81, 82, 93, 82, 77	4	4	6	8
UOB, Neg, EW, n=2, 1, 2, 3, 1, 7	2	1	2	3
UG, 1+ or 1/4 G/DL, BL, n=92, 94, 95, 106, 93, 96	0	0	0	0
UG, 3+ or 1 G/DL, BL, n=92, 94, 95, 106, 93, 96	0	2	1	0
UG, 4+ or 2 more G/DL, n=92, 94, 95, 106, 93, 96	0	1	0	0
UG, Neg, BL, n=92, 94, 95, 106, 93, 96	90	91	94	105
UG, Trace, BL, n=92, 94, 95, 106, 93, 96	1	0	0	1
UG, Trace or 1/10 G/DL, BL, n=92, 94, 95,106,93,96	1	0	0	0
UG 1+ or 1/4 G/DL, W8, n=71, 81, 82, 93, 82, 77	0	1	1	0
UG, 3+ or 1 G/DL, W8, n=71, 81, 82, 93, 82, 77	0	3	1	0
UG, Neg, W8, n=71, 81, 82, 93, 82, 77	71	77	80	92
UG, Trace, W8, n=71, 81, 82, 93, 82, 77	0	0	0	0
UG, Trace or 1/10 G/DL, W8, n=71, 81, 82,93,82,77	0	0	0	1
UG, Neg, EW, n=2, 1, 2, 3, 1, 7	2	1	2	3
UK, 1+, BL, n=92, 94, 95, 106, 93, 96	0	0	1	1
UK, 2+, BL, n=92, 94, 95, 106, 93, 96	0	0	0	0
UK, Neg, BL, n=92, 94, 95, 106, 93, 96	91	89	92	104
UK, Trace, BL, n=92, 94, 95, 106, 93, 96	1	5	2	1
UK, 2+, W8, n=71, 81, 82, 93, 82, 77	0	0	0	1
UK, Neg, W8, n=71, 81, 82, 93, 82, 77	67	77	78	91

UK, Trace, W8, n=71, 81, 82, 93, 82, 77	4	4	4	1
UK, Neg, EW, n=2, 1, 2, 3, 1, 7	2	1	2	3
UP, 1+, BL, n=92, 94, 95, 106, 93, 96	7	7	6	8
UP, 2+, BL, n=92, 94, 95, 106, 93, 96	0	0	2	1
UP, 3+, BL, n=92, 94, 95, 106, 93, 96	1	1	0	0
UP, Neg, BL, n=92, 94, 95, 106, 93, 96	70	76	80	89
UP, Trace, BL, n=92, 94, 95, 106, 93, 96	14	10	7	8
UP, 1+, W8, n=71, 81, 82, 93, 82, 77	3	2	5	1
UP, 2+, W8, n=71, 81, 82, 93, 82, 77	2	1	0	1
UP, 3+, W8, n=71, 81, 82, 93, 82, 77	0	0	0	0
UP, Neg, W8,n=71, 81, 82, 93, 82, 77	60	70	68	78
UP, Trace, W8, n=71, 81, 82, 93, 82, 77	6	8	9	13
UP, Neg, EW, n=2, 1, 2, 3, 1, 7	2	1	2	3
UP, Trace, EW, n=2, 1, 2, 3, 1, 7	0	0	0	0
UWBC, 1+, BL, n=92, 94, 95, 106, 93, 96	1	1	6	1
UWBC, 2+, BL, n=92, 94, 95, 106, 93, 96	1	3	1	7
UWBC, 3+, BL, n=92, 94, 95, 106, 93, 96	0	3	2	2
UWBC, Mod, BL, n=92, 94, 95, 106, 93, 96	0	0	0	0
UWBC, Neg, BL, n=92, 94, 95, 106, 93, 96	88	84	82	92
UWBC, Trace, BL, n=92, 94, 95, 106, 93, 96	2	3	4	4
UWBC, 1+, W8, n=71, 81, 82, 93, 82, 77	1	3	2	3
UWBC, 2+, W8, n=71, 81, 82, 93, 82, 77	1	1	4	3
UWBC, 3+, W8, n=71, 81, 82, 93, 82, 77	0	0	2	1
UWBC, Neg, W8, n=71, 81, 82, 93, 82, 77	66	71	69	81
UWBC, Small, W8, n=71, 81, 82, 93, 82, 77	1	0	1	0
UWBC, Trace, W8, n=71, 81, 82, 93, 82, 77	2	6	4	5
UWBC, 2+, EW, n=2, 1, 2, 3, 1, 7	0	1	0	0
UWBC, Neg, EW, n=2, 1, 2, 3, 1, 7	2	0	2	3

