Clinical trial results:
A 52 week Randomised, Double-blind, Placebo-controlled Study to Investigate the Efficacy and Safety of GSK1605786A in the Maintenance of Remission in Subjects with Crohn's Disease

Summary

EudraCT number	2010-022383-12
Trial protocol	NL DE NO BE SE GB DK CZ HU GR AT ES PL PT EE IT SK BG
Global end of trial date	23 October 2013

Results information

Result version number	v1
This version publication date	26 February 2016
First version publication date	18 March 2015

Trial information

Trial identification

Sponsor protocol code	CCX114157

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01316939
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

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	05 February 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 October 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

• To assess the efficacy of GSK1605786A compared with placebo in maintaining clinical remission in subjects with Crohn’s disease over 52 weeks.

Protection of trial subjects:

Subjects were allowed to continue use of certain background medications to manage their Crohn’s disease.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 May 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 13
Country: Number of subjects enrolled	Austria: 6
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Canada: 15
Country: Number of subjects enrolled	Czech Republic: 16
Country: Number of subjects enrolled	Denmark: 9
Country: Number of subjects enrolled	Estonia: 4
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Hong Kong: 4
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Israel: 5
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Japan: 7
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	New Zealand: 5
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Russian Federation: 8
Country: Number of subjects enrolled	Slovakia: 13

Country: Number of subjects enrolled	South Africa: 1
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	Ukraine: 7
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	United States: 41
Worldwide total number of subjects	229
EEA total number of subjects	113

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)	222
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were eligible to enter the study if they had achieved clinical response (Crohn's Disease Activity Index [CDAI] decrease >=100 points) and/or clinical remission (CDAI <150) for their moderately-to-severely active disease at the end of 12 weeks of treatment in the induction studies CCX114151 or CCX114643.

Pre-assignment

Screening details:

Participants were randomized at Baseline (Week 0) to receive placebo or one of two possible dosage regimens of GSK1605786A: 500 milligrams (mg) once daily (QD) or 500 mg twice daily (BID) for 52-weeks.

Period 1

Period 1 title	Overall Study (52 Week Treatment Period) (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 matching placebo via 2 oral capsules for 52 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received 2 capsules of matching placebo via oral capsules for 52 weeks

Arm title	GSK1605786A 500 mg QD

Arm description:

Participants received GSK1605786A a total of 500 milligrams (mg), administered as 2 250 mg oral capsules once daily (QD) for 52 weeks

Arm type	Active comparator
Investigational medicinal product name	GSK1605786A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

500 mg once daily oral administration

Arm title	GSK1605786A 500 mg BID

Arm description:

Participants received GSK1605786A a total of 500 mg, administered as 2 250 mg oral capsules, twice daily (BID) for 52 weeks

Arm type	Active comparator

Investigational medicinal product name	GSK1605786A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

500 mg twice daily, oral administration

Number of subjects in period 1	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID
Started	76	77	76
Completed	13	9	7
Not completed	63	68	69
Physician decision	2	2	1
Protocol Defined Stopping Criteria	1	-	1
Adverse event, non-fatal	9	12	11
Lost to follow-up	-	-	2
Study Closed/Terminated	26	25	23
Lack of efficacy	24	25	25
Withdrawal by subject	1	3	6
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo via 2 oral capsules for 52 weeks	
Reporting group title	GSK1605786A 500 mg QD
Reporting group description:	
Participants received GSK1605786A a total of 500 milligrams (mg), administered as 2 250 mg oral capsules once daily (QD) for 52 weeks	
Reporting group title	GSK1605786A 500 mg BID
Reporting group description:	
Participants received GSK1605786A a total of 500 mg, administered as 2 250 mg oral capsules, twice daily (BID) for 52 weeks	

Reporting group values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID
Number of subjects	76	77	76
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	38.2	36.7	38.8
standard deviation	± 13.2	± 13	± 12.75
Gender categorical Units: Subjects			
Female	46	35	42
Male	30	42	34
Race, Customized Units: Subjects			
White-Caucasian/European	69	64	68
White-Arabic/North African	1	3	1
Black	2	1	0
Asian-East	1	4	5
Asian-Japanese	3	3	1
Am. Indian/native Alaskan	0	0	1
Missing	0	2	0

Reporting group values	Total		
Number of subjects	229		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	123		
Male	106		
Race, Customized Units: Subjects			
White-Caucasian/European	201		
White-Arabic/North African	5		
Black	3		
Asian-East	10		
Asian-Japanese	7		
Am. Indian/native Alaskan	1		
Missing	2		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo via 2 oral capsules for 52 weeks	
Reporting group title	GSK1605786A 500 mg QD
Reporting group description:	
Participants received GSK1605786A a total of 500 milligrams (mg), administered as 2 250 mg oral capsules once daily (QD) for 52 weeks	
Reporting group title	GSK1605786A 500 mg BID
Reporting group description:	
Participants received GSK1605786A a total of 500 mg, administered as 2 250 mg oral capsules, twice daily (BID) for 52 weeks	
Subject analysis set title	Intent to Treat population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The Intent-to-Treat (ITT) population consisted of all participants randomised to treatment who had achieved a clinical response (CDAI decrease from baseline of >=100 points) or achieved clinical remission (CDAI <150 points) in Study CCX114151 or Study CCX114643.	
Subject analysis set title	Saftey population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Population comprised of all participants who were randomised and took at least one dose of treatment during the study; i.e., those participants with no treatment start date are excluded from this population.	

Primary: Percentage of participants that achieved clinical remission at both Weeks 28 and 52 of the 52-Week Treatment Period

End point title	Percentage of participants that achieved clinical remission at both Weeks 28 and 52 of the 52-Week Treatment Period
End point description:	
Clinical remission is defined as a Crohn’s Disease Activity Index (CDAI) score of <150 points. The CDAI is a scoring system to measure disease severity with scores of >=220 to <=450 describing the moderately-to-severely active population, a score of >450 is considered severe. The score is algorithmically derived from the sum of participants'-reported Crohn’s disease symptoms recorded over 7 days and investigator recorded assessments of the participants’ condition, laboratory parameters and use of anti-diarrhoeal medication. Missing efficacy data (premature discontinuation or otherwise) were imputed using a “no effect” imputation where missing equals no response or no change in response. The Intent-to-Treat (ITT) population consisted of all participants randomised to treatment who had achieved a clinical response (CDAI decrease from baseline of >=100 points) or achieved clinical remission (CDAI <150 points) in Study CCX114151 or Study CCX114643.	
End point type	Primary
End point timeframe:	
Weeks 28 and 52	

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76[1]	77[2]	76[3]	
Units: Percentage of participants				
number (not applicable)	10.5	6.5	3.9	

Notes:

[1] - ITT population

[2] - ITT population

[3] - ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.9
upper limit	4.8

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.8
upper limit	1.6

Secondary: Percentage of participants in clinical remission and not taking corticosteroids at both Weeks 28 and 52 of the 52-Week Treatment Period

End point title	Percentage of participants in clinical remission and not taking corticosteroids at both Weeks 28 and 52 of the 52-Week Treatment Period

End point description:

Clinical remission is defined as a CDAI score of <150 points. The CDAI is a scoring system to measure disease severity with scores of >=220 to <=450 describing the moderately-to-severely active population. The score is algorithmically derived from the sum of participants'-reported Crohn’s disease symptoms recorded over 7 days and investigator recorded assessments of the participants’ condition, laboratory parameters and use of anti-diarrhoeal medication. Missing efficacy data (premature discontinuation or otherwise) were imputed using a “no effect” imputation where missing equals no response or no change in response. Percentage of participants in clinical remission and not taking corticosteroids at both Weeks 28 and 52 of the 52-week Treatment Period were presented. A participant was considered to be not taking corticosteroids at Weeks 28 and 52 if the participant has not taken a

corticosteroid for the 8 days prior to and the day of the CDAI assessment for each of Weeks 28 and 52.

End point type	Secondary

End point timeframe:
Weeks 28 and 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76[4]	77[5]	76[6]	
Units: Percentage of participants				
number (not applicable)	9.2	5.2	3.9	

Notes:
[4] - ITT population
[5] - ITT population
[6] - ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.2
upper limit	4.2

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.1
upper limit	2.6

Secondary: Percentage of participants in clinical remission at both Weeks 28 and 52 of the 52-Week Treatment Period among those participants who were in clinical remission at Baseline

End point title	Percentage of participants in clinical remission at both Weeks 28 and 52 of the 52-Week Treatment Period among those participants who were in clinical remission at Baseline

End point description:

Clinical remission is defined as a CDAI score of <150 points. The CDAI is a scoring system to measure disease severity with scores of >=220 to <=450 describing the moderately-to-severely active population. The score is algorithmically derived from the sum of participants'-reported Crohn's disease symptoms recorded over 7 days and investigator recorded assessments of the participants' condition, laboratory parameters and use of anti-diarrhoeal medication. Missing efficacy data (premature discontinuation or otherwise) were imputed using a "no effect" imputation where missing equals no response or no change in response. The percentage of participants who were in clinical remission at Baseline and at both Weeks 28 and 52 of the 52-week treatment period were presented. Baseline (Week 0) is defined as the results taken at the End of Study Visit of the Induction Study. Because the Induction Study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Baseline, Weeks 28 and 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[7]	0[8]	0[9]	
Units: Percentage of participants				
number (not applicable)				

Notes:

[7] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.
[8] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.
[9] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants in clinical remission at all visits (continuous clinical remission) during the 52-Week Treatment Period among participants in clinical remission at Baseline (BL)

End point title	Percentage of participants in clinical remission at all visits (continuous clinical remission) during the 52-Week Treatment Period among participants in clinical remission at Baseline (BL)

End point description:

Clinical remission is defined as a CDAI score of <150 points. The CDAI is a scoring system to measure disease severity with scores of >=220 to <=450 describing the moderately-to-severely active population. The score is algorithmically derived from the sum of participants'-reported Crohn's disease symptoms recorded over 7 days and investigator recorded assessments of the participants' condition, laboratory parameters and use of anti-diarrhoeal medication. Missing efficacy data (premature discontinuation or otherwise) were imputed using a "no effect" imputation where missing equals no response or no change in response. The percentage of participants who were in clinical remission at BL and at all visits during 52-eek Treatment Period were presented. BL (Week 0) is the results taken at the End of Study Visit of Induction Study. CDAI score was measured at Weeks 0, 4, 8, 12, 28, 36, 44 and 52. Because the Induction study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

BL (Week 0) and Weeks 4, 8, 12, 28, 36, 44 and 52.

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[10]	0[11]	0[12]	
Units: Percentage of participants				
number (not applicable)				

Notes:

[10] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.
[11] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.
[12] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants in clinical remission at Week 52

End point title	Percentage of participants in clinical remission at Week 52

End point description:

Clinical remission is defined as a CDAI score of <150 points. The CDAI is a scoring system to measure disease severity with scores of >=220 to <=450 describing the moderately-to-severely active population. The score is algorithmically derived from the sum of participants'-reported Crohn's disease symptoms recorded over 7 days and investigator recorded assessments of the participants' condition, laboratory parameters and use of anti-diarrhoeal medication. Missing efficacy data (premature discontinuation or otherwise) were imputed using a "no effect" imputation where missing equals no response or no change in response.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76[13]	77[14]	76[15]	
Units: Percentage of participants				
number (not applicable)	11.8	7.8	6.6	

Notes:

[13] - ITT Population

[14] - ITT Population

[15] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GSK1605786A 500 mg QD v Placebo

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.5
upper limit	5.4

Statistical analysis title	Statistical analysis 2
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.4
upper limit	3.9

Secondary: Percentage of participants with a clinical response at both Weeks 28 and 52 of the 52-Week Treatment Period

End point title	Percentage of participants with a clinical response at both Weeks 28 and 52 of the 52-Week Treatment Period

End point description:

Clinical response is defined as a CDAI score decrease from a Baseline value of >=100 points. The CDAI is a scoring system to measure disease severity with scores of >=220 to <=450 describing the moderately-to-severely active population. The score is algorithmically derived from the sum of participants'-reported Crohn’s disease symptoms recorded over 7 days and investigator recorded assessments of the participants’ condition, laboratory parameters and use of anti-diarrhoeal medication. Missing efficacy data (premature discontinuation or otherwise) were imputed using a “no effect” imputation where missing equals no response or no change in response. Because the study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Weeks 28 and 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[16]	0[17]	0[18]	
Units: Percentage of participants				
number (not applicable)				

Notes:

[16] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.
[17] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.
[18] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to induction of clinical response at both Weeks 28 and 52 of the 52-Week Treatment Period

End point title	Time to induction of clinical response at both Weeks 28 and 52 of the 52-Week Treatment Period

End point description:

Clinical response is defined as a CDAI score decrease from a Baseline value of >=100 points. The CDAI is a scoring system to measure disease severity with scores of >=220 to <=450 describing the moderately-to-severely active population. The score is algorithmically derived from the sum of participants'-reported Crohn’s disease symptoms recorded over 7 days and investigator recorded assessments of the participants’ condition, laboratory parameters and use of anti-diarrhoeal medication. Missing efficacy data (premature discontinuation or otherwise) were imputed using a “no effect” imputation where missing equals no response or no change in response. Because the study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Weeks 28 and 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[19]	0[20]	0[21]	
Units: Percentage of participants				
number (not applicable)				

Notes:

[19] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.
[20] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.
[21] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CDAI score at Weeks 4, 8, 12, 20, 28, 36, 44, and 52

End point title	Change from Baseline in CDAI score at Weeks 4, 8, 12, 20, 28, 36, 44, and 52

End point description:

The CDAI is a scoring system to measure disease severity with scores of >=220 to <=450 describing the moderately-to-severely active population. The score is algorithmically derived from the sum of participants-reported Crohn's disease symptoms recorded over 7 days and investigator recorded assessments of the participant's condition, laboratory parameters and use of anti-diarrhoeal medication. Because the study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 20, 28, 36, 44, and 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[22]	0[23]	0[24]	
Units: Score on scale				
number (not applicable)				

Notes:

[22] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.
[23] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.
[24] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) total score at Week 52

End point title	Change from Baseline in Inflammatory Bowel Disease Questionnaire (IBDQ) total score at Week 52

End point description:

The IBDQ is a 32-item IBD-specific health related quality of life instrument evaluating general activities of daily living, intestinal function, social performance, personal interactions, and emotional status. The IBDQ questionnaire was completed by each participant at Baseline and at Weeks 28, and 52 (or final visit if the participant withdrew prematurely). Item responses are summed for a total score and also averaged among four dimensions: 1) bowel function (10 items), 2) systemic symptoms (5 items), social function (5 items), and 4) emotional status (12 items). Change from Baseline was calculated as the Week 52 IBDQ score minus the score at Baseline. Baseline (Week 0) is defined as the results taken at the End of Study Visit of the Induction Study. Because the Induction Study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Baseline (Week 0) and Week 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[25]	0[26]	0[27]	
Units: Score on scale				
number (not applicable)				

Notes:

[25] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.
[26] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.
[27] - ITT Population, because the study was terminated prematurely, summary statistics were not compiled.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any adverse event (AE) and any serious adverse event (SAE)

End point title	Number of participants with any adverse event (AE) and any serious adverse event (SAE)

End point description:

An AE is defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. A SAE is defined as any untoward medical occurrence that, at any dose, results in death; was life threatening; required hospitalization or prolongation of existing hospitalization; resulted in disability/incapacity; was a congenital anomaly/birth defect. The Safety Population comprised of all participants who were randomised and took at least one dose of treatment during the study; i.e., those participants with no treatment start date are excluded from this population.

End point type	Secondary

End point timeframe:

From the start of study medication until and 4 weeks post treatment (up to Week 56)

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76[28]	77[29]	76[30]	
Units: Participants				
number (not applicable)				
Any AE	55	50	54	
Any SAE	1	3	2	

Notes:

[28] - Safety Population

[29] - Safety Population

[30] - Safety Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

tatistical analysis provided for Any AE

Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.384
Method	Fisher exact

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Statistical analysis provided for Any AE	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Statistical analysis provided for Any SAE	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.62
Method	Fisher exact

Statistical analysis title	Statistical analysis 4
Statistical analysis description: Statistical analysis provided for Any SAE	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

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

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

End point description:

Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) values were obtained as part of vital sign monitoring and measured after the participant was at rest in the supine position for at least 5 minutes. Change from Baseline measurements in SBP and DBP were assessed at Weeks 4, 8, 12, 20, 28, 36, 44, 52 and 4 weeks post-treatment. Baseline (Week 0) is defined as the results taken at the End of Study Visit of the Induction Study. Change from Baseline was calculated as the post-Baseline value minus the value at Baseline.

End point type	Secondary

End point timeframe:

Baseline and Weeks 4, 8, 12, 20, 28, 36, 44, 52 and 4 weeks post-treatment (assessed up to Week 56)

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76[31]	77[32]	76[33]	
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP, Week 4, n=74, 75, 74	-1.6 (± 13.08)	-0.9 (± 10.15)	1.2 (± 11.06)	
SBP, Week 8, n=61, 61, 61	-2.7 (± 13.75)	0.7 (± 12.17)	0.5 (± 12.91)	
SBP, Week 12, n=55, 48, 48	-0.9 (± 11.93)	0.9 (± 11.31)	1.1 (± 13.53)	
SBP, Week 20, n=44, 39, 37	-3 (± 12.7)	-0.7 (± 10.52)	2 (± 9.64)	
SBP, Week 28, n=33, 25, 24	2.2 (± 10.62)	1.2 (± 10.47)	4.6 (± 11.63)	
SBP, Week 36, n=24, 21, 13	0.7 (± 13.5)	2.1 (± 9.49)	1.8 (± 15.76)	
SBP, Week 44, n=19, 14, 10	-0.1 (± 12.59)	-1.6 (± 13.35)	0 (± 13.18)	
SBP, Week 52, n=15, 9, 7	-1.6 (± 13.8)	1 (± 9.29)	2.3 (± 13.25)	
SBP, 4 weeks post treatment, n=33, 29, 27	-0.5 (± 13.19)	-1.3 (± 11.21)	2 (± 11.09)	
DBP, Week 4, n=74, 75, 74	-2 (± 9.9)	-2 (± 9.54)	-0.1 (± 9.05)	
DBP, Week 8, n=61, 61, 61	-0.1 (± 10.39)	-0.6 (± 8.78)	-1.3 (± 8.03)	
DBP, Week 12, n=55, 48, 48	-0.4 (± 10.22)	-1.5 (± 6.68)	-0.8 (± 10.12)	
DBP, Week 20, n=44, 39, 37	-1.1 (± 9.33)	-2 (± 8.31)	0.1 (± 8.17)	
DBP, Week 28, n=33, 25, 24	2.4 (± 8)	-1.2 (± 10.05)	2 (± 6.13)	
DBP, Week 36, n=24, 21, 13	-0.2 (± 9.94)	-0.5 (± 10.01)	0.8 (± 9.04)	
DBP, Week 44, n=19, 14, 10	0.1 (± 12.09)	-3 (± 7.91)	-0.1 (± 10.29)	
DBP, Week 52, n=15, 9, 7	-0.7 (± 8.99)	-1.4 (± 8.4)	2.4 (± 8)	
DBP, 4 weeks post treatment, n=33, 29, 27	0.2 (± 9.05)	0.1 (± 7.12)	1.3 (± 9.53)	

Notes:

[31] - Safety Population. Only participants available at the specified time points were analyzed (n=X,X, X).

[32] - Safety Population. Only participants available at the specified time points were analyzed (n=X,X, X).

[33] - Safety Population. Only participants available at the specified time points were analyzed (n=X,X, X).

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in heart rate (HR)

End point title	Change from Baseline in heart rate (HR)

End point description:

Heart Rate (HR) values were obtained as part of vital sign monitoring and measured after the participant

was at rest in the supine position for at least 5 minutes. Change from Baseline in HR was assessed at Weeks 4, 8, 12, 20, 28, 36, 44, 52 and 4 weeks post-treatment. Baseline (Week 0) is defined as the results taken at the End of Study Visit of the Induction Study. Change from Baseline was calculated as the post-Baseline value minus the value at Baseline.

End point type	Secondary

End point timeframe:

Baseline and Weeks 4, 8, 12, 20, 28, 36, 44, 52 and 4 weeks post-treatment (assessed up to Week 56)

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76[34]	77[35]	76[36]	
Units: beats per minute				
arithmetic mean (standard deviation)				
HR, Week 4, n=73, 74, 74	1.8 (± 11.06)	-2.2 (± 11.96)	0 (± 10.17)	
HR, Week 8, n=61, 61, 61	0.9 (± 10.85)	-0.4 (± 12.23)	-0.2 (± 12.93)	
HR, Week 12, n=54, 48, 48	0.9 (± 10.27)	-2.4 (± 11.25)	-0.5 (± 11.24)	
HR, Week 20, n=44, 39, 37	-1 (± 9.59)	-0.8 (± 14.49)	-0.4 (± 13.83)	
HR, Week 28, n=33, 25, 24	1.3 (± 11.65)	0.5 (± 15.07)	-0.7 (± 11.56)	
HR, Week 36, n=24, 21, 13	-2.8 (± 9.92)	2.4 (± 9.45)	2.5 (± 8.11)	
HR, Week 44, n=19, 14, 10	2 (± 10.96)	2.6 (± 5.85)	1.4 (± 11.22)	
HR, Week 52, n=15, 9, 7	1.6 (± 8.87)	-0.1 (± 7.77)	4.1 (± 8.55)	
HR, 4 week post treatment, n=33, 29, 27	-1.1 (± 8.79)	1.5 (± 12.04)	-3.1 (± 8.43)	

Notes:

[34] - Safety Population. Only participants available at the specified time points were analyzed (n=X,X, X).
[35] - Safety Population. Only participants available at the specified time points were analyzed (n=X,X, X).
[36] - Safety Population. Only participants available at the specified time points were analyzed (n=X,X, X).