Notes:

[103] - ITT Population

[104] - ITT Population

[105] - ITT Population

[106] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[107]	102[108]		
Units: Participants				
UOB, 1+, BL, n=92, 94, 95, 106, 93, 96	3	2		
UOB, 2+, BL, n=92, 94, 95, 106, 93, 96	1	1		
UOB, 3+, BL, n=92, 94, 95, 106, 93, 96	2	2		
UOB, 4+, BL, n=92, 94, 95, 106, 93, 96	0	0		

UOB, Mod, BL, n=92, 94, 95, 106, 93, 96	0	1		
UOB, Neg, BL, n=92, 94, 95, 106, 93, 96	81	82		
UOB, Small, BL, n=92, 94, 95, 106, 93, 96	1	0		
UOB, Trace, BL, n=92, 94, 95, 106, 93, 96	5	8		
UOB, 1+, W8, n=71, 81, 82, 93, 82, 77	4	3		
UOB, 2+, W8, n=71, 81, 82, 93, 82, 77	2	3		
UOB, 3+, W8, n=71, 81, 82, 93, 82, 77	0	1		
UOB, Large, W8, n=71, 81, 82, 93, 82, 77	1	0		
UOB, Mod, W8, n=71, 81, 82, 93, 82, 77	1	0		
UOB, Neg, W8, n=71, 81, 82, 93, 82, 77	69	66		
UOB, Trace, W8, n=71, 81, 82, 93, 82, 77	5	4		
UOB, Neg, EW, n=2, 1, 2, 3, 1, 7	1	7		
UG, 1+ or 1/4 G/DL, BL, n=92, 94, 95, 106, 93, 96	0	1		
UG, 3+ or 1 G/DL, BL, n=92, 94, 95, 106, 93, 96	0	1		
UG, 4+ or 2 more G/DL, n=92, 94, 95, 106, 93, 96	0	0		
UG, Neg, BL, n=92, 94, 95, 106, 93, 96	91	94		
UG, Trace, BL, n=92, 94, 95, 106, 93, 96	1	0		
UG, Trace or 1/10 G/DL, BL, n=92, 94, 95,106,93,96	1	0		
UG 1+ or 1/4 G/DL, W8, n=71, 81, 82, 93, 82, 77	0	0		
UG, 3+ or 1 G/DL, W8, n=71, 81, 82, 93, 82, 77	0	1		
UG, Neg, W8, n=71, 81, 82, 93, 82, 77	78	76		
UG, Trace, W8, n=71, 81, 82, 93, 82, 77	2	0		
UG, Trace or 1/10 G/DL, W8, n=71, 81, 82,93,82,77	2	0		
UG, Neg, EW, n=2, 1, 2, 3, 1, 7	1	7		
UK, 1+, BL, n=92, 94, 95, 106, 93, 96	1	0		
UK, 2+, BL, n=92, 94, 95, 106, 93, 96	1	0		
UK, Neg, BL, n=92, 94, 95, 106, 93, 96	90	95		
UK, Trace, BL, n=92, 94, 95, 106, 93, 96	1	1		
UK, 2+, W8, n=71, 81, 82, 93, 82, 77	0	0		
UK, Neg, W8, n=71, 81, 82, 93, 82, 77	79	69		
UK, Trace, W8, n=71, 81, 82, 93, 82, 77	3	8		
UK, Neg, EW, n=2, 1, 2, 3, 1, 7	1	7		
UP, 1+, BL, n=92, 94, 95, 106, 93, 96	5	4		
UP, 2+, BL, n=92, 94, 95, 106, 93, 96	1	0		
UP, 3+, BL, n=92, 94, 95, 106, 93, 96	0	0		
UP, Neg, BL, n=92, 94, 95, 106, 93, 96	80	78		
UP, Trace, BL, n=92, 94, 95, 106, 93, 96	7	14		
UP, 1+, W8, n=71, 81, 82, 93, 82, 77	4	2		

UP, 2+, W8, n=71, 81, 82, 93, 82, 77	1	0		
UP, 3+, W8, n=71, 81, 82, 93, 82, 77	1	0		
UP, Neg, W8,n=71, 81, 82, 93, 82, 77	64	71		
UP, Trace, W8, n=71, 81, 82, 93, 82, 77	12	4		
UP, Neg, EW, n=2, 1, 2, 3, 1, 7	1	5		
UP, Trace, EW, n=2, 1, 2, 3, 1, 7	0	2		
UWBC, 1+, BL, n=92, 94, 95, 106, 93, 96	6	3		
UWBC, 2+, BL, n=92, 94, 95, 106, 93, 96	2	3		
UWBC, 3+, BL, n=92, 94, 95, 106, 93, 96	1	2		
UWBC, Mod, BL, n=92, 94, 95, 106, 93, 96	1	0		
UWBC, Neg, BL, n=92, 94, 95, 106, 93, 96	81	85		
UWBC, Trace, BL, n=92, 94, 95, 106, 93, 96	2	3		
UWBC, 1+, W8, n=71, 81, 82, 93, 82, 77	7	4		
UWBC, 2+, W8, n=71, 81, 82, 93, 82, 77	2	3		
UWBC, 3+, W8, n=71, 81, 82, 93, 82, 77	0	1		
UWBC, Neg, W8, n=71, 81, 82, 93, 82, 77	67	67		
UWBC, Small, W8, n=71, 81, 82, 93, 82, 77	0	0		
UWBC, Trace, W8, n=71, 81, 82, 93, 82, 77	6	2		
UWBC, 2+, EW, n=2, 1, 2, 3, 1, 7	0	1		
UWBC, Neg, EW, n=2, 1, 2, 3, 1, 7	1	6		

Notes:

[107] - ITT Population

[108] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Urine specific gravity at Baseline and Week 8/Early Withdrawal

End point title	Urine specific gravity at Baseline and Week 8/Early Withdrawal

End point description:

Urine samples were collected for the measurement of urine specific gravity by dipstick method at Baseline and at Week 8/Early Withdrawal. The Baseline value was the measurement taken at screening (Visit 1). Specific gravity is a measure of the amount of material dissolved in the urine. Specific gravity is the ratio of the density (mass of a unit volume) of a substance to the density (mass of the same unit volume) of a reference substance. Normal urine has a specific gravity between 1.010 and 1.020. Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline and Week 8/Early Withdrawal

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[109]	97[110]	100[111]	110[112]
Units: ratio				
arithmetic mean (standard deviation)				
Baseline, n=92, 94, 95, 106, 93, 96	1.023 (± 0.00707)	1.024 (± 0.0069)	1.0236 (± 0.00682)	1.023 (± 0.00687)
Week 8, n=71, 81, 82, 93, 82, 77	1.0238 (± 0.00731)	1.0227 (± 0.00735)	1.023 (± 0.00714)	1.0223 (± 0.00738)
EW, n=2, 1, 2, 3, 1, 7	1.0265 (± 0.00071)	1.0121 (± 0)	1.02 (± 0.00141)	1.0233 (± 0.00987)

Notes:

[109] - ITT Population

[110] - ITT Population

[111] - ITT Population

[112] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[113]	102[114]		
Units: ratio				
arithmetic mean (standard deviation)				
Baseline, n=92, 94, 95, 106, 93, 96	1.0242 (± 0.0062)	1.0227 (± 0.0076)		
Week 8, n=71, 81, 82, 93, 82, 77	1.0235 (± 0.00727)	1.0217 (± 0.00751)		
EW, n=2, 1, 2, 3, 1, 7	1.019 (± 0)	1.024 (± 0.00653)		

Notes:

[113] - ITT Population

[114] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Urine pH at Baseline and Week 8/Early Withdrawal

End point title	Urine pH at Baseline and Week 8/Early Withdrawal

End point description:

Urine samples were collected for the measurement of urine pH by dipstick method at Baseline and at Week 8/Early Withdrawal. The Baseline value was the measurement taken at screening (Visit 1). Urine pH is an acid-base measurement. pH is measured on a numeric scale ranging from 0 to 14; values on the scale refer to the degree of alkalinity or acidity. A pH of 7 is neutral. A pH less than 7 is acidic, and a pH greater than 7 is basic. Normal urine has a slightly acid pH (5.0 - 6.0). Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline and Week 8/Early Withdrawal

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94[115]	97[116]	100[117]	110[118]
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline, n=92, 94, 95, 106, 93, 96	6.04 (± 0.487)	6.05 (± 0.418)	6.06 (± 0.455)	6.13 (± 0.488)
Week 8, n=71, 81, 82, 93, 82, 77	6.03 (± 0.422)	6.01 (± 0.418)	6.12 (± 0.462)	6.06 (± 0.435)
EW, n=2, 1, 2, 3, 1, 7	6 (± 0.707)	6 (± 0)	5.75 (± 0.354)	6.83 (± 0.289)