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with shifts from Baseline for the indicated hematology parameters

End point title	Number of participants with shifts from Baseline for the indicated hematology parameters

End point description:

Hematology parameters measured included platelets (PLS), neutrophils (NL), lymphocytes (LMP), monocytes (MONO), eosinophils (EOS), basophils(BASO), hematocrit (HCT), band cells (BC), red blood cell (RBC) count, hemoglobin (HGB), white blood cell (WBC) count, and segmented (seg) NL. The Baseline value is defined as the value obtained at Week 0. The number of participants with the indicated hematology parameters data reference range shifts from Baseline (defined as shift to low, shift to normal or no change, shift to high) until 4 weeks post treatment are presented.

End point type	Secondary

End point timeframe:

From Baseline until 4 weeks post-treatment (assessed up to Week 56)

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76[37]	77[38]	76[39]	
Units: Participants				
number (not applicable)				
PLS, shift to low, n=76, 76, 75	1	1	0	
PLS, shift to normal or no change, n=76, 76, 75	69	63	61	
PLS, shift to high, n=64, 61, 68	6	12	14	
NL, shift to low, n=76, 76, 74	3	2	1	
NL, shift to normal or no change, n=76, 76, 75	51	55	54	
NL, shift to high, n=49, 47, 51	22	20	20	
LMP, shift to low, n=51, 49, 50	19	19	14	
LMP, shift to normal or no change, n=76, 76, 75	54	55	60	
LMP, shift to high, n=75, 76, 74	3	2	2	
MONO, shift to low, n=76, 76, 75	0	0	0	
MONO, shift to normal or no change, n=76, 76, 75	69	72	68	
MONO, shift to high, n=73, 75, 73	7	4	7	
EOS, shift to low, n=0, 0, 0	0	0	0	
EOS, shift to normal or no change, n=76, 76, 75	73	69	73	
EOS, shift to high, n=74, 76, 75	3	7	2	
BASO, shift to low, n=0, 0, 0	0	0	0	
BASO, shift to normal or no change, n=76, 76, 75	76	76	74	
BASO, shift to high, n=76, 76, 75	0	0	1	
HCT, shift to low, n=49, 43, 51	13	10	11	
HCT, shift to normal or no change, n=76, 76, 75	63	65	62	
HCT, shift to high, n=75, 76, 73	1	1	2	
BC, shift to low, n=0, 0, 0	0	0	0	
BC, shift to normal or no change, n=1, 0, 0	1	0	0	
BC, shift to high, n=0, 0, 0	0	0	0	
RBC, shift to low, n=37, 40, 42	8	6	9	
RBC, shift to normal or no change, n=54, 56, 53	45	50	42	
RBC, shift to high, n=54, 55, 53	1	0	2	
HGB, shift to low, n=37, 35, 47	15	13	11	
HGB, shift to normal or no change, n=76, 76, 75	60	63	64	
HGB, shift to high, n=75, 76, 75	1	0	0	
WBC, shift to low, n=71, 75, 71	4	5	7	
WBC, shift to normal or no change, n=76, 76, 75	63	59	62	
WBC, shift to high, n=63, 62, 65	9	12	6	
Seg NL, shift to low, n=76, 76, 74	3	2	1	
Seg NL, shift to normal or no change, n=76, 76, 75	51	55	54	
Seg NL, shift to high, n=49, 47, 51	22	20	20	

Notes:
[37] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X , X)
[38] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X , X)
[39] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X , X)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Statistical analysis provided for PLS, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Statistical analysis provided for PLS, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Statistical analysis provided for PLS, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.23
Method	Fisher exact

Statistical analysis title	Statistical analysis 4
Statistical analysis description:	
Statistical analysis provided for PLS, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.105
Method	Fisher exact

Statistical analysis title	Statistical analysis 5
Statistical analysis description: Statistical analysis provided for PLS, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.129
Method	Fisher exact

Statistical analysis title	Statistical analysis 6
Statistical analysis description: Statistical analysis provided for PLS, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.091
Method	Fisher exact

Statistical analysis title	Statistical analysis 7
Statistical analysis description: Statistical analysis provided for NL, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 8
Statistical analysis description: Statistical analysis provided for NL, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.62
Method	Fisher exact

Statistical analysis title	Statistical analysis 9
Statistical analysis description:	
Statistical analysis provided for NL, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.597
Method	Fisher exact

Statistical analysis title	Statistical analysis 10
Statistical analysis description:	
Statistical analysis provided for NL, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.597
Method	Fisher exact

Statistical analysis title	Statistical analysis 11
Statistical analysis description:	
Statistical analysis provided for NL, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.84
Method	Fisher exact

Statistical analysis title	Statistical analysis 12
Statistical analysis description:	
Statistical analysis provided for NL, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.686
Method	Fisher exact

Statistical analysis title	Statistical analysis 13
Statistical analysis description:	
Statistical analysis provided for LMP, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 14
Statistical analysis description:	
Statistical analysis provided for LMP, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.397
Method	Fisher exact

Statistical analysis title	Statistical analysis 15
Statistical analysis description:	
Statistical analysis provided for LMP, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 16
Statistical analysis description:	
Statistical analysis provided for LMP, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.257
Method	Fisher exact

Statistical analysis title	Statistical analysis 17
Statistical analysis description:	
Statistical analysis provided for LMP, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.681
Method	Fisher exact

Statistical analysis title	Statistical analysis 18
Statistical analysis description:	
Statistical analysis provided for LMP, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 19
Statistical analysis description:	
Statistical analysis provided for MONO, shift to low. None of the participants had MONO, shift to low.	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [40]
Method	Fisher exact

Notes:

[40] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 20
Statistical analysis description:	
Statistical analysis provided for MONO, shift to low. None of the participants had MONO, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [41]
Method	Fisher exact

Notes:

[41] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 21
Statistical analysis description:	
Statistical analysis provided for MONO, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.533
Method	Fisher exact

Statistical analysis title	Statistical analysis 22
Statistical analysis description:	
Statistical analysis provided for MONO, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 23
Statistical analysis description:	
Statistical analysis provided for MONO, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.364
Method	Fisher exact

Statistical analysis title	Statistical analysis 24
Statistical analysis description:	
Statistical analysis provided for MONO, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 25
Statistical analysis description:	
Statistical analysis provided for EOS, shift to low. None of the participants had EOS, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [42]
Method	Fisher exact

Notes:

[42] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 26
Statistical analysis description:	
Statistical analysis provided for EOS, shift to low. None of the participants had EOS, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [43]
Method	Fisher exact

Notes:

[43] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 27
Statistical analysis description:	
Statistical analysis provided for EOS, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.327
Method	Fisher exact

Statistical analysis title	Statistical analysis 28
Statistical analysis description:	
Statistical analysis provided for EOS, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 29
Statistical analysis description:	
Statistical analysis provided for EOS, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.327
Method	Fisher exact

Statistical analysis title	Statistical analysis 30
Statistical analysis description:	
Statistical analysis provided for EOS, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.681
Method	Fisher exact

Statistical analysis title	Statistical analysis 31
Statistical analysis description:	
Statistical analysis provided for BASO, shift to low. None of the participants had BASO, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [44]
Method	Fisher exact

Notes:

[44] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 32
Statistical analysis description:	
Statistical analysis provided for BASO, shift to low. None of the participants had BASO, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [45]
Method	Fisher exact

Notes:

[45] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 33

Statistical analysis description:

Statistical analysis provided for BASO, shift to normal or no change. None of the participants had BASO, shift to normal or no change

Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [46]
Method	Fisher exact

Notes:

[46] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 34

Statistical analysis description:

Statistical analysis provided for BASO, shift to normal or no change

Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.497
Method	Fisher exact

Statistical analysis title	Statistical analysis 35

Statistical analysis description:

Statistical analysis provided for BASO, shift to high. None of the participants had BASO, shift to high

Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [47]
Method	Fisher exact

Notes:

[47] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 36

Statistical analysis description:

Statistical analysis provided for BASO, shift to high

Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.497
Method	Fisher exact

Statistical analysis title	Statistical analysis 37
Statistical analysis description:	
Statistical analysis provided for HCT, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.811
Method	Fisher exact

Statistical analysis title	Statistical analysis 38
Statistical analysis description:	
Statistical analysis provided for HCT, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.642
Method	Fisher exact

Statistical analysis title	Statistical analysis 39
Statistical analysis description:	
Statistical analysis provided for HCT, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.824
Method	Fisher exact

Statistical analysis title	Statistical analysis 40
Statistical analysis description:	
Statistical analysis provided for HCT, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 41
Statistical analysis description:	
Statistical analysis provided for HCT, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 42
Statistical analysis description:	
Statistical analysis provided for HCT, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.617
Method	Fisher exact

Statistical analysis title	Statistical analysis 43
Statistical analysis description:	
Statistical analysis provided for BC, shift to low. None of the participants had BC, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [48]
Method	Fisher exact

Notes:

[48] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 44
Statistical analysis description:	
Statistical analysis provided for BC, shift to low. None of the participants had BC, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [49]
Method	Fisher exact

Notes:

[49] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 45

Statistical analysis description:

Statistical analysis provided for BC, shift to normal or no change

Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [50]
Method	Fisher exact

Notes:

[50] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 46

Statistical analysis description:

Statistical analysis provided for BC, shift to normal or no change

Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [51]
Method	Fisher exact

Notes:

[51] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 47

Statistical analysis description:

Statistical analysis provided for BC, shift to high. None of the participants had BC, shift to high

Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [52]
Method	Fisher exact

Notes:

[52] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 48

Statistical analysis description:

Statistical analysis provided for BC, shift to high. None of the participants had BC, shift to high

Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [53]
Method	Fisher exact

Notes:

[53] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 49
Statistical analysis description:	
Statistical analysis provided for RBC, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.559
Method	Fisher exact

Statistical analysis title	Statistical analysis 50
Statistical analysis description:	
Statistical analysis provided for RBC, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 51
Statistical analysis description:	
Statistical analysis provided for RBC, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.414
Method	Fisher exact

Statistical analysis title	Statistical analysis 52
Statistical analysis description:	
Statistical analysis provided for RBC, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.628
Method	Fisher exact

Statistical analysis title	Statistical analysis 53
Statistical analysis description:	
Statistical analysis provided for RBC, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.495
Method	Fisher exact

Statistical analysis title	Statistical analysis 54
Statistical analysis description:	
Statistical analysis provided for RBC, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.618
Method	Fisher exact

Statistical analysis title	Statistical analysis 55
Statistical analysis description:	
Statistical analysis provided for HGB, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.812
Method	Fisher exact

Statistical analysis title	Statistical analysis 56
Statistical analysis description:	
Statistical analysis provided for HGB, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.103
Method	Fisher exact

Statistical analysis title	Statistical analysis 57
Statistical analysis description:	
Statistical analysis provided for HGB, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.68
Method	Fisher exact

Statistical analysis title	Statistical analysis 58
Statistical analysis description:	
Statistical analysis provided for HGB, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.396
Method	Fisher exact

Statistical analysis title	Statistical analysis 59
Statistical analysis description:	
Statistical analysis provided for HGB, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.497
Method	Fisher exact

Statistical analysis title	Statistical analysis 60
Statistical analysis description:	
Statistical analysis provided for HGB, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 61
Statistical analysis description:	
Statistical analysis provided for WBC, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 62
Statistical analysis description:	
Statistical analysis provided for WBC, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.532
Method	Fisher exact

Statistical analysis title	Statistical analysis 63
Statistical analysis description:	
Statistical analysis provided for WBC, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.541
Method	Fisher exact

Statistical analysis title	Statistical analysis 64
Statistical analysis description:	
Statistical analysis provided for WBC, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 65
Statistical analysis description:	
Statistical analysis provided for WBC, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.482
Method	Fisher exact

Statistical analysis title	Statistical analysis 66
Statistical analysis description:	
Statistical analysis provided for WBC, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.42
Method	Fisher exact

Statistical analysis title	Statistical analysis 67
Statistical analysis description:	
Statistical analysis provided for Seg NL, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 68
Statistical analysis description:	
Statistical analysis provided for Seg NL, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.62
Method	Fisher exact

Statistical analysis title	Statistical analysis 69
Statistical analysis description:	
Statistical analysis provided for Seg NL, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.597
Method	Fisher exact

Statistical analysis title	Statistical analysis 70
Statistical analysis description:	
Statistical analysis provided for Seg NL, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.597
Method	Fisher exact

Statistical analysis title	Statistical analysis 71
Statistical analysis description:	
Statistical analysis provided for Seg NL, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.84
Method	Fisher exact

Statistical analysis title	Statistical analysis 72
Statistical analysis description:	
Statistical analysis provided for Seg NL, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.686
Method	Fisher exact

Secondary: Number of participants with shifts from Baseline for the indicated clinical chemistry parameters

End point title	Number of participants with shifts from Baseline for the indicated clinical chemistry parameters

End point description:

Clinical chemistry parameters included total protein (TP), phosphorous (PPR), albumin (ALB), sodium (Na), potassium (K), chloride (Cl), calcium (Ca), glucose (GL), gamma-glutamyl transferase (GGT), total bilirubin (TB), direct bilirubin (DB), alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN)/urea (U), creatinine (CRE), uric acid (UA), bicarbonate (BIC), lactate dehydrogenase (LD), cholesterol (CHO), and creatine kinase (CK). The Baseline value is defined as the value obtained at Week 0. The number of participants with the indicated clinical chemistry parameters' data reference range shifts from Baseline (defined as shift to low, shift to normal or no change, or shift to high) until 4 weeks post-treatment are presented.

End point type	Secondary

End point timeframe:

From Baseline until 4 week post-treatment (assessed up to Week 56)

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76[54]	77[55]	76[56]	
Units: Participants				
number (not applicable)				
TP, shift to low, n=73, 71, 68	3	7	5	
TP, shift to normal or no change, n=76, 75, 75	73	67	70	
TP, shift to high, n=76, 75, 75	0	1	0	
PPR, shift to low, n=69, 74, 73	2	9	13	
PPR, shift to normal or no change, n=76, 75, 75	66	63	59	
PPR, shift to high, n=76, 72, 73	8	3	3	
ALB, shift to low, n=75, 71, 74	1	2	3	
ALB, shift to normal or no change, n=76, 75, 75	71	69	71	
ALB, shift to high, n=75, 75, 73	4	4	1	
Na, shift to low, n=74, 75, 73	0	1	3	
Na, shift to normal or no change, n=76, 75, 75	75	73	72	
Na, shift to high, n=76, 75, 74	1	1	0	
K, shift to low, n=76, 73, 75	4	1	4	
K, shift to normal or no change, n=76, 75, 75	68	74	67	
K, shift to high, n=76, 75, 73	4	0	4	
Cl, shift to low, n=76, 75, 75	0	0	1	

Cl, shift to normal or no change, n=76, 75, 75	67	67	63	
Cl, shift to high, n=74, 71, 70	9	8	11	
Ca, shift to low, n=72, 72, 71	3	5	7	
Ca, shift to normal or no change, n=76, 75, 75	71	68	65	
Ca, shift to high, n=75, 75, 75	2	2	3	
GL, shift to low, n=74, 73, 71	6	8	12	
GL, shift to normal or no change, n=76, 75, 75	58	52	56	
GL, shift to high, n=70, 69, 73	13	16	10	
GGT, shift to low, n=0, 0, 0	0	0	0	
GGT, shift to normal or no change, n=76, 77, 76	71	71	66	
GGT, shift to high, n=68, 68, 71	5	6	10	
TB, shift to low, n=0, 0, 0	0	0	0	
TB, shift to normal or no change, n=76, 77, 76	72	74	74	
TB, shift to high, n=75, 77, 74	4	3	2	
DB, shift to low, n=0, 0, 0	0	0	0	
DB, shift to normal or no change, n=76, 77, 76	75	76	75	
DB, shift to high, n=76, 77, 75	1	1	1	
ALP, shift to low, n=76, 76, 76	0	0	0	
ALP, shift to normal or no change, n=76, 77, 76	68	73	69	
ALP, shift to high, n=75, 76, 74	8	4	7	
ALT, shift to low, n=0, 0, 0	0	0	0	
ALT, shift to normal or no change, n=76, 77, 76	71	74	68	
ALT, shift to high, n=74, 77, 74	5	3	8	
AST, shift to low, n=0, 0, 0	0	0	0	
AST, shift to normal or no change, n=76, 77, 76	67	75	71	
AST, shift to high, n=74, 76, 76	9	2	5	
BUN/U, shift to low, n=71, 71, 68	4	6	5	
BUN/U, shift to normal or no change, n=76, 75, 75	71	69	69	
BUN/U, shift to high, n=76, 75, 75	1	0	2	
CRE, shift to low, n=65, 63, 59	6	8	12	
CRE, shift to normal or no change, n=76, 75, 75	69	67	63	
CRE, shift to high, n=76, 75, 74	1	0	0	
UA, shift to low, n=74, 72, 69	3	3	3	
UA, shift to normal or no change, n=76,75,75	73	71	68	
UA, shift to high, n=72, 75, 74	0	1	4	
BIC, shift to low, n=70, 70, 67	21	16	18	
BIC, shift to normal or no change, n=76,75,75	55	59	57	
BIC, shift to high, n=76, 74, 75	0	0	0	
LD, shift to low, n=0, 0, 0	0	0	0	
LD, shift to normal or no change, n=76,75,75	75	74	74	
LD, shift to high, n=75,73,75	1	1	1	
CHO, shift to low, n=0, 0, 0	0	0	0	

CHO, shift to normal or no change, n=76,75,75	69	71	64	
CHO, shift to high, n=57, 61, 68	7	4	11	
CK, shift to low, n=0, 0, 0	0	0	0	
CK, shift to normal or no change, n=76,75,75	69	71	67	
CK, shift to high, n=74, 73, 74	7	4	8	

Notes:

[54] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

[55] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

[56] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Statistical analysis provided for TP, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.205
Method	Fisher exact

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Statistical analysis provided for TP, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.482
Method	Fisher exact

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Statistical analysis provided for TP, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.13
Method	Fisher exact

Statistical analysis title	Statistical analysis 4
Statistical analysis description: Statistical analysis provided for TP, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.494
Method	Fisher exact

Statistical analysis title	Statistical analysis 5
Statistical analysis description: Statistical analysis provided for TP, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.497
Method	Fisher exact

Statistical analysis title	Statistical analysis 6
Statistical analysis description: Statistical analysis provided for TP, shift to high. None of the participants had TP, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [57]
Method	Fisher exact

Notes:

[57] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 7
Statistical analysis description: Statistical analysis provided for PPR, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.057
Method	Fisher exact

Statistical analysis title	Statistical analysis 8
Statistical analysis description:	
Statistical analysis provided for PPR, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	Fisher exact

Statistical analysis title	Statistical analysis 9
Statistical analysis description:	
Statistical analysis provided for PPR, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.652
Method	Fisher exact

Statistical analysis title	Statistical analysis 10
Statistical analysis description:	
Statistical analysis provided for PPR, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.202
Method	Fisher exact

Statistical analysis title	Statistical analysis 11
Statistical analysis description:	
Statistical analysis provided for PPR, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.211
Method	Fisher exact

Statistical analysis title	Statistical analysis 12
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.21
Method	Fisher exact

Statistical analysis title	Statistical analysis 13
Statistical analysis description: Statistical analysis provided for ALB, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.612
Method	Fisher exact

Statistical analysis title	Statistical analysis 14
Statistical analysis description: Statistical analysis provided for ALB, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.367
Method	Fisher exact

Statistical analysis title	Statistical analysis 15
Statistical analysis description: Statistical analysis provided for ALB, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.765
Method	Fisher exact

Statistical analysis title	Statistical analysis 16
Statistical analysis description:	
Statistical analysis provided for ALB, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 17
Statistical analysis description:	
Statistical analysis provided for ALB, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 18
Statistical analysis description:	
Statistical analysis provided for ALB, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.367
Method	Fisher exact

Statistical analysis title	Statistical analysis 19
Statistical analysis description:	
Statistical analysis provided for Na, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 20
Statistical analysis description:	
Statistical analysis provided for Na, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.366
Method	Fisher exact

Statistical analysis title	Statistical analysis 21
Statistical analysis description:	
Statistical analysis provided for Na, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.62
Method	Fisher exact

Statistical analysis title	Statistical analysis 22
Statistical analysis description:	
Statistical analysis provided for Na, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.367
Method	Fisher exact

Statistical analysis title	Statistical analysis 23
Statistical analysis description:	
Statistical analysis provided for Na, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.497
Method	Fisher exact

Statistical analysis title	Statistical analysis 24
Statistical analysis description:	
Statistical analysis provided for Na, shift to high. None of the participants had Na, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [58]
Method	Fisher exact

Notes:

[58] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 25
Statistical analysis description:	
Statistical analysis provided for K, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.367
Method	Fisher exact

Statistical analysis title	Statistical analysis 26
Statistical analysis description:	
Statistical analysis provided for K, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 27
Statistical analysis description:	
Statistical analysis provided for K, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.034
Method	Fisher exact

Statistical analysis title	Statistical analysis 28
Statistical analysis description: Statistical analysis provided for K, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 29
Statistical analysis description: Statistical analysis provided for K, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.12
Method	Fisher exact

Statistical analysis title	Statistical analysis 30
Statistical analysis description: Statistical analysis provided for K, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 31
Statistical analysis description: Statistical analysis provided for Cl, shift to low. None of the participants had Cl, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [59]
Method	Fisher exact

Notes:

[59] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 32
Statistical analysis description:	
Statistical analysis provided for Cl, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.497
Method	Fisher exact

Statistical analysis title	Statistical analysis 33
Statistical analysis description:	
Statistical analysis provided for Cl, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 34
Statistical analysis description:	
Statistical analysis provided for Cl, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.49
Method	Fisher exact

Statistical analysis title	Statistical analysis 35
Statistical analysis description:	
Statistical analysis provided for Cl, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 36
Statistical analysis description:	
Statistical analysis provided for Cl, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.632
Method	Fisher exact

Statistical analysis title	Statistical analysis 37
Statistical analysis description:	
Statistical analysis provided for Ca, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.719
Method	Fisher exact

Statistical analysis title	Statistical analysis 38
Statistical analysis description:	
Statistical analysis provided for Ca, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.208
Method	Fisher exact

Statistical analysis title	Statistical analysis 39
Statistical analysis description:	
Statistical analysis provided for Ca, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.564
Method	Fisher exact

Statistical analysis title	Statistical analysis 40
Statistical analysis description:	
Statistical analysis provided for Ca, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.185
Method	Fisher exact

Statistical analysis title	Statistical analysis 41
Statistical analysis description:	
Statistical analysis provided for Ca, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 42
Statistical analysis description:	
Statistical analysis provided for Ca, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 43
Statistical analysis description:	
Statistical analysis provided for GL, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.587
Method	Fisher exact

Statistical analysis title	Statistical analysis 44
Statistical analysis description:	
Statistical analysis provided for GL, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.134
Method	Fisher exact

Statistical analysis title	Statistical analysis 45
Statistical analysis description:	
Statistical analysis provided for GL, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.365
Method	Fisher exact

Statistical analysis title	Statistical analysis 46
Statistical analysis description:	
Statistical analysis provided for GL, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.852
Method	Fisher exact

Statistical analysis title	Statistical analysis 47
Statistical analysis description:	
Statistical analysis provided for GL, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.537
Method	Fisher exact

Statistical analysis title	Statistical analysis 48
Statistical analysis description:	
Statistical analysis provided for GL, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.498
Method	Fisher exact

Statistical analysis title	Statistical analysis 49
Statistical analysis description:	
Statistical analysis provided for GGT, shift to low. None of the participants had GGT, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [60]
Method	Fisher exact

Notes:

[60] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 50
Statistical analysis description:	
Statistical analysis provided for GGT, shift to low. None of the participants had GGT, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [61]
Method	Fisher exact

Notes:

[61] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 51
Statistical analysis description:	
Statistical analysis provided for GGT, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 52
Statistical analysis description: Statistical analysis provided for GGT, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.276
Method	Fisher exact

Statistical analysis title	Statistical analysis 53
Statistical analysis description: Statistical analysis provided for GGT, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 54
Statistical analysis description: Statistical analysis provided for GGT, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.276
Method	Fisher exact

Statistical analysis title	Statistical analysis 55
Statistical analysis description: Statistical analysis provided for TB, shift to low. None of the participants had TB, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [62]
Method	Fisher exact

Notes:

[62] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 56

Statistical analysis description:

Statistical analysis provided for TB, shift to low. None of the participants had TB, shift to low

Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [63]
Method	Fisher exact

Notes:

[63] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 57

Statistical analysis description:

Statistical analysis provided for TB, shift to normal or no change

Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.719
Method	Fisher exact

Statistical analysis title	Statistical analysis 58

Statistical analysis description:

Statistical analysis provided for TB, shift to normal or no change

Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.681
Method	Fisher exact

Statistical analysis title	Statistical analysis 59

Statistical analysis description:

Statistical analysis provided for TB, shift to high

Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.717
Method	Fisher exact

Statistical analysis title	Statistical analysis 60
Statistical analysis description:	
Statistical analysis provided for TB, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.681
Method	Fisher exact

Statistical analysis title	Statistical analysis 61
Statistical analysis description:	
Statistical analysis provided for DB, shift to low. None of the participants had DB, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [64]
Method	Fisher exact

Notes:

[64] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 62
Statistical analysis description:	
Statistical analysis provided for DB, shift to low. None of the participants had DB, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [65]
Method	Fisher exact

Notes:

[65] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 63
Statistical analysis description:	
Statistical analysis provided for DB, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 64
Statistical analysis description: Statistical analysis provided for DB, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 65
Statistical analysis description: Statistical analysis provided for DB, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 66
Statistical analysis description: Statistical analysis provided for DB, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 67
Statistical analysis description: Statistical analysis provided for ALP, shift to low. None of the participants had ALP, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [66]
Method	Fisher exact

Notes:

[66] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 68

Statistical analysis description:

Statistical analysis provided for ALP, shift to low. None of the participants had ALP, shift to low

Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [67]
Method	Fisher exact

Notes:

[67] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 69

Statistical analysis description:

Statistical analysis provided for ALP, shift to normal or no change

Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.246
Method	Fisher exact

Statistical analysis title	Statistical analysis 70

Statistical analysis description:

Statistical analysis provided for ALP, shift to normal or no change

Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 71

Statistical analysis description:

Statistical analysis provided for ALP, shift to high

Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.245
Method	Fisher exact

Statistical analysis title	Statistical analysis 72
Statistical analysis description:	
Statistical analysis provided for ALP, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 73
Statistical analysis description:	
Statistical analysis provided for ALT, shift to low. None of the participants had ALT, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [68]
Method	Fisher exact

Notes:

[68] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 74
Statistical analysis description:	
Statistical analysis provided for ALT, shift to low. None of the participants had ALT, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [69]
Method	Fisher exact

Notes:

[69] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 75
Statistical analysis description:	
Statistical analysis provided for ALT, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.495
Method	Fisher exact

Statistical analysis title	Statistical analysis 76
Statistical analysis description:	
Statistical analysis provided for ALT, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.564
Method	Fisher exact

Statistical analysis title	Statistical analysis 77
Statistical analysis description:	
Statistical analysis provided for ALT, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.489
Method	Fisher exact

Statistical analysis title	Statistical analysis 78
Statistical analysis description:	
Statistical analysis provided for ALT, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.563
Method	Fisher exact

Statistical analysis title	Statistical analysis 79
Statistical analysis description:	
Statistical analysis provided for AST, shift to low. None of the participants had AST, shift to low.	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [70]
Method	Fisher exact

Notes:

[70] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 80

Statistical analysis description:

Statistical analysis provided for AST, shift to low. None of the participants had AST, shift to low.

Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [71]
Method	Fisher exact

Notes:

[71] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 81

Statistical analysis description:

Statistical analysis provided for AST, shift to normal or no change

Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.031
Method	Fisher exact

Statistical analysis title	Statistical analysis 82

Statistical analysis description:

Statistical analysis provided for AST, shift to normal or no change

Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.401
Method	Fisher exact

Statistical analysis title	Statistical analysis 83

Statistical analysis description:

Statistical analysis provided for AST, shift to high

Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.03
Method	Fisher exact

Statistical analysis title	Statistical analysis 84
Statistical analysis description:	
Statistical analysis provided for AST, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.273
Method	Fisher exact

Statistical analysis title	Statistical analysis 85
Statistical analysis description:	
Statistical analysis provided for BUN/U, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.745
Method	Fisher exact

Statistical analysis title	Statistical analysis 86
Statistical analysis description:	
Statistical analysis provided for BUN/U, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.741
Method	Fisher exact

Statistical analysis title	Statistical analysis 87
Statistical analysis description:	
Statistical analysis provided for BUN/U, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.765
Method	Fisher exact

Statistical analysis title	Statistical analysis 88
Statistical analysis description:	
Statistical analysis provided for BUN/U, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.765
Method	Fisher exact

Statistical analysis title	Statistical analysis 89
Statistical analysis description:	
Statistical analysis provided for BUN/U, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 90
Statistical analysis description:	
Statistical analysis provided for BUN/U, shift to high	
Comparison groups	GSK1605786A 500 mg BID v Placebo
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.62
Method	Fisher exact

Statistical analysis title	Statistical analysis 91
Statistical analysis description:	
Statistical analysis provided for CRE, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.581
Method	Fisher exact

Statistical analysis title	Statistical analysis 92
Statistical analysis description:	
Statistical analysis provided for CRE, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.124
Method	Fisher exact

Statistical analysis title	Statistical analysis 93
Statistical analysis description:	
Statistical analysis provided for CRE, shift to normal or no change	
Comparison groups	GSK1605786A 500 mg QD v Placebo
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.792
Method	Fisher exact

Statistical analysis title	Statistical analysis 94
Statistical analysis description:	
Statistical analysis provided for CRE, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.23
Method	Fisher exact

Statistical analysis title	Statistical analysis 95
Statistical analysis description:	
Statistical analysis provided for CRE, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 96
Statistical analysis description:	
Statistical analysis provided for CRE, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 97
Statistical analysis description:	
Statistical analysis provided for UA, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 98
Statistical analysis description:	
Statistical analysis provided for UA, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 99
Statistical analysis description:	
Statistical analysis provided for UA, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.719
Method	Fisher exact

Statistical analysis title	Statistical analysis 100
Statistical analysis description:	
Statistical analysis provided for UA, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.209
Method	Fisher exact

Statistical analysis title	Statistical analysis 101
Statistical analysis description:	
Statistical analysis provided for UA, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 102
Statistical analysis description:	
Statistical analysis provided for UA, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.12
Method	Fisher exact

Statistical analysis title	Statistical analysis 103
Statistical analysis description:	
Statistical analysis provided for BIC, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.444
Method	Fisher exact

Statistical analysis title	Statistical analysis 104
Statistical analysis description: Statistical analysis provided for BIC, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.709
Method	Fisher exact

Statistical analysis title	Statistical analysis 105
Statistical analysis description: Statistical analysis provided for BIC, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.45
Method	Fisher exact

Statistical analysis title	Statistical analysis 106
Statistical analysis description: Statistical analysis provided for BIC, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.711
Method	Fisher exact

Statistical analysis title	Statistical analysis 107
Statistical analysis description: Statistical analysis provided for BIC, shift to high. None of the participants had BIC, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [72]
Method	Fisher exact

Notes:

[72] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 108

Statistical analysis description:

Statistical analysis provided for BIC, shift to high. None of the participants had BIC, shift to high

Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [73]
Method	Fisher exact

Notes:

[73] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 109

Statistical analysis description:

Statistical analysis provided for LD, shift to low. None of the participants had LD, shift to low

Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [74]
Method	Fisher exact

Notes:

[74] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 110

Statistical analysis description:

Statistical analysis provided for LD, shift to low. None of the participants had LD, shift to low

Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [75]
Method	Fisher exact

Notes:

[75] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 111

Statistical analysis description:

Statistical analysis provided for LD, shift to normal or no change

Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 112
Statistical analysis description:	
Statistical analysis provided for LD, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 113
Statistical analysis description:	
Statistical analysis provided for LD, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 114
Statistical analysis description:	
Statistical analysis provided for LD, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Statistical analysis title	Statistical analysis 115
Statistical analysis description:	
Statistical analysis provided for CHO, shift to low. None of the participants had CHO, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [76]
Method	Fisher exact

Notes:

[76] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 116

Statistical analysis description:

Statistical analysis provided for CHO, shift to low. None of the participants had CHO, shift to low

Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [77]
Method	Fisher exact

Notes:

[77] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 117

Statistical analysis description:

Statistical analysis provided for CHO, shift to normal or no change

Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.533
Method	Fisher exact

Statistical analysis title	Statistical analysis 118

Statistical analysis description:

Statistical analysis provided for CHO, shift to normal or no change

Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.327
Method	Fisher exact

Statistical analysis title	Statistical analysis 119

Statistical analysis description:

Statistical analysis provided for CHO, shift to high

Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.351
Method	Fisher exact

Statistical analysis title	Statistical analysis 120
Statistical analysis description:	
Statistical analysis provided for CHO, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.615
Method	Fisher exact

Statistical analysis title	Statistical analysis 121
Statistical analysis description:	
Statistical analysis provided for CK, shift to low. None of the participants had CK, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [78]
Method	Fisher exact

Notes:

[78] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 122
Statistical analysis description:	
Statistical analysis provided for CK, shift to low. None of the participants had CK, shift to low	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 9999 [79]
Method	Fisher exact

Notes:

[79] - A P-value of 9999 indicates a value of N/A or that it could not be calculated.

Statistical analysis title	Statistical analysis 123
Statistical analysis description:	
Statistical analysis provided for CK, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg QD

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.533
Method	Fisher exact

Statistical analysis title	Statistical analysis 124
Statistical analysis description:	
Statistical analysis provided for CK, shift to normal or no change	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.792
Method	Fisher exact

Statistical analysis title	Statistical analysis 125
Statistical analysis description:	
Statistical analysis provided for CK, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg QD
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.533
Method	Fisher exact

Statistical analysis title	Statistical analysis 126
Statistical analysis description:	
Statistical analysis provided for CK, shift to high	
Comparison groups	Placebo v GSK1605786A 500 mg BID
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	other
P-value	> 0.999
Method	Fisher exact

Secondary: Change from Baseline in ALT, AST, ALP, and GGT

End point title	Change from Baseline in ALT, AST, ALP, and GGT

End point description:

Changes in Baseline in ALP, ALT, AST and GGT were assessed to monitor liver function. Blood samples were taken at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52 and 4 Weeks post-treatment. Baseline (Week 0) is defined as the results taken at End of Study Visit of Induction Study.

Change from Baseline was calculated as the post-Baseline value at the timepoint indicated minus the value at Baseline.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52 and 4 Weeks post-treatment (assessed up to Week 56)

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76[80]	77[81]	76[82]	
Units: International Unit per Liter (IU/L)				
arithmetic mean (standard deviation)				
ALT, Week 2, n=74, 75, 74	-1 (± 14.7)	0.3 (± 5.88)	0.2 (± 6.27)	
ALT, Week 4, n=71, 67, 71	0.2 (± 8.93)	-0.6 (± 4.83)	-0.1 (± 6.94)	
ALT, Week 6, n=64, 61, 63	0.4 (± 11.92)	1.1 (± 6.66)	0.3 (± 7.35)	
ALT, Week 8, n=61, 56, 57	0 (± 9.46)	-0.2 (± 6.2)	1 (± 6.43)	
ALT, Week 10, n=56, 49, 51	-2.1 (± 8.15)	-0.5 (± 5.24)	0.9 (± 7.33)	
ALT, Week 12, n=51, 45, 48	-2.7 (± 8.6)	-0.6 (± 5.13)	0.6 (± 7.4)	
ALT, Week 16, n=48, 41, 42	-1.4 (± 9)	0.5 (± 7.69)	0.4 (± 4.98)	
ALT, Week 20, n=43, 36, 36	-2.7 (± 8.85)	-0.4 (± 7.07)	1.4 (± 4.59)	
ALT, Week 24, n=37, 32, 29	-1.3 (± 9.94)	-0.2 (± 6.25)	2.3 (± 6.19)	
ALT, Week 28, n=31, 26, 23	-1.6 (± 10.08)	-0.2 (± 5.91)	0.3 (± 5.12)	
ALT, Week 32, n=26, 23, 19	-2.3 (± 9.48)	-0.8 (± 6.81)	11.1 (± 35.32)	
ALT, Week 36, n=23, 19, 13	-2.3 (± 8.17)	-0.6 (± 7.46)	5.4 (± 10.74)	
ALT, Week 40, n=23, 15, 10	-3.4 (± 10.74)	0.1 (± 10.24)	6 (± 10.13)	
ALT, Week 44, n=18, 14, 9	-3.2 (± 13.37)	-1.5 (± 7.72)	0.3 (± 4.82)	
ALT, Week 48, n=14, 11, 8	-3.8 (± 13.98)	-2 (± 12.21)	-0.6 (± 6.52)	
ALT, Week 52, n=14, 9, 7	-5.1 (± 11.47)	-1.2 (± 11.41)	-1.3 (± 5.22)	
ALT, 4 week post treatment, n=33, 31, 28	-5.8 (± 28.79)	0.4 (± 8.11)	10.3 (± 41.19)	
AST, Week 2, n=74, 75, 74	0.4 (± 12.18)	0.3 (± 3.76)	0.6 (± 5.41)	
AST, Week 4, n=71, 67, 71	0.5 (± 7.19)	0.1 (± 4.24)	-0.2 (± 5.45)	
AST, Week 6, n=64, 61, 63	1.2 (± 9.18)	0.8 (± 3.99)	-0.1 (± 3.94)	
AST, Week 8, n=61, 56, 57	0.1 (± 6.39)	0 (± 4.07)	1 (± 4.58)	
AST, Week 10, n=56, 49, 50	-0.7 (± 5.17)	0.6 (± 3.94)	0.8 (± 4.18)	
AST, Week 12, n=51, 45, 48	0.4 (± 8.38)	0.5 (± 5.97)	1.1 (± 6.11)	
AST, Week 16, n=48, 41, 42	0 (± 7.57)	1.5 (± 5.29)	0.4 (± 4.24)	
AST, Week 20, n=43, 36, 36	-0.2 (± 7.18)	0.8 (± 4.74)	0.2 (± 5.02)	
AST, Week 24, n=37, 32, 29	0 (± 8.35)	0.2 (± 4.52)	1.7 (± 6.21)	
AST, Week 28, n=31, 26, 23	1.3 (± 10.01)	0.5 (± 4.52)	-0.9 (± 4.42)	
AST, Week 32, n=26, 23, 19	-0.2 (± 7.06)	-0.6 (± 6.67)	4.9 (± 17.5)	
AST, Week 36, n=22, 19, 13	0 (± 8.17)	0.3 (± 4.36)	3.3 (± 7)	
AST, Week 40, n=23, 15, 10	-0.7 (± 9.95)	-0.5 (± 3.66)	3.8 (± 8.43)	
AST, Week 44, n=18, 14, 9	-1.3 (± 7.14)	-0.8 (± 5.03)	-0.8 (± 4.09)	
AST, Week 48, n=14, 11, 8	-0.1 (± 11.65)	-3.4 (± 8.87)	-0.4 (± 6.32)	
AST, Week 52, n=14, 9, 7	-1.4 (± 10.05)	-0.9 (± 3.98)	-1 (± 2.83)	
AST, 4 week post treatment, n=33, 31, 28	-2.5 (± 17.99)	-0.3 (± 4.13)	5.4 (± 20.7)	
ALP, Week 2, n=74, 75, 74	-0.2 (± 7.42)	1.3 (± 9.54)	0.4 (± 9.96)	

ALP, Week 4, n=71, 67, 71	0.1 (± 9.3)	2 (± 10.63)	0.4 (± 11)	
ALP, Week 6, n=64, 61, 63	1 (± 11.21)	3.6 (± 11.28)	1 (± 11.16)	
ALP, Week 8, n=61, 56, 57	1.7 (± 12.04)	3.9 (± 12.61)	0.2 (± 11.21)	
ALP, Week 10, n=56, 49, 51	-1.4 (± 10.54)	5.6 (± 12.55)	2.8 (± 12.93)	
ALP, Week 12, n=51, 45, 48	1.2 (± 10.99)	5.6 (± 14.85)	2.4 (± 11.38)	
ALP, Week 16, n=48, 41, 42	1.5 (± 13.71)	7.2 (± 13.16)	3.4 (± 13.23)	
ALP, Week 20, n=43, 36, 36	3.7 (± 13.7)	9.3 (± 16.74)	2 (± 12.8)	
ALP, Week 24, n=37, 32, 29	1.9 (± 13.77)	9.2 (± 17.74)	3.4 (± 11)	
ALP, Week 28, n=31, 26, 23	1.9 (± 16.62)	12.2 (± 16.71)	-0.6 (± 12.53)	
ALP, Week 32, n=26, 23, 19	-1 (± 16.55)	10.5 (± 19.52)	4.3 (± 9.63)	
ALP, Week 36, n=23, 19, 13	2.3 (± 18.43)	9.4 (± 16.98)	6.3 (± 13.11)	
ALP, Week 40, n=23, 15, 10	1.5 (± 18.6)	6.5 (± 6.71)	-0.2 (± 9.14)	
ALP, Week 44, n=18, 14, 9	2.6 (± 17.32)	6 (± 9.88)	-3.6 (± 8.31)	
ALP, Week 48, n=14, 11, 8	10.6 (± 23.54)	1.1 (± 19.93)	-5.5 (± 11.25)	
ALP, Week 52, n=14, 9, 7	2.1 (± 13.76)	3.9 (± 10.28)	3.9 (± 9.58)	
ALP, 4 week post treatment, n=33, 31, 28	3.5 (± 12.84)	3.8 (± 14.98)	4.9 (± 8.29)	
GGT, Week 2, n=74, 75, 74	-3 (± 8.06)	1.8 (± 13.22)	0.4 (± 8.89)	
GGT, Week 4, n=71, 67, 71	-4.2 (± 9.86)	-0.4 (± 12.58)	2.1 (± 11.32)	
GGT, Week 6, n=64, 61, 63	-5 (± 15.47)	1.7 (± 13.1)	1.9 (± 10.5)	
GGT, Week 8, n=61, 56, 57	-1.2 (± 24.86)	1.1 (± 16.05)	2 (± 7.55)	
GGT, Week 10, n=56, 49, 51	-6.2 (± 11.03)	0.7 (± 14.38)	2.2 (± 6.71)	
GGT, Week 12, n=51, 45, 48	-8.2 (± 15)	0.5 (± 14.94)	2.3 (± 8.21)	
GGT, Week 16, n=48, 41, 42	-3.4 (± 19.57)	-0.9 (± 12.17)	3.7 (± 8.72)	
GGT, Week 20, n=43, 36, 36	-6.5 (± 17.94)	-1.9 (± 11.95)	2.9 (± 8.57)	
GGT, Week 24, n=37, 32, 29	-6.4 (± 15.11)	-3 (± 19.17)	2.6 (± 7.95)	
GGT, Week 28, n=31, 26, 23	-7.8 (± 25.33)	-4.3 (± 17.17)	1.3 (± 6.56)	
GGT, Week 32, n=26, 23, 19	-13.2 (± 31.99)	-9 (± 31.31)	6.5 (± 13.53)	
GGT, Week 36, n=23, 19, 13	-9 (± 27.65)	-6.7 (± 18.39)	11 (± 13.38)	
GGT, Week 40, n=23, 15, 10	-11.7 (± 21.56)	-6.1 (± 18.98)	8.9 (± 10.49)	
GGT, Week 44, n=18, 14, 9	-7.4 (± 15.82)	-8.6 (± 20.03)	4.4 (± 9.15)	
GGT, Week 48, n=14, 11, 8	-4.4 (± 9.8)	-13.5 (± 40.87)	4.1 (± 9.3)	
GGT, Week 52, n=14, 9, 7	-10.4 (± 19.75)	0 (± 11.64)	8.3 (± 10.4)	
GGT, 4 week post treatment, n=33, 31, 26	-4.2 (± 12.03)	-3.4 (± 13.5)	0.8 (± 21.68)	

Notes:

[80] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

[81] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

[82] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total bilirubin

End point title	Change from Baseline in total bilirubin

End point description:

Changes in Baseline in TB were assessed to monitor liver function. Blood samples were taken at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52 and 4 Weeks post-treatment. Baseline (Week

0) is defined as the results taken at End of Study Visit of Induction Study. Change from Baseline was calculated as the post-Baseline value at the timepoint indicated minus the value at Baseline.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52 and 4 Weeks post treatment (assessed up to Week 56)

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76[83]	77[84]	76[85]	
Units: micromole/Liter (umol/L)				
arithmetic mean (standard deviation)				
TB, Week 2, n=74, 75, 74	0.7 (± 3.21)	0 (± 2.09)	-0.7 (± 2.48)	
TB, Week 4, n=71, 67, 71	0.7 (± 3.46)	0 (± 2.33)	-0.1 (± 2.24)	
TB, Week 6, n=64, 61, 63	0.9 (± 2.29)	0.1 (± 2.6)	-0.4 (± 2.95)	
TB, Week 8, n=61, 56, 57	1 (± 3.38)	0.2 (± 2.49)	0 (± 2.31)	
TB, Week 10, n=56, 49, 51	0.9 (± 3.46)	0.5 (± 3.25)	-0.1 (± 3.27)	
TB, Week 12, n=51, 45, 48	0.8 (± 2.7)	0.2 (± 2.42)	0.6 (± 3.33)	
TB, Week 16, n=48, 41, 42	0.8 (± 3.75)	0.8 (± 2.99)	-0.2 (± 2)	
TB, Week 20, n=43, 36, 36	1.4 (± 3.07)	0.9 (± 3.25)	0.4 (± 2.89)	
TB, Week 24, n=37, 32, 29	1 (± 3.26)	0.8 (± 2.63)	0.8 (± 4.27)	
TB, Week 28, n=31, 26, 23	0.8 (± 3.37)	0.4 (± 2.08)	0.2 (± 4.3)	
TB, Week 32, n=26, 23, 19	0.5 (± 2.37)	0.2 (± 2.41)	0.8 (± 5.7)	
TB, Week 36, n=23, 19, 13	0.4 (± 2.62)	0.6 (± 3.09)	0.5 (± 2.44)	
TB, Week 40, n=23, 15, 10	0.7 (± 2.52)	-0.5 (± 2.67)	0.7 (± 3.16)	
TB, Week 44, n=18, 14, 9	1.4 (± 2.79)	0 (± 1.66)	1 (± 6.44)	
TB, Week 48, n=14, 11, 8	1 (± 4.49)	-1.4 (± 3.35)	-1.5 (± 6.97)	
TB, Week 52, n=14, 9, 7	0.7 (± 4.81)	0.6 (± 1.42)	-1.7 (± 9.53)	
TB, 4 week post treatment, n=33, 31, 28	0.2 (± 3.69)	1.4 (± 2.81)	1.8 (± 3.47)	

Notes:

[83] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

[84] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

[85] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in albumin (ALB)

End point title	Change from Baseline in albumin (ALB)

End point description:

Changes in Baseline in ALB were assessed to monitor liver function. Blood samples were taken at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52 and 4 Weeks post-treatment. Baseline (Week 0) is defined as the results taken at End of Study Visit of Induction Study. Change from Baseline was calculated as the post-Baseline value at the timepoint indicated minus the value at Baseline.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52 and 4 Weeks post

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76[86]	77[87]	76[88]	
Units: Gram/Liter (G/L)				
arithmetic mean (standard deviation)				
ALB, Week 2, n=4, 8, 7	-0.3 (± 1.26)	0 (± 2.51)	-0.1 (± 1.35)	
ALB, Week 4, n=70, 66, 69	0.7 (± 2.2)	0.1 (± 2.39)	-0.2 (± 2.3)	
ALB, Week 6, n=1, 3, 7	-1 (± 0)	-1 (± 2)	-0.6 (± 2.3)	
ALB, Week 8, n=61, 56, 57	0.2 (± 2.44)	0.3 (± 2.37)	-0.6 (± 2.63)	
ALB, Week 10, n=6, 4, 5	-2 (± 2.97)	-1.5 (± 2.08)	-1.4 (± 1.34)	
ALB, Week 12, n=50, 45, 48	0 (± 2.48)	0 (± 2.43)	0 (± 2.7)	
ALB, Week 16, n=3, 5, 4	-3 (± 2.65)	-1 (± 3)	-1.5 (± 2.52)	
ALB, Week 20, n=43, 35, 36	0.4 (± 2.02)	0.7 (± 2.78)	0 (± 2.42)	
ALB, Week 24, n=5, 4, 3	-0.2 (± 4.55)	-2.3 (± 4.35)	-4 (± 3.61)	
ALB, Week 28, n=30, 24, 23	0.1 (± 2.06)	0.1 (± 4.47)	0.5 (± 2.89)	
ALB, Week 32, n=0, 3, 0	0 (± 0)	-4 (± 4.36)	0 (± 0)	
ALB, Week 36, n=23, 19, 13	-0.2 (± 2.78)	0.7 (± 4.01)	0.4 (± 2.79)	
ALB, Week 40, n=2, 0, 0	0.5 (± 2.12)	0 (± 0)	0 (± 0)	
ALB, Week 44, n=18, 14, 8	-0.2 (± 2.55)	0 (± 2.69)	0.4 (± 2.33)	
ALB, Week 48, n=1, 1, 1	2 (± 0)	1 (± 0)	1 (± 0)	
ALB, Week 52, n=14, 9, 7	-0.1 (± 2.14)	-1.3 (± 1.94)	1.9 (± 2.27)	
ALB, 4 week post treatment, n=33, 31, 26	-1 (± 2.48)	-0.5 (± 3.52)	-0.2 (± 3.03)	

Notes:

[86] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

[87] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

[88] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal 12-lead electrocardiogram (ECG) findings at Baseline and Weeks 28 and 52

End point title	Number of participants with abnormal 12-lead electrocardiogram (ECG) findings at Baseline and Weeks 28 and 52

End point description:

A 12-lead ECG was recorded in a supine position after the participant was kept at rest in this position for at least 5 minutes. Data are presented as clinically significant (CS) or not clinically significant (NCS) abnormal findings. The study investigator determined if the abnormal ECG finding was CS or NCS. Baseline (Week 0) is defined as the results taken at End of Study Visit of Induction Study.

End point type	Secondary

End point timeframe:

Baseline and Weeks 28 and 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76[89]	77[90]	76[91]	
Units: Participants				
number (not applicable)				
BL (Week 0), Normal, n=76, 77, 76	62	69	54	
BL (Week 0), Abnormal NCS, n=76, 77, 76	13	8	54	
BL (Week 0), Abnormal CS, n=76, 77, 76	1	0	2	
Week 28, Normal, n=32, 23, 24	27	16	20	
Week 28, Abnormal NCS, n=32, 23, 24	5	7	4	
Week 28, Abnormal CS, n=32, 23, 24	0	0	0	
Week 52, Normal, n=14, 8, 7	12	8	6	
Week 52, Abnormal NCS, n=14, 8, 7	2	0	1	
Week 52, Abnormal CS, n=14, 8, 7	0	0	0	

Notes:

[89] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

[90] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

[91] - Safety Population. Only participants available at the specified time points were analyzed(n=X, X, X)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Short Form – 36 version 2 (SF-36v2) at Weeks 28 and 52

End point title	Change from Baseline in Short Form – 36 version 2 (SF-36v2) at Weeks 28 and 52

End point description:

The SF-36v2 is a 36-item general health related quality of life instrument focusing on 7 health concept scales and one general health indicator scale. This provides information about how participants feel, and how well they have been able to perform their usual activities, over the past 4 weeks. Scores on each item are summed and averaged (range = 0-100). The higher scores represents better health state and better functioning. Change from Baseline was calculated as the value at indicated time point minus the value at Baseline.Baseline (Week 0) is defined as the results taken at End of Study Visit of Induction Study. Because the study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Baseline and Weeks 28 and 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[92]	0[93]	0[94]	
Units: Score on scale				
number (not applicable)				

Notes:

[92] - ITT Population

[93] - ITT Population

[94] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in EQ-5D at Weeks 28 and 52

End point title	Change from Baseline in EQ-5D at Weeks 28 and 52

End point description:

The EQ-5D provides a simple, self-reported descriptive profile and a single index value for health status. The EQ-5D consists of two parts comprising the EQ-5D descriptive system and the EQ visual analogue scale(VAS). The EQ-5D descriptive system comprises 5 dimensions of health (mobility, self-care, usual activities, and pain/discomfort anxiety/depression). Each dimension has three levels(no problems, some/moderate problems,extreme problems). A unique EQ-5D health state index value is calculated by subtracting from 1 the instrument's predefined coefficients corresponding to the response level for each dimension. The EQ VAS records the respondents self-rated health status on a vertical graduated scale(0=worst imaginable-100=best imaginable). Change from BL was calculated as the value at indicated time point minus the value at BL. BL(Week 0) is defined as the results taken at the End of Induction Study visit. The study was terminated prematurely so summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Baseline and Weeks 28 and 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[95]	0[96]	0[97]	
Units: Score on scale				
number (not applicable)				

Notes:

[95] - ITT Population

[96] - ITT Population

[97] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Work Productivity and Activity Impairment-CD (WPAI-CD) at Weeks 28 and 52

End point title	Change from Baseline in Work Productivity and Activity Impairment-CD (WPAI-CD) at Weeks 28 and 52

End point description:

The WPAI-CD questionnaire assesses the impact of disease on work productivity and activity and

consists of 6 items: employment status, hours missed due to Crohn's disease, hours missed for other reasons, hours worked, lost productivity, and daily activity impairment due to Crohn's disease. The following scores are calculated and expressed as percentages (with higher scores indicating more productivity loss): absenteeism, presenteeism (impairment while at work), work productivity loss (absenteeism + presenteeism), and daily activity impairment. Change from Baseline was calculated as the value at indicated time point minus the value at Baseline. Baseline (Week 0) is defined as the results taken at End of Study Visit of Induction Study. Because the study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Baseline and Weeks 28 and 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[98]	0[99]	0[100]	
Units: Score on scale				
number (not applicable)				

Notes:

[98] - ITT Population

[99] - ITT Population

[100] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who received of disability benefits or health-related resources at Weeks 28 and 52

End point title	Number of participants who received of disability benefits or health-related resources at Weeks 28 and 52

End point description:

The summary of the number of participants who received disability benefits, or with all cause and Crohn's disease-related hospitalisations, surgeries, and out-patient visits was planned to compare between each GSK1605786A dose group and placebo using Fisher's exact test. Because the Induction Study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Weeks 28 and 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[101]	0[102]	0[103]	
Units: Participants				
number (not applicable)				

Notes:

[101] - ITT Population

[102] - ITT Population

[103] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of hospital visits

End point title	Duration of hospital visits

End point description:

The duration of hospital visits was planned to summarize by treatment group using a five-number summary and compare between each GSK1605786A dose group and placebo using Wilcoxon rank sum tests. Because the study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Baseline to Weeks 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[104]	0[105]	0[106]	
Units: Days				
number (not applicable)				

Notes:

[104] - ITT Population

[105] - ITT Population

[106] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in C-reactive protein concentration at Weeks 28 and 52

End point title	Change from Baseline in C-reactive protein concentration at Weeks 28 and 52

End point description:

Blood samples were collected for the measurement of c-reactive protein at Baseline and Weeks 28 and 52. Baseline (Week 0) is defined as the results taken at End of Study Visit of Induction Study. Change from Baseline was calculated as the value at indicated time point minus the value at Baseline. Because the study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Baseline and Weeks 28 and 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[107]	0[108]	0[109]	
Units: Milligrams per liter				
number (not applicable)				

Notes:

[107] - ITT Population

[108] - ITT Population

[109] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in faecal calprotectin at Week 28 and 52

End point title	Change from Baseline in faecal calprotectin at Week 28 and 52

End point description:

Blood samples were collected for the measurement of c-reactive protein at Baseline and Weeks 28 and 52. Baseline (Week 0) is defined as the results taken at End of Study Visit of Induction Study. Change from Baseline was calculated as the value at indicated time point minus the value at Baseline. Because the study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Baseline and Weeks 28 and 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[110]	0[111]	0[112]	
Units: microgram per gram				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[110] - ITT Population

[111] - ITT Population

[112] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) of GSK1605786A

End point title	Pharmacokinetics (PK) of GSK1605786A

End point description:

The PK analyses was planned to perform to characterize the PK of the study drug GSK1605786A in the participant population. PK is defined as the concentration of drug in a participant's blood at certain time points after the drug was taken by mouth. These PK analyses was not conducted following the early termination of the study. Because the study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Baseline and Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[113]	0[114]	0[115]	
Units: microgram per gram				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[113] - ITT Population

[114] - ITT Population

[115] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacogenetic analyses

End point title	Pharmacogenetic analyses

End point description:

Sample for the pharmacogenetic analyses was collected during prior induction study was planned to use. The pharmacogenetic analyses was planned to perform to investigate the relationship between the genetic markers with the safety and efficacy response to GSK1605786A. These pharmacogenetic analyses was not conducted following the early termination of the study. Because the study was terminated prematurely, summary statistics were not compiled.

End point type	Secondary

End point timeframe:

Post randomization any time during early two weeks

End point values	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[116]	0[117]	0[118]	
Units: presence or absence of certain genes				
number (not applicable)				

Notes:

[116] - ITT Population

[117] - ITT Population

[118] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the start of study medication until and 4 weeks post treatment (up to Week 56)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo via 2 oral capsules for 52 weeks	
Reporting group title	GSK1605786A 500 mg QD
Reporting group description:	
Participants received GSK1605786A a total of 500 milligrams (mg), administered as 2 250 mg oral capsules once daily (QD) for 52 weeks	
Reporting group title	GSK1605786A 500 mg BID
Reporting group description:	
Participants received GSK1605786A a total of 500 mg, administered as 2 250 mg oral capsules, twice daily (BID) for 52 weeks	

Serious adverse events	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 76 (1.32%)	3 / 77 (3.90%)	2 / 76 (2.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 77 (0.00%)	0 / 76 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn's disease			

subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	0 / 76 (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
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 77 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 76 (0.00%)	1 / 77 (1.30%)	0 / 76 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 77 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	GSK1605786A 500 mg QD	GSK1605786A 500 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 76 (71.05%)	48 / 77 (62.34%)	54 / 76 (71.05%)
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 76 (7.89%)	3 / 77 (3.90%)	9 / 76 (11.84%)
occurrences (all)	7	8	19
General disorders and administration site conditions			
Abdominal pain			
subjects affected / exposed	10 / 76 (13.16%)	5 / 77 (6.49%)	9 / 76 (11.84%)
occurrences (all)	11	7	10
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 76 (0.00%)	2 / 77 (2.60%)	4 / 76 (5.26%)
occurrences (all)	0	2	4

Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	13 / 76 (17.11%)	12 / 77 (15.58%)	10 / 76 (13.16%)
occurrences (all)	14	13	11
Diarrhoea			
subjects affected / exposed	8 / 76 (10.53%)	3 / 77 (3.90%)	3 / 76 (3.95%)
occurrences (all)	9	3	5
Nausea			
subjects affected / exposed	6 / 76 (7.89%)	1 / 77 (1.30%)	6 / 76 (7.89%)
occurrences (all)	8	2	12
Vomiting			
subjects affected / exposed	4 / 76 (5.26%)	2 / 77 (2.60%)	3 / 76 (3.95%)
occurrences (all)	5	2	4
Toothache			
subjects affected / exposed	3 / 76 (3.95%)	0 / 77 (0.00%)	4 / 76 (5.26%)
occurrences (all)	3	0	4
Dyspepsia			
subjects affected / exposed	1 / 76 (1.32%)	4 / 77 (5.19%)	1 / 76 (1.32%)
occurrences (all)	2	4	2
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	7 / 76 (9.21%)	2 / 77 (2.60%)	1 / 76 (1.32%)
occurrences (all)	7	2	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 76 (10.53%)	5 / 77 (6.49%)	4 / 76 (5.26%)
occurrences (all)	11	7	5
Back pain			
subjects affected / exposed	4 / 76 (5.26%)	4 / 77 (5.19%)	5 / 76 (6.58%)
occurrences (all)	4	4	5
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 76 (11.84%)	9 / 77 (11.69%)	9 / 76 (11.84%)
occurrences (all)	12	11	12
Influenza			

subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1	4 / 77 (5.19%) 4	2 / 76 (2.63%) 2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 July 2011	To update sponsor departmental and contact information, include revised information and to correct previous errors vand minor typographical and protocol errors, update secondary objectives for health outcomes, include work productivity and activity impairment assessment, update secondary objectives to include biomarkers of inflammation, include exploratory objective of assessment of fistula closure to clarify that this will be an exploratory objective of this study, update approximation of number of subjects required for screening based on current screen failure rate, amend 50% limitation of enrolment of subjects receiving prior treatment with an anti-TNF agent, include only subjects who discontinued due to loss or lack of efficacy, clarify for other secondary efficacy endpoints that changes in IBDQ total score will be assessed at Week 8 in addition to Week 12, clarify for safety endpoints that changes in body weight and temperature will be performed only in relation to CDAI scoring and not as a separate assessment, include assessment of liver function test parameters as a safety endpoint, clarify that changes in CRP concentrations will also be assessed at Weeks 4 and 8, clarify that the investigator should conduct a Follow-up visit in addition to an Early Withdrawal visit for safety follow up, remove specification of version of Investigator Brochure as this document will be updated throughout the life of the study. Investigators should refer to most recent version of the Investigator Brochure, amend Inclusion Criteria as follows: clarify the criterion for determination of an elevated CRP laboratory value, allow subjects to qualify based on current evidence of active disease by either endoscopic assessment or inflammatory biomarkers. Subjects who do not qualify based on endoscopic assessment may be eligible if the CRP and faecal calprotectin criteria are met, updated criteria for acceptable contraceptive methods of birth control according to sponsor standards
27 July 2011	Amend Exclusion Criteria as follows: clarify criteria for fixed symptomatic stenoses and stricture, to clarify that prohibited medications should not be taken throughout the study,to specify the duration of the wash-out period for previous use of biologics based on scheduling of randomisation visit,to include criterion to prohibit use of digoxin or related cardiac glycosides(e.g digitoxin, deslanoside, lanatoside C, metildigoxin) within 7 days prior to screening, to clarify that subjects should not receive immunisation with a live vaccine, with the exception of influenza vaccine, for the duration of the study to ensure subject safety, correct typographical error in exclusion of alkaline phosphatase to > 1.5 times the upper limit of normal,to specify that Investigators should confirm that subjects continue to meet the requirements for Exclusion Criterion #20 based on Week 0 liver function test results, subjects who do not continue to meet this criterion should be withdrawn from the study, to clarify testing procedures for exclusion on basis of a positive test for Hepatitis C, clarify exclusion criterion for subject with Bundle Branch Block and to include information on procedures for QTc assessment, update withdrawal and stopping criteria and testing procedures for liver chemistry abnormalities and ECG findings to be consistent with revisions to GSK standard withdrawal criteria, clarify permitted treatment with oral antibiotics for Crohn's disease and the allowable use of short courses of oral antibiotics for intercurrent To include use of digoxin or related cardiac glycosides(e.g digitoxin, deslanoside, lanatoside C, metildigoxin) as prohibited medications, correct errors in the Time and Events table for consistency with protocol text or to clarify study procedures, increase potential duration of Screening period to allow sufficient time for scheduling of ileocolonoscopy for subjects who do not qualify on the basis of biomarker testing.

27 July 2011	To clarify that information on obtaining haematocrit values for CDAI determination is available in the SPM, To clarify that subjects should initiate study drug administration the evening of the day of the randomisation visit, To provide clarification that adverse events should be collected at the Week 16 visit and to provide additional clarification regarding reporting of worsening of Crohn's disease as an adverse event, To include information on reporting and analyses of Disease-related events common in Crohn's disease for consistency with new FDA safety reporting guidance. Protocol-specified events related to worsening of Crohn's disease will not be reported as SAEs, To clarify assessments at Early Withdrawal and Follow-up visits, To clarify process for pharmacokinetics sample collection, To provide additional clarification on data handling, To include additional information on analyses of components of SF-36v2 and disability benefit data To provide additional clarification on IDMC purpose and safety review, To amend CDAI to clarify that investigator should assess symptoms/findings for subject based on current conditions and fever should be documented if present over the past week, To include most recent version of IBDQ which is being utilised in the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 August 2013	Discontinue investigational product and discontinue enrollment of new subjects. 4 September 2013 - Study Termination.	-

Notes:

Limitations and caveats

None reported