Notes:

[115] - ITT Population

[116] - ITT Population

[117] - ITT Population

[118] - ITT Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95[119]	102[120]		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline, n=92, 94, 95, 106, 93, 96	6.05 (± 0.489)	6.08 (± 0.415)		
Week 8, n=71, 81, 82, 93, 82, 77	6.06 (± 0.523)	5.96 (± 0.342)		
EW, n=2, 1, 2, 3, 1, 7	7.5 (± 0)	5.86 (± 0.556)		

Notes:

[119] - ITT Population

[120] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: 24-hour urinary cortisol excretion at Baseline and Week 8

End point title	24-hour urinary cortisol excretion at Baseline and Week 8

End point description:

A 24-hour urine sample was collected for the measurement of 24 hr urinary cortisol excretion at the following scheduled time points: within 7 days prior to Study Visits 3 (Week 0) and Visit 8 (Week 8). The Baseline value for 24 hr urinary cortisol was taken from Visit 3. Urine Cortisol (UC) Population: all participants whose urine samples did not have confounding factors that could affect the interpretation of results.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66[121]	72[122]	72[123]	76[124]
Units: Nanomoles per 24 hours (nmol/24 hours)				
median (full range (min-max))				

Baseline	70.2 (10.1 to 382.7)	74.45 (6.1 to 645.2)	65.8 (5.9 to 341.1)	65.56 (8.8 to 457.3)
Week 8	79.25 (7.5 to 275)	76.74 (5.2 to 306.6)	79.15 (13.9 to 680.9)	81 (10.6 to 506.6)

Notes:

[121] - UC Population

[122] - UC Population

[123] - UC Population

[124] - UC Population

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69[125]	70[126]		
Units: Nanomoles per 24 hours (nmol/24 hours)				
median (full range (min-max))				
Baseline	66.8 (4.6 to 396.2)	66.2 (6.4 to 338.6)		
Week 8	62.1 (8 to 366.7)	82.14 (4.7 to 231)		

Notes:

[125] - UC Population

[126] - UC Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) at Week 8

End point title	Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) at Week 8

End point description:

Change from Baseline was calculated as the Week 8 value minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline and Week 8

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78[127]	85[128]	91[129]	98[130]
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP	-2.5 (± 9.29)	1.5 (± 10.54)	0.9 (± 10.35)	-0.4 (± 10.46)
DBP	-1.1 (± 8.16)	0.3 (± 7.65)	0.2 (± 7.5)	-0.3 (± 8.41)

Notes:

[127] - ITT Population. Only those participants available at the specified time points were analyzed.

[128] - ITT Population. Only those participants available at the specified time points were analyzed.

[129] - ITT Population. Only those participants available at the specified time points were analyzed.

[130] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86[131]	84[132]		
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP	1.4 (± 9.53)	0.2 (± 10.64)		
DBP	0.1 (± 8.5)	-0.2 (± 8.55)		

Notes:

[131] - ITT Population. Only those participants available at the specified time points were analyzed.

[132] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in heart rate at Week 8

End point title	Change from Baseline in heart rate at Week 8
End point description:	
Change from Baseline was calculated as the Week 8 value minus the Baseline value.	
End point type	Secondary
End point timeframe:	
Baseline and Week 8	

End point values	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD	GW685698X 100 µg OD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78[133]	85[134]	91[135]	98[136]
Units: Beats per minute				
arithmetic mean (standard deviation)	2.9 (± 9.23)	0.4 (± 8.26)	1.5 (± 8.35)	0.8 (± 8.12)

Notes:

[133] - ITT Population. Only those participants available at the specified time points were analyzed.

[134] - ITT Population. Only those participants available at the specified time points were analyzed.

[135] - ITT Population. Only those participants available at the specified time points were analyzed.

[136] - ITT Population. Only those participants available at the specified time points were analyzed.

End point values	GW685698X 200 µg OD	FP 100 µg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86[137]	84[138]		
Units: Beats per minute				
arithmetic mean (standard deviation)	-2.3 (± 8.32)	0.8 (± 9.14)		

Notes:

[137] - ITT Population. Only those participants available at the specified time points were analyzed.

[138] - ITT Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious AEs were collected from the start of study medication to the end of the the treatment period (up to Week 8).

Adverse event reporting additional description:

SAEs and non-serious AEs were reported for members of the Intent-to-Treat (ITT) Population, comprised of all participants randomized to treatment who received at least one dose of trial medication during the treatment period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo once daily (OD) in the evening from the dry powder inhaler (DPI) and placebo twice daily (BID) from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol inhalation aerosol to be used as needed throughout the study.

Reporting group title	GW685698X 25 µg OD

Reporting group description:

Participants received GW685698X 25 micrograms (µg) OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Reporting group title	GW685698X 50 µg OD

Reporting group description:

Participants received GW685698X 50 µg OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Reporting group title	GW685698X 100 µg OD

Reporting group description:

Participants received GW685698X 100 µg OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Reporting group title	GW685698X 200 µg OD

Reporting group description:

Participants received GW685698X 200 µg OD in the evening from the DPI and placebo BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Reporting group title	FP 100 µg BID

Reporting group description:

Participants received fluticasone propionate (FP) 100 µg BID from the DISKUS/ACCUHALER (one inhalation in the morning and one inhalation in the evening) plus placebo OD in the evening from the DPI for 8 weeks. In addition, participants were provided supplemental albuterol/salbutamol aerosol to be used as needed throughout the study.

Serious adverse events	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 94 (0.00%)	1 / 97 (1.03%)	0 / 100 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Snake bite			
subjects affected / exposed	0 / 94 (0.00%)	1 / 97 (1.03%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 94 (0.00%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 94 (0.00%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 94 (0.00%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	GW685698X 100 µg OD	GW685698X 200 µg OD	FP 100 µg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 110 (0.91%)	0 / 95 (0.00%)	2 / 102 (1.96%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Snake bite			
subjects affected / exposed	0 / 110 (0.00%)	0 / 95 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 110 (0.00%)	0 / 95 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 110 (0.00%)	0 / 95 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 110 (0.00%)	0 / 95 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 110 (0.00%)	0 / 95 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 110 (0.91%)	0 / 95 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Placebo	GW685698X 25 µg OD	GW685698X 50 µg OD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 94 (11.70%)	6 / 97 (6.19%)	8 / 100 (8.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 94 (10.64%)	6 / 97 (6.19%)	6 / 100 (6.00%)
occurrences (all)	15	7	14
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 94 (1.06%)	0 / 97 (0.00%)	1 / 100 (1.00%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 94 (0.00%)	0 / 97 (0.00%)	3 / 100 (3.00%)
occurrences (all)	0	0	4
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 94 (1.06%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	GW685698X 100 µg OD	GW685698X 200 µg OD	FP 100 µg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 110 (15.45%)	9 / 95 (9.47%)	16 / 102 (15.69%)
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 110 (10.91%)	5 / 95 (5.26%)	12 / 102 (11.76%)
occurrences (all)	22	6	18
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			

subjects affected / exposed	4 / 110 (3.64%)	3 / 95 (3.16%)	2 / 102 (1.96%)
occurrences (all)	4	3	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 110 (0.00%)	1 / 95 (1.05%)	1 / 102 (0.98%)
occurrences (all)	0	1	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 110 (3.64%)	3 / 95 (3.16%)	2 / 102 (1.96%)
occurrences (all)	4	4	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2007	• To clarify examination of oropharynx and vital signs assessments at Clinic Visit 1 and Clinic Visits 3 through 8 (Summary); • Amended Study Entry Criteria to exclude female subjects who are lactating • Clarified exclusion criteria for randomization to treatment (Protocol Section 4.3.2 number 6) • Clarified the fasting laboratory assessment (footnote number 7) is only for clinical chemistry • Clarified PK sampling at Visits 5 and 8 only and not at the Early Withdrawal Visit • Clarified that Lung Function testing is to be performed at Clinic Visit 1 and Clinic Visits 3 through 8 (Protocol Section 6.2.1) • Amended AE collection to start as Visit 3
24 October 2007	• Amended once-daily GW685698X (FF) administration from morning to evening • Amended timing of clinic lung function assessments from morning to evening • Amended fasting requirements for chemistry laboratory assessments • Amended the time of dosing documentation required for pharmacokinetic blood samples • Clarify details of Urinary Cortisol Population • Amended PEF trough analysis from morning to evening
21 March 2008	• To amend to allow for a Visit 1 screening period to be performed any time of day and to allow for re-screening if subjects fail lung function assessments at Visit 1. • Clarification of Lung Function reversibility procedure. • Amend respiratory infection exclusion criterion. • To allow use of long-acting anti-histamines. • Amend IP compliance at Visit 6. • To clarify timing of clinical laboratory assessments

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported