Clinical trial results:
An adaptive Phase II study to evaluate the efficacy, pharmacodynamics, safety and tolerability of GSK2586184 in patients with mild to moderate systemic lupus erythematosus.

Summary

EudraCT number	2012-001645-41
Trial protocol	DE HU SE ES GR EE CZ PL
Global end of trial date	31 March 2014

Results information

Result version number	v2 (current)
This version publication date	26 March 2016
First version publication date	01 July 2015
Version creation reason	• Correction of full data set Minor corrections required.

Trial information

Trial identification

Sponsor protocol code	JAK115919

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01777256
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	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	09 July 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 March 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

• To estimate the relationship between dose of GSK2586184 and pharmacodynamic effect on expression of selected messenger ribonucleic acid (mRNA) transcripts following 2 weeks of treatment in SLE patients
• To estimate the relationship between dose of GSK2586184 and clinical response as assessed by SELENA SLEDAI score following 12 weeks of treatment in SLE patients
• To evaluate the safety and tolerability of repeat doses of GSK2586184 in SLE patients.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 March 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Czech Republic: 2
Country: Number of subjects enrolled	Estonia: 3
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Greece: 6
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Peru: 14
Worldwide total number of subjects	50
EEA total number of subjects	32

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)	50
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants (par) with a clinical diagnosis of systemic lupus erythematosus (SLE) according to the American College of Rheumatology classification criteria were enrolled. Enrolled par with clinically active SLE were randomised in a 1:1:1:1:1 ratio to receive twice daily doses of GSK2586184 (50 milligram (mg), 100 mg, 200 mg, 400 mg) or placebo.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK2586184 50 mg BID

Arm description:

Participants received a combination of 2 film coated tablets, so that each participant received a total of 50 milligram (mg) of GSK2586184, twice daily (BID) with food for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	GSK2586184
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Either 50mg or 200mg oral tablets taken twice daily with food

Arm title	GSK2586184 100 mg BID

Arm description:

Participants received a combination of 2 film coated tablets, so that each participant received a total of 100 mg of GSK2586184, BID with food for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	GSK2586184
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Either 50mg or 200mg oral tablets taken twice daily with food

Arm title	GSK2586184 200 mg BID

Arm description:

Participants received a combination of 2 film coated tablets, so that each participant received a total of 200 mg of GSK2586184, BID with food for 12 weeks.

Arm type	Experimental

Investigational medicinal product name	GSK2586184
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Either 50mg or 200mg oral tablets taken twice daily with food

Arm title	GSK2586184 400 mg BID

Arm description:

Participants received a combination of 2 film coated tablets, so that each participant received a total of 400 mg of GSK2586184, BID with food for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	GSK2586184
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Either 50mg or 200mg oral tablets taken twice daily with food

Arm title	Placebo

Arm description:

Participants received a combination of 2 film coated tablets of GSK2586184 matching placebo, BID with food for 12 weeks.

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

Dosage and administration details:

Placebo - Either 50mg or 200mg oral tablets taken twice daily with food

Number of subjects in period 1	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID
Started	9	10	10
Completed	4	5	4
Not completed	5	5	6
Study closed/terminated	4	4	-
Consent withdrawn by subject	-	-	1
Physician decision	-	-	-
Adverse event, non-fatal	1	1	4
Lost to follow-up	-	-	-
Protocol deviation	-	-	1

Number of subjects in period 1	GSK2586184 400 mg BID	Placebo
Started	10	11

Completed	4	5
Not completed	6	6
Study closed/terminated	3	5
Consent withdrawn by subject	1	-
Physician decision	1	-
Adverse event, non-fatal	1	-
Lost to follow-up	-	1
Protocol deviation	-	-

Baseline characteristics

Reporting groups	
Reporting group title	GSK2586184 50 mg BID
Reporting group description:	
Participants received a combination of 2 film coated tablets, so that each participant received a total of 50 milligram (mg) of GSK2586184, twice daily (BID) with food for 12 weeks.	
Reporting group title	GSK2586184 100 mg BID
Reporting group description:	
Participants received a combination of 2 film coated tablets, so that each participant received a total of 100 mg of GSK2586184, BID with food for 12 weeks.	
Reporting group title	GSK2586184 200 mg BID
Reporting group description:	
Participants received a combination of 2 film coated tablets, so that each participant received a total of 200 mg of GSK2586184, BID with food for 12 weeks.	
Reporting group title	GSK2586184 400 mg BID
Reporting group description:	
Participants received a combination of 2 film coated tablets, so that each participant received a total of 400 mg of GSK2586184, BID with food for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received a combination of 2 film coated tablets of GSK2586184 matching placebo, BID with food for 12 weeks.	

Reporting group values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID
Number of subjects	9	10	10
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	38	43.1	37.3
standard deviation	± 12.55	± 11.23	± 7.15
Gender categorical Units: Subjects			
Female	9	10	10
Male	0	0	0
Race Units: Subjects			
American Indian or Alaskan Native	2	2	3
Asian - Central/South Asian Heritage	1	0	0
Asian - East Asian Heritage	0	0	0
White - White/Caucasian/European Heritage	6	6	7
Mixed Race	0	2	0

Reporting group values	GSK2586184 400 mg BID	Placebo	Total
Number of subjects	10	11	50

Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	47.5	36.9	
standard deviation	± 10.99	± 10.14	-
Gender categorical Units: Subjects			
Female	10	11	50
Male	0	0	0
Race Units: Subjects			
American Indian or Alaskan Native	1	4	12
Asian - Central/South Asian Heritage	0	0	1
Asian - East Asian Heritage	1	0	1
White - White/Caucasian/European Heritage	8	7	34
Mixed Race	0	0	2

End points

End points reporting groups

Reporting group title	GSK2586184 50 mg BID
Reporting group description:	
Participants received a combination of 2 film coated tablets, so that each participant received a total of 50 milligram (mg) of GSK2586184, twice daily (BID) with food for 12 weeks.	
Reporting group title	GSK2586184 100 mg BID
Reporting group description:	
Participants received a combination of 2 film coated tablets, so that each participant received a total of 100 mg of GSK2586184, BID with food for 12 weeks.	
Reporting group title	GSK2586184 200 mg BID
Reporting group description:	
Participants received a combination of 2 film coated tablets, so that each participant received a total of 200 mg of GSK2586184, BID with food for 12 weeks.	
Reporting group title	GSK2586184 400 mg BID
Reporting group description:	
Participants received a combination of 2 film coated tablets, so that each participant received a total of 400 mg of GSK2586184, BID with food for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received a combination of 2 film coated tablets of GSK2586184 matching placebo, BID with food for 12 weeks.	

Primary: Percentage Inhibition from Baseline of interferon (IFN) Transcriptional Biomarkers at Week 2

End point title	Percentage Inhibition from Baseline of interferon (IFN) Transcriptional Biomarkers at Week 2
End point description:	
Mean reduction (40%) from Baseline of the IFN transcriptional signature biomarker was monitored at Week 2. Percentage (Per) inhibition (=[(Day x–Baseline)/Baseline]*-100), was the Per reduction from baseline (Day1) and evaluated in any pre-designated panels of genes i.e. Addenbrookes 1, Addenbrookes 2, JAK439, PD, Panel Stripping, Flare and Transcription. Analysis was performed using a repeated measures model with covariates of treatment, baseline, Day, Day by baseline and Day by treatment interactions. Only those Par available at the specified time points were analysed (n=X,X,X,X,X). Different Par may have been analysed at different time points, so the overall number of Par analysed reflects everyone in the Intent To Treat (ITT) Population i.e. Par randomised to treatment, received >=1 dose of study medication and had >=1 valid post dose assessment	
End point type	Primary
End point timeframe:	
Baseline and Week 2	

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8[1]	10[2]	9[3]	9[4]
Units: Percentage				
arithmetic mean (standard deviation)				
Panel1	1.55 (± 7.621)	0.53 (± 8.048)	0.15 (± 11.338)	4.83 (± 6.315)

Panel2	1.1 (± 8.526)	0.64 (± 7.804)	0.38 (± 11.696)	4.48 (± 6.697)
Panel3	0.31 (± 6.814)	0.49 (± 5.147)	1.22 (± 12.014)	3.98 (± 5.847)
Panel4	-0.48 (± 5.215)	-0.27 (± 4.461)	-1.91 (± 11.685)	2.08 (± 5.586)
Panel5	0.73 (± 7.682)	0.29 (± 7.789)	0.16 (± 12.227)	5.29 (± 6.825)
Panel6	1.07 (± 6.419)	0.82 (± 6.428)	1.24 (± 10.849)	5.64 (± 6.008)
Panel7	0.77 (± 1.835)	-1 (± 2.318)	-1.06 (± 6.948)	0.6 (± 1.503)

Notes:

[1] - ITT Population

[2] - ITT Population

[3] - ITT Population

[4] - ITT Population

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	9[5]			
Units: Percentage				
arithmetic mean (standard deviation)				
Panel1	-1.21 (± 7.543)			
Panel2	-1.05 (± 7.657)			
Panel3	-0.46 (± 5.36)			
Panel4	-1.02 (± 5.182)			
Panel5	-1.14 (± 7.242)			
Panel6	-0.94 (± 6.425)			
Panel7	-0.3 (± 1.645)			

Notes:

[5] - ITT Population

Statistical analyses

Statistical analysis title	Analysis 1
Comparison groups	Placebo v GSK2586184 50 mg BID
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority[6]
Parameter estimate	Mean difference (final values)
Point estimate	2.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.31
upper limit	9.81

Notes:
[6] - Panel 1: Placebo vs GSK2586184 50 mg BID at Week 2

Statistical analysis title	Analysis 2
Comparison groups	Placebo v GSK2586184 100 mg BID
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority[7]
Parameter estimate	Mean difference (final values)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.19
upper limit	8.3

Notes:
[7] - Panel 1: Placebo vs GSK2586184 100 mg BID at Week 2

Statistical analysis title	Analysis 3
Comparison groups	Placebo v GSK2586184 200 mg BID
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[8]
Parameter estimate	Mean difference (final values)
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.37
upper limit	6.56

Notes:
[8] - Panel 1: Placebo vs GSK2586184 200 mg BID at Week 2

Statistical analysis title	Analysis 4
Comparison groups	Placebo v GSK2586184 400 mg BID
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[9]
Parameter estimate	Mean difference (final values)
Point estimate	5.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.46
upper limit	12.25

Notes:
[9] - Panel 1: Placebo vs GSK2586184 400 mg BID at Week 2

Statistical analysis title	Analysis 5

Comparison groups	Placebo v GSK2586184 50 mg BID
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority[10]
Parameter estimate	Mean difference (final values)
Point estimate	2.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.52
upper limit	9.56

Notes:

[10] - Panel 2: Placebo vs GSK2586184 50 mg BID at Week 2

Statistical analysis title	Analysis 6
Comparison groups	Placebo v GSK2586184 100 mg BID
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority[11]
Parameter estimate	Mean difference (final values)
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.86
upper limit	8.54

Notes:

[11] - Panel 2: Placebo vs GSK2586184 100 mg BID at Week 2

Statistical analysis title	Analysis 7
Comparison groups	Placebo v GSK2586184 200 mg BID
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[12]
Parameter estimate	Mean difference (final values)
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.95
upper limit	6.99

Notes:

[12] - Panel 2: Placebo vs GSK2586184 200 mg BID at Week 2

Statistical analysis title	Analysis 8
Comparison groups	Placebo v GSK2586184 400 mg BID

Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[13]
Parameter estimate	Mean difference (final values)
Point estimate	4.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.55
upper limit	12.11

Notes:

[13] - Panel 2: Placebo vs GSK2586184 400 mg BID at Week 2

Statistical analysis title	Analysis 9
Comparison groups	Placebo v GSK2586184 50 mg BID
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority[14]
Parameter estimate	Mean difference (final values)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.2
upper limit	7.16

Notes:

[14] - Panel 3: Placebo vs GSK2586184 50 mg BID at Week 2

Statistical analysis title	Analysis 10
Comparison groups	Placebo v GSK2586184 100 mg BID
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority[15]
Parameter estimate	Mean difference (final values)
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.13
upper limit	6.65

Notes:

[15] - Panel 3: Placebo vs GSK2586184 100 mg BID at Week 2

Statistical analysis title	Analysis 11
Comparison groups	Placebo v GSK2586184 200 mg BID

Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[16]
Parameter estimate	Mean difference (final values)
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.06
upper limit	6.19

Notes:

[16] - Panel 3: Placebo vs GSK2586184 200 mg BID at Week 2

Statistical analysis title	Analysis 12
Comparison groups	Placebo v GSK2586184 400 mg BID
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[17]
Parameter estimate	Mean difference (final values)
Point estimate	4.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.99
upper limit	10.03

Notes:

[17] - Panel 3: Placebo vs GSK2586184 400 mg BID at Week 2

Statistical analysis title	Analysis 13
Comparison groups	Placebo v GSK2586184 50 mg BID
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority[18]
Parameter estimate	Mean difference (final values)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.42
upper limit	5.87

Notes:

[18] - Panel 4: Placebo vs GSK25865184 50 mg BID at Week 2

Statistical analysis title	Analysis 14
Comparison groups	Placebo v GSK2586184 100 mg BID

Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority[19]
Parameter estimate	Mean difference (final values)
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.32
upper limit	5.46

Notes:

[19] - Panel 4: Placebo vs GSK2586184 100 mg BID at Week 2

Statistical analysis title	Analysis 15
Comparison groups	Placebo v GSK2586184 200 mg BID
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[20]
Parameter estimate	Mean difference (final values)
Point estimate	-2.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.41
upper limit	2.76

Notes:

[20] - Panel 4: Placebo vs GSK2586184 200 mg BID at Week 2

Statistical analysis title	Analysis 16
Comparison groups	Placebo v GSK2586184 400 mg BID
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[21]
Parameter estimate	Mean difference (final values)
Point estimate	2.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.01
upper limit	8

Notes:

[21] - Panel 4: Placebo vs GSK2586184 400 mg BID at Week 2

Statistical analysis title	Analysis 17
Comparison groups	Placebo v GSK2586184 50 mg BID

Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority[22]
Parameter estimate	Mean difference (final values)
Point estimate	1.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.53
upper limit	9.42

Notes:

[22] - Panel 5: Placebo vs GSK2586184 50 mg BID at Week 2

Statistical analysis title	Analysis 18
Comparison groups	Placebo v GSK2586184 100 mg BID
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority[23]
Parameter estimate	Mean difference (final values)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.85
upper limit	8.41

Notes:

[23] - Panel 5: Placebo vs GSK2586184 100 mg BID at Week 2

Statistical analysis title	Analysis 19
Comparison groups	Placebo v GSK2586184 200 mg BID
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[24]
Parameter estimate	Mean difference (final values)
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.7
upper limit	7.04

Notes:

[24] - Panel 5: Placebo vs GSK2586184 200 mg BID at Week 2

Statistical analysis title	Analysis 20
Comparison groups	Placebo v GSK2586184 400 mg BID

Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[25]
Parameter estimate	Mean difference (final values)
Point estimate	5.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.45
upper limit	13.06

Notes:

[25] - Panel 5: Placebo vs GSK2586184 400 mg BID at Week 2

Statistical analysis title	Analysis 21
Comparison groups	Placebo v GSK2586184 50 mg BID
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority[26]
Parameter estimate	Mean difference (final values)
Point estimate	2.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.56
upper limit	8.61

Notes:

[26] - Panel 6: Placebo vs GSK2586184 50 mg BID at Week 2

Statistical analysis title	Analysis 22
Comparison groups	Placebo v GSK2586184 100 mg BID
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority[27]
Parameter estimate	Mean difference (final values)
Point estimate	1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.71
upper limit	7.86

Notes:

[27] - Panel 6: Placebo vs GSK2586184 100 mg BID at Week 2

Statistical analysis title	Analysis 23
Comparison groups	Placebo v GSK2586184 200 mg BID

Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[28]
Parameter estimate	Mean difference (final values)
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.84
upper limit	7.15

Notes:

[28] - Panel 6: Placebo vs GSK2586184 200 mg BID at Week 2

Statistical analysis title	Analysis 24
Comparison groups	Placebo v GSK2586184 400 mg BID
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[29]
Parameter estimate	Mean difference (final values)
Point estimate	5.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	12.32

Notes:

[29] - Panel 6: Placebo vs GSK2586184 400 mg BID at Week 2

Statistical analysis title	Analysis 25
Comparison groups	Placebo v GSK2586184 50 mg BID
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority[30]
Parameter estimate	Mean difference (final values)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.18
upper limit	3.45

Notes:

[30] - Panel 7: Placebo vs GSK2586184 50 mg BID at Week 2

Statistical analysis title	Analysis 26
Comparison groups	Placebo v GSK2586184 100 mg BID

Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority[31]
Parameter estimate	Mean difference (final values)
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	2.17

Notes:

[31] - Panel 7: Placebo vs GSK2586184 100 mg BID at Week 2

Statistical analysis title	Analysis 27
Comparison groups	Placebo v GSK2586184 200 mg BID
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[32]
Parameter estimate	Mean difference (final values)
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.85
upper limit	1.68

Notes:

[32] - Panel 7: Placebo vs GSK2586184 200 mg BID at Week 2

Statistical analysis title	Analysis 28
Comparison groups	Placebo v GSK2586184 400 mg BID
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority[33]
Parameter estimate	Mean difference (final values)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.41
upper limit	3.09

Notes:

[33] - Panel 7: Placebo vs GSK2586184 400 mg BID at Week 2

Primary: Change from Baseline of SELENA SLEDAI score at indicated timepoints up to Week 16.

End point title	Change from Baseline of SELENA SLEDAI score at indicated timepoints up to Week 16.[34]

End point description:

The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) is a validated index for assessing SLE disease activity. It is a weighted index in which signs and symptoms, laboratory tests, and physician’s assessment for each of 9 organ systems are given a weighted score and summed, if present

at the time of the visit or in the preceding 10 days. Modified version of SLEDAI is Safety of Estrogen in Lupus National Assessment (SELENA) SLEDAI where the maximum theoretical score for the SELENA SLEDAI was 105 with 0 indicating inactive disease. Baseline value is defined as Day 1 (pre-dose) SELENA SLEDAI score. Only those Par available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different Par may have been analysed at different time points, so the overall number of Par analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 2, 4, 6, 8, 10, 12 and 16

Notes:

[34] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[35]	10[36]	10[37]	10[38]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week2, n=9,8,9,9,9	-2 (± 3.43)	-1 (± 3.02)	0.3 (± 3.46)	-2.4 (± 2.19)
Week4, n=7,8,7,8,8	-1.9 (± 4.85)	-1.5 (± 2.33)	-0.6 (± 2.99)	-3.5 (± 3.16)
Week6, n=7,7,6,8,8	-3.3 (± 3.3)	-1.9 (± 2.61)	-2 (± 5.66)	-3 (± 3.55)
Week8, n=6,7,4,7,7	-4.2 (± 2.86)	-3 (± 2.65)	-3.5 (± 5.74)	-3.4 (± 3.21)
Week10, n=5,6,4,6,6	-3.6 (± 3.29)	-4.2 (± 1.33)	-2 (± 6.93)	-3.7 (± 3.44)
Week12, n=4,5,4,5,5	-4.5 (± 4.43)	-6.2 (± 6.1)	-3 (± 6.83)	-4.6 (± 4.98)
Week16, n=9,10,9,8,10	-3.7 (± 4.42)	-4.9 (± 4.72)	-3.7 (± 6.08)	-7 (± 3.55)

Notes:

[35] - ITT Population.

[36] - ITT Population.

[37] - ITT Population.

[38] - ITT Population.

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[39]			
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week2, n=9,8,9,9,9	-1.3 (± 3.46)			
Week4, n=7,8,7,8,8	-2.8 (± 3.69)			
Week6, n=7,7,6,8,8	-2.8 (± 3.2)			
Week8, n=6,7,4,7,7	-4 (± 3.83)			
Week10, n=5,6,4,6,6	-5.2 (± 3.82)			
Week12, n=4,5,4,5,5	-3.6 (± 3.58)			
Week16, n=9,10,9,8,10	-3.4 (± 3.66)			

Notes:

[39] - ITT Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in systolic blood pressure and diastolic blood

pressure at the indicated time points up to Week 16

End point title	Change from Baseline in systolic blood pressure and diastolic blood pressure at the indicated time points up to Week 16[40]

End point description:

Change from Baseline in systolic blood pressure (BP) and diastolic BP is summarised for each post-Baseline assessment up to Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 2, 4, 6, 8, 10, 12 and 16

Notes:

[40] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[41]	10[42]	10[43]	10[44]
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
Sitting Systolic BP, Week2, n=8,8,6,8,7	-1.25 (± 6.944)	-1.13 (± 7.624)	3.5 (± 11.895)	-2.25 (± 7.573)
Sitting Systolic BP, Week4, n=6,6,7,8,7	3.33 (± 10.838)	-2.83 (± 11.737)	-0.57 (± 5.318)	-6.75 (± 12.43)
Sitting Systolic BP, Week6, n=6,8,5,8,8	3.83 (± 8.841)	-2.25 (± 7.421)	5 (± 11.225)	0.5 (± 7.728)
Sitting Systolic BP, Week8, n=7,5,8,8,7	-3.57 (± 4.65)	-1.4 (± 11.546)	-0.38 (± 10.309)	-4.75 (± 12.556)
Sitting Systolic BP, Week10, n=5,6,3,5,7	-1.2 (± 11.692)	-1.5 (± 16.159)	2 (± 8.185)	-1.4 (± 18.064)
Sitting Systolic BP, Week12, n=6,5,6,7,6	-2.5 (± 10.895)	-1.8 (± 9.176)	2.5 (± 8.118)	-2.57 (± 13.477)
Sitting Systolic BP, Week16, n=4,5,2,4,5	-0.75 (± 9.215)	-2.8 (± 8.758)	7 (± 2.828)	-10.75 (± 19.276)
Supine Systolic BP, Week2, n=1,2,3,1,3	0 (± 99999)	-10 (± 0)	-9.67 (± 8.963)	5 (± 99999)
Supine Systolic BP, Week4, n=2,2,1,0,3	0 (± 7.071)	-15 (± 7.071)	0 (± 99999)	99999 (± 99999)
Supine Systolic BP, Week6, n=1,2,1,1,0	9 (± 99999)	-10 (± 0)	0 (± 99999)	2 (± 99999)
Supine Systolic BP, Week8, n=1,2,1,1,2	5 (± 99999)	-10 (± 14.142)	-10 (± 99999)	0 (± 99999)
Supine Systolic BP, Week10, n=2,2,1,1,1	10 (± 14.142)	-5 (± 7.071)	0 (± 99999)	0 (± 99999)
Supine Systolic BP, Week12, n=1,2,1,1,1	5 (± 99999)	-10 (± 0)	-10 (± 99999)	-2 (± 99999)
Supine Systolic BP, Week16, n=1,1,1,1,1	0 (± 99999)	-10 (± 99999)	0 (± 99999)	2 (± 99999)
Sitting Diastolic BP, Week2, n=8,8,6,8,7	-0.63 (± 8.667)	0.25 (± 6.944)	-0.33 (± 7.202)	-8.5 (± 10.268)
Sitting Diastolic BP, Week4, n=6,6,7,8,7	5.17 (± 6.824)	-1.83 (± 8.773)	-0.43 (± 5.94)	-6.63 (± 12.094)
Sitting Diastolic BP, Week6, n=6,8,5,8,8	-1.67 (± 3.933)	4 (± 3.817)	-1.6 (± 3.782)	-0.38 (± 8.331)
Sitting Diastolic BP, Week8, n=7,5,8,8,7	1 (± 11.255)	-2 (± 8.276)	-0.38 (± 4.596)	-2 (± 10.515)

Sitting Diastolic BP, Week10, n=5,6,3,5,7	-2.8 (± 6.419)	-2.17 (± 12.073)	4.33 (± 3.786)	1 (± 11.662)
Sitting Diastolic BP, Week12, n=6,5,6,7,6	-2 (± 5.06)	-1.2 (± 3.271)	-2 (± 4.98)	-1 (± 9.539)
Sitting Diastolic BP, Week16, n=4,5,2,4,5	-2.5 (± 2.646)	-3.6 (± 8.792)	2 (± 7.071)	-0.25 (± 16.681)
Supine Diastolic BP, Week2, n=1,2,3,1,3	-10 (± 99999)	-5 (± 7.071)	-3.67 (± 5.508)	-5 (± 99999)
Supine Diastolic BP, Week4, n=2,2,1,0,3	-5 (± 7.071)	-6 (± 5.657)	-20 (± 99999)	99999 (± 99999)
Supine Diastolic BP, Week6, n=1,2,1,1,0	0 (± 99999)	-10 (± 2.828)	-10 (± 99999)	-10 (± 99999)
Supine Diastolic BP, Week8, n=1,2,1,1,2	0 (± 99999)	-6 (± 5.657)	-10 (± 99999)	5 (± 99999)
Supine Diastolic BP, Week10, n=2,2,1,1,1	2.5 (± 10.607)	-11 (± 1.414)	-10 (± 99999)	-15 (± 99999)
Supine Diastolic BP, Week12, n=1,2,1,1,1	0 (± 99999)	-6 (± 8.485)	-20 (± 99999)	-5 (± 99999)
Supine Diastolic BP, Week16, n=1,1,1,1,1	-5 (± 99999)	-12 (± 99999)	-10 (± 99999)	0 (± 99999)

Notes:

[41] - ITT Population. "Not available (NA)" data is presented as "99999"

[42] - ITT Population. "Not available (NA)" data is presented as "99999"

[43] - ITT Population. "Not available (NA)" data is presented as "99999"

[44] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[45]			
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
Sitting Systolic BP, Week2, n=8,8,6,8,7	-0.29 (± 5.09)			
Sitting Systolic BP, Week4, n=6,6,7,8,7	7.14 (± 7.448)			
Sitting Systolic BP, Week6, n=6,8,5,8,8	12.63 (± 16.151)			
Sitting Systolic BP, Week8, n=7,5,8,8,7	4.14 (± 11.067)			
Sitting Systolic BP, Week10, n=5,6,3,5,7	6.29 (± 15.649)			
Sitting Systolic BP, Week12, n=6,5,6,7,6	2.17 (± 10.265)			
Sitting Systolic BP, Week16, n=4,5,2,4,5	7.2 (± 14.957)			
Supine Systolic BP, Week2, n=1,2,3,1,3	11 (± 18.248)			
Supine Systolic BP, Week4, n=2,2,1,0,3	11.67 (± 25.658)			
Supine Systolic BP, Week6, n=1,2,1,1,0	99999 (± 99999)			
Supine Systolic BP, Week8, n=1,2,1,1,2	7.5 (± 17.678)			
Supine Systolic BP, Week10, n=2,2,1,1,1	10 (± 99999)			
Supine Systolic BP, Week12, n=1,2,1,1,1	20 (± 99999)			
Supine Systolic BP, Week16, n=1,1,1,1,1	18 (± 99999)			
Sitting Diastolic BP, Week2, n=8,8,6,8,7	2.57 (± 4.826)			
Sitting Diastolic BP, Week4, n=6,6,7,8,7	7 (± 8.813)			
Sitting Diastolic BP, Week6, n=6,8,5,8,8	2.25 (± 8.155)			

Sitting Diastolic BP, Week8, n=7,5,8,8,7	3.43 (± 4.685)			
Sitting Diastolic BP, Week10, n=5,6,3,5,7	6.71 (± 10.812)			
Sitting Diastolic BP, Week12, n=6,5,6,7,6	1.5 (± 3.507)			
Sitting Diastolic BP, Week16, n=4,5,2,4,5	11.4 (± 12.422)			
Supine Diastolic BP, Week2, n=1,2,3,1,3	5 (± 8.66)			
Supine Diastolic BP, Week4, n=2,2,1,0,3	1.33 (± 12.662)			
Supine Diastolic BP, Week6, n=1,2,1,1,0	99999 (± 99999)			
Supine Diastolic BP, Week8, n=1,2,1,1,2	5 (± 7.071)			
Supine Diastolic BP, Week10, n=2,2,1,1,1	10 (± 99999)			
Supine Diastolic BP, Week12, n=1,2,1,1,1	5 (± 99999)			
Supine Diastolic BP, Week16, n=1,1,1,1,1	8 (± 99999)			

Notes:

[45] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in heart rate at the indicated time points up to Week 16

End point title	Change from Baseline in heart rate at the indicated time points up to Week 16[46]

End point description:

Change from Baseline in sitting and supine heart rate is summarised for each post-Baseline assessment up to Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 2, 4, 6, 8, 10, 12 and 16

Notes:

[46] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[47]	10[48]	10[49]	10[50]
Units: Beats per minute				
arithmetic mean (standard deviation)				
Sitting Heart Rate, Week2, n=8,8,6,8,7	5.25 (± 6.541)	-2.13 (± 7.357)	-0.5 (± 10.035)	-2.38 (± 9.68)
Sitting Heart Rate, Week4, n=6,6,7,8,7	2 (± 8.786)	-0.67 (± 12.58)	3.43 (± 11.574)	-2.75 (± 8.924)

Sitting Heart Rate, Week6, n=6,8,5,8,8	1.17 (± 4.07)	-3.13 (± 9.094)	-0.4 (± 6.58)	-2.38 (± 10.474)
Sitting Heart Rate, Week8, n=7,5,8,8,7	7.43 (± 10.907)	-5.6 (± 10.139)	-1 (± 7.151)	2 (± 16.318)
Sitting Heart Rate, Week10, n=5,6,3,5,7	2.2 (± 8.228)	-5.33 (± 7.866)	0.67 (± 5.686)	2.2 (± 6.87)
Sitting Heart Rate, Week12, n=6,5,6,7,6	1 (± 10.881)	-6 (± 6)	5 (± 9.529)	-2.14 (± 9.668)
Sitting Heart Rate, Week16, n=4,5,2,4,5	-5.5 (± 8.737)	-3.8 (± 3.194)	-3 (± 2.828)	9.5 (± 13.229)
Supine Heart Rate, Week2, n=1,2,3,1,3	7 (± 99999)	-1 (± 2.828)	2.67 (± 5.774)	1 (± 99999)
Supine Heart Rate, Week4, n=2,2,1,0,3	-2 (± 1.414)	0 (± 1.414)	4 (± 99999)	99999 (± 99999)
Supine Heart Rate, Week6, n=1,2,1,1,0	4 (± 99999)	-1.5 (± 0.707)	6 (± 99999)	-8 (± 99999)
Supine Heart Rate, Week8, n=1,2,1,1,2	-8 (± 99999)	-0.5 (± 3.536)	12 (± 99999)	-11 (± 99999)
Supine Heart Rate, Week10, n=2,2,1,1,1	-4.5 (± 9.192)	-0.5 (± 0.707)	10 (± 99999)	-8 (± 99999)
Supine Heart Rate, Week12, n=1,2,1,1,1	0 (± 99999)	-1 (± 1.414)	7 (± 99999)	-9 (± 99999)
Supine Heart Rate, Week16, n=1,1,1,1,1	-8 (± 99999)	-2 (± 99999)	8 (± 99999)	-6 (± 99999)

Notes:

[47] - ITT Population. "Not available (NA)" data is presented as "99999"

[48] - ITT Population. "Not available (NA)" data is presented as "99999"

[49] - ITT Population. "Not available (NA)" data is presented as "99999"

[50] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[51]			
Units: Beats per minute				
arithmetic mean (standard deviation)				
Sitting Heart Rate, Week2, n=8,8,6,8,7	6.29 (± 13.45)			
Sitting Heart Rate, Week4, n=6,6,7,8,7	3.86 (± 15.869)			
Sitting Heart Rate, Week6, n=6,8,5,8,8	4.88 (± 12.933)			
Sitting Heart Rate, Week8, n=7,5,8,8,7	3.43 (± 19.372)			
Sitting Heart Rate, Week10, n=5,6,3,5,7	1.43 (± 17.116)			
Sitting Heart Rate, Week12, n=6,5,6,7,6	-2 (± 19.463)			
Sitting Heart Rate, Week16, n=4,5,2,4,5	8 (± 19.3)			
Supine Heart Rate, Week2, n=1,2,3,1,3	-6.33 (± 6.658)			
Supine Heart Rate, Week4, n=2,2,1,0,3	-3.33 (± 7.638)			
Supine Heart Rate, Week6, n=1,2,1,1,0	99999 (± 99999)			
Supine Heart Rate, Week8, n=1,2,1,1,2	-4 (± 1.414)			
Supine Heart Rate, Week10, n=2,2,1,1,1	-7 (± 99999)			
Supine Heart Rate, Week12, n=1,2,1,1,1	-1 (± 99999)			
Supine Heart Rate, Week16, n=1,1,1,1,1	0 (± 99999)			

Notes:

[51] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in temperature at the indicated time points up to Week 16

End point title	Change from Baseline in temperature at the indicated time points up to Week 16[52]

End point description:

Change from Baseline in temperature is summarised for each post-Baseline assessment up to Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 2, 4, 6, 8, 10, 12 and 16

Notes:

[52] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[53]	10[54]	10[55]	10[56]
Units: Celsius				
arithmetic mean (standard deviation)				
Temperature, Week2, n=9,10,9,9,10	0.04 (± 0.279)	0.26 (± 0.556)	-0.01 (± 0.271)	-0.08 (± 0.299)
Temperature, Week4, n=8,8,8,8,10	-0.06 (± 0.316)	0.34 (± 0.59)	0.19 (± 0.352)	0.09 (± 0.125)
Temperature, Week6, n=7,10,6,9,8	-0.01 (± 0.273)	0.12 (± 0.162)	0.2 (± 0.253)	0.18 (± 0.244)
Temperature, Week8, n=8,7,9,9,9	0.04 (± 0.119)	0.06 (± 0.611)	0.07 (± 0.212)	0.04 (± 0.159)
Temperature, Week10, n=7,8,4,6,8	0.04 (± 0.207)	0.11 (± 0.275)	0.23 (± 0.189)	0.07 (± 0.151)
Temperature, Week12, n=7,7,7,8,7	0.09 (± 0.241)	0.3 (± 0.733)	0.1 (± 0.258)	0.08 (± 0.292)
Temperature, Week16, n=5,6,3,5,6	-0.1 (± 0.1)	0.2 (± 0.369)	-0.13 (± 0.379)	0.04 (± 0.261)

Notes:

[53] - ITT Population. "Not available (NA)" data is presented as "99999"

[54] - ITT Population. "Not available (NA)" data is presented as "99999"

[55] - ITT Population. "Not available (NA)" data is presented as "99999"

[56] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[57]			

Units: Celsius				
arithmetic mean (standard deviation)				
Temperature, Week2, n=9,10,9,9,10	0.15 (± 0.331)			
Temperature, Week4, n=8,8,8,8,10	-0.02 (± 0.326)			
Temperature, Week6, n=7,10,6,9,8	0.24 (± 0.389)			
Temperature, Week8, n=8,7,9,9,9	0.18 (± 0.319)			
Temperature, Week10, n=7,8,4,6,8	0.18 (± 0.238)			
Temperature, Week12, n=7,7,7,8,7	0.09 (± 0.308)			
Temperature, Week16, n=5,6,3,5,6	0.05 (± 0.235)			

Notes:

[57] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in albumin, globulin and protein at the indicated time points up to Week 16

End point title	Change from Baseline in albumin, globulin and protein at the indicated time points up to Week 16[58]

End point description:

Change from Baseline in the albumin, globulin and protein values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[58] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[59]	10[60]	10[61]	10[62]
Units: Grams per liter				
arithmetic mean (standard deviation)				
Albumin; Week2; n=9,9,9,9,10	-0.4 (± 1.88)	0.2 (± 2.22)	-0.6 (± 2.19)	0.9 (± 2.2)
Albumin; Week3; n=1,1,1,0,0	-2 (± 99999)	-4 (± 99999)	1 (± 99999)	99999 (± 99999)
Albumin; Week4; n=8,9,8,9,9	1.3 (± 2.05)	0.4 (± 2.55)	-1 (± 1.36)	1.1 (± 2.09)
Albumin; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	2 (± 99999)	-3 (± 99999)
Albumin; Week6; n=7,10,6,10,8	-1 (± 2)	0.7 (± 2.31)	2.3 (± 2.5)	1 (± 3.13)
Albumin; Week8; n=8,7,9,9,9	1.3 (± 2.55)	-0.1 (± 2.34)	0.2 (± 1.79)	1.8 (± 4.02)
Albumin; Week10; n=7,8,4,7,8	-0.4 (± 2.15)	0.3 (± 2.82)	-0.3 (± 0.96)	1.7 (± 3.73)
Albumin; Week12; n=7,7,7,8,7	-0.4 (± 1.51)	0.6 (± 3.21)	-0.4 (± 2.57)	1 (± 3.66)
Albumin; Week16; n=5,6,3,6,6	-1.4 (± 2.88)	-1.5 (± 3.33)	-3 (± 1.73)	0.3 (± 3.01)
Globulin; Week2; n=9,9,9,9,10	-1.7 (± 3.2)	-0.6 (± 2.55)	0.2 (± 2.28)	-1.6 (± 2.96)

Globulin; Week3; n=1,1,1,0,0	2 (± 99999)	0 (± 99999)	-6 (± 99999)	99999 (± 99999)
Globulin; Week4; n=8,9,8,9,9	-2.1 (± 3.44)	-1.1 (± 3.18)	-1.8 (± 3.06)	-2.6 (± 1.67)
Globulin; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	-0.7 (± 99999)	-3 (± 99999)
Globulin; Week6; n=7,10,6,10,8	-1 (± 1.83)	-0.3 (± 2.11)	-1.5 (± 3.33)	-3.4 (± 3.24)
Globulin; Week8; n=8,7,9,9,9	-1.6 (± 3.78)	-1.7 (± 1.7)	-2.6 (± 3.13)	-2.6 (± 2.3)
Globulin; Week10; n=7,8,4,7,8	-2.1 (± 2.79)	-0.5 (± 2.27)	-0.8 (± 1.26)	-3.1 (± 1.46)
Globulin; Week12; n=7,7,7,8,7	-0.3 (± 2.29)	-0.6 (± 3.46)	-0.7 (± 5.15)	-1.5 (± 3.02)
Globulin; Week16; n=5,6,3,6,6	-0.6 (± 1.67)	0.3 (± 2.34)	-0.7 (± 1.15)	-2 (± 4.1)
Protein; Week2; n=9,9,9,9,10	-2.1 (± 3.95)	-0.3 (± 3.81)	-0.3 (± 3.81)	-0.7 (± 4.82)
Protein; Week3; n=1,1,1,0,0	0 (± 99999)	-4 (± 99999)	-5 (± 99999)	99999 (± 99999)
Protein; Week4; n=8,9,8,9,9	-0.9 (± 2.9)	-0.7 (± 4.44)	-1.9 (± 2.23)	-1.4 (± 3.4)
Protein; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	-5 (± 99999)	-6 (± 99999)
Protein; Week6; n=7,10,6,10,8	-2 (± 3.46)	0.4 (± 2.8)	0.8 (± 2.93)	-2.4 (± 5.8)
Protein; Week8; n=8,7,9,9,9	-0.4 (± 3.29)	-1.9 (± 2.54)	-2.3 (± 3.84)	-0.8 (± 5.21)
Protein; Week10; n=7,8,4,7,8	-2.6 (± 4.47)	-0.3 (± 3.69)	-1 (± 1.15)	-1.4 (± 4.39)
Protein; Week12; n=7,7,7,8,7	-0.7 (± 3.68)	0 (± 3.42)	-1.1 (± 3.53)	-0.5 (± 4)
Protein; Week16; n=5,6,3,6,6	-2 (± 4.36)	-1.2 (± 3.25)	-3.7 (± 1.53)	-1.7 (± 4.5)

Notes:

[59] - ITT Population. "Not available (NA)" data is presented as "99999"

[60] - ITT Population. "Not available (NA)" data is presented as "99999"

[61] - ITT Population. "Not available (NA)" data is presented as "99999"

[62] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[63]			
Units: Grams per liter				
arithmetic mean (standard deviation)				
Albumin; Week2; n=9,9,9,9,10	-1.2 (± 2.15)			
Albumin; Week3; n=1,1,1,0,0	99999 (± 99999)			
Albumin; Week4; n=8,9,8,9,9	-1.4 (± 3.09)			
Albumin; Week5; n=0,0,1,1,1	2 (± 99999)			
Albumin; Week6; n=7,10,6,10,8	-0.9 (± 2.85)			
Albumin; Week8; n=8,7,9,9,9	-2.1 (± 1.9)			
Albumin; Week10; n=7,8,4,7,8	-2.1 (± 1.55)			
Albumin; Week12; n=7,7,7,8,7	-2.6 (± 3.1)			
Albumin; Week16; n=5,6,3,6,6	-2.5 (± 2.74)			
Globulin; Week2; n=9,9,9,9,10	1.1 (± 1.79)			
Globulin; Week3; n=1,1,1,0,0	99999 (± 99999)			
Globulin; Week4; n=8,9,8,9,9	0.3 (± 2.92)			
Globulin; Week5; n=0,0,1,1,1	3 (± 99999)			
Globulin; Week6; n=7,10,6,10,8	1.5 (± 2)			
Globulin; Week8; n=8,7,9,9,9	-0.7 (± 2.29)			
Globulin; Week10; n=7,8,4,7,8	0.1 (± 1.64)			
Globulin; Week12; n=7,7,7,8,7	-0.4 (± 1.62)			
Globulin; Week16; n=5,6,3,6,6	0.8 (± 2.23)			
Protein; Week2; n=9,9,9,9,10	-0.1 (± 3.14)			

Protein; Week3; n=1,1,1,0,0	99999 (± 99999)			
Protein; Week4; n=8,9,8,9,9	-1.1 (± 3.52)			
Protein; Week5; n=0,0,1,1,1	5 (± 99999)			
Protein; Week6; n=7,10,6,10,8	0.6 (± 2.83)			
Protein; Week8; n=8,7,9,9,9	-2.8 (± 3.42)			
Protein; Week10; n=7,8,4,7,8	-2 (± 2.45)			
Protein; Week12; n=7,7,7,8,7	-3 (± 3.32)			
Protein; Week16; n=5,6,3,6,6	-1.7 (± 3.44)			

Notes:

[63] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in alkaline phosphatase, alanine amino transferase, aspartate amino transferase, creatine kinase, gamma glutamyl transferase and lactate dehydrogenase at the indicated time points up to Week 16

End point title	Change from Baseline in alkaline phosphatase, alanine amino transferase, aspartate amino transferase, creatine kinase, gamma glutamyl transferase and lactate dehydrogenase at the indicated time points up to Week 16[64]

End point description:

Change from Baseline in the alkaline phosphatase (ALP), alanine amino transferase (ALT), aspartate amino transferase (AST), creatine kinase (CK), gamma glutamyl transferase (GGT) and lactate dehydrogenase (LDH) values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[64] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[65]	10[66]	10[67]	10[68]
Units: International units per liter				
arithmetic mean (standard deviation)				
ALP; Week2; n=9,9,9,9,10	-4.2 (± 6.2)	1.7 (± 16.53)	-5.8 (± 13.64)	-4.1 (± 5.64)
ALP; Week3; n=1,1,1,0,0	5 (± 99999)	-10 (± 99999)	-59 (± 99999)	99999 (± 99999)
ALP; Week4; n=8,9,8,9,9	-0.9 (± 7.47)	-4.4 (± 6.52)	24.6 (± 102.06)	-3 (± 11.64)
ALP; Week5; n=0,0,3,1,1	99999 (± 99999)	99999 (± 99999)	27.7 (± 122.66)	12 (± 99999)
ALP; Week6; n=7,10,7,10,8	-3.1 (± 7.27)	-5.1 (± 4.95)	-4.4 (± 35.58)	-6.9 (± 10.76)
ALP; Week8; n=9,7,9,9,9	-5.3 (± 7.89)	-8.1 (± 5.87)	-13 (± 26)	-5.9 (± 7.06)
ALP; Week10; n=7,8,4,7,8	-5.3 (± 12.62)	-7.8 (± 7.83)	-16.3 (± 9.29)	-12.4 (± 10.66)

ALP; Week12; n=7,7,7,8,7	-2.7 (± 9.07)	-6.4 (± 12.99)	-19.6 (± 24.23)	-10.4 (± 8.75)
ALP; Week16; n=5,6,3,6,6	1.2 (± 6.42)	-9.8 (± 9.83)	-8.3 (± 2.52)	-9.2 (± 16.75)
ALT; Week2; n=9,9,9,9,10	10.4 (± 28.1)	24.1 (± 65.25)	35.3 (± 68.85)	10.7 (± 23.49)
ALT; Week3; n=1,1,1,0,0	5 (± 99999)	-2 (± 99999)	5 (± 99999)	99999 (± 99999)
ALT; Week4; n=8,9,8,9,9	0 (± 5.63)	1.8 (± 13.71)	67.3 (± 156.91)	7.7 (± 17.15)
ALT; Week5; n=0,0,3,1,1	99999 (± 99999)	99999 (± 99999)	40 (± 67.18)	17 (± 99999)
ALT; Week6; n=7,10,7,10,8	56.1 (± 149.97)	1 (± 4.67)	9.3 (± 27.37)	27.37 (± 4.36)
ALT; Week8; n=9,7,9,9,9	-0.4 (± 4.98)	1.3 (± 9.95)	-2.3 (± 13.02)	0.8 (± 3.11)
ALT; Week10; n=7,8,4,7,8	4.3 (± 13.31)	-2.4 (± 6.99)	1.8 (± 4.27)	1.3 (± 3.9)
ALT; Week12; n=7,7,7,8,7	9.6 (± 24.79)	-1.6 (± 6.16)	-5.3 (± 11.87)	4 (± 5.32)
ALT; Week16; n=5,6,3,6,6	2 (± 6.44)	3.5 (± 14.45)	2.3 (± 3.79)	-1.2 (± 5.31)
AST; Week2; n=9,9,9,9,10	9.7 (± 21.6)	37.6 (± 106.14)	37.7 (± 61.72)	14.8 (± 23.69)
AST; Week3; n=1,1,1,0,0	6 (± 99999)	2 (± 99999)	-24 (± 99999)	99999 (± 99999)
AST; Week4; n=8,9,8,9,9	-2.8 (± 5.85)	-0.1 (± 3.14)	25.9 (± 68.92)	5 (± 3.04)
AST; Week5; n=0,0,3,1,1	99999 (± 99999)	99999 (± 99999)	-4.3 (± 16.92)	-1 (± 99999)
AST; Week6; n=7,10,7,10,8	25.6 (± 66.39)	1.4 (± 4.2)	5 (± 23.47)	2.5 (± 7.49)
AST; Week8; n=9,7,9,9,9	1 (± 6.71)	2.7 (± 7.48)	-3.2 (± 10.8)	4 (± 4.66)
AST; Week10; n=7,8,4,7,8	4.4 (± 7.61)	-0.9 (± 5.22)	2.5 (± 5)	4.9 (± 3.29)
AST; Week12; n=7,7,7,8,7	8 (± 17.95)	1.1 (± 5.79)	-2 (± 11.55)	8.5 (± 7.03)
AST; Week16; n=5,6,3,6,6	1.6 (± 6.66)	0.3 (± 9.52)	2.3 (± 3.06)	-0.2 (± 3.25)
CK; Week2; n=9,9,9,9,10	7.4 (± 10.51)	287.9 (± 809.45)	38.9 (± 53.16)	41.9 (± 31.62)
CK; Week3; n=1,1,1,0,0	0 (± 99999)	-27 (± 99999)	-30 (± 99999)	99999 (± 99999)
CK; Week4; n=8,9,8,9,9	2.6 (± 15.18)	25.1 (± 15.14)	19.3 (± 26.12)	55.9 (± 54.49)
CK; Week5; n=0,0,3,1,1	99999 (± 99999)	99999 (± 99999)	83 (± 154.15)	-19 (± 99999)
CK; Week6; n=7,10,7,10,8	21.3 (± 30.6)	16.8 (± 17.16)	26.3 (± 37.3)	59.9 (± 125.28)
CK; Week8; n=9,7,9,9,9	12.5 (± 17.03)	27.6 (± 26.79)	21.4 (± 53.68)	68.4 (± 57.07)
CK; Week10; n=7,8,4,7,8	18.7 (± 20.25)	34.5 (± 31)	53.3 (± 45.68)	81.1 (± 63.2)
CK; Week12; n=7,7,7,8,7	21.7 (± 24.56)	28.9 (± 20.36)	12.9 (± 50.7)	173.6 (± 265.21)
CK; Week16; n=5,6,3,6,6	25.6 (± 39.6)	15.7 (± 10.52)	-4.3 (± 19.14)	18.5 (± 25.56)
GGT; Week2; n=9,9,9,9,10	1 (± 4.74)	15.7 (± 45.96)	5.9 (± 18.1)	0.2 (± 4.92)
GGT; Week3; n=1,1,1,0,0	0 (± 99999)	-2 (± 99999)	19 (± 99999)	99999 (± 99999)
GGT; Week4; n=8,9,8,9,9	0.5 (± 4.14)	4.6 (± 25.5)	82.8 (± 197.06)	6.4 (± 25.04)
GGT; Week5; n=0,0,3,1,1	99999 (± 99999)	99999 (± 99999)	-25 (± 99999)	42 (± 99999)
GGT; Week6; n=7,10,7,10,8	5 (± 14.05)	1.2 (± 12.74)	1.2 (± 20.68)	3.1 (± 8.17)
GGT; Week8; n=9,7,9,9,9	-1.5 (± 8.67)	-0.3 (± 11.25)	7.2 (± 29.11)	0.9 (± 5.62)
GGT; Week10; n=7,8,4,7,8	-0.3 (± 3.73)	-4.1 (± 8.53)	0.8 (± 6.18)	-2.6 (± 2.76)
GGT; Week12; n=7,7,7,8,7	3.4 (± 13.2)	-4.3 (± 8.86)	-5.3 (± 16.5)	-1.5 (± 3.93)
GGT; Week16; n=5,6,3,6,6	0.8 (± 3.96)	-2.5 (± 5.09)	2 (± 5.2)	-1.3 (± 4.27)
LDH; Week2; n=9,9,9,9,10	7.7 (± 21.75)	61.3 (± 148.63)	73.1 (± 70.39)	49.3 (± 62.86)
LDH; Week3; n=1,1,1,0,0	18 (± 99999)	6 (± 99999)	-2 (± 99999)	99999 (± 99999)

LDH; Week4; n=8,9,8,9,9	-17.6 (± 55.64)	11.6 (± 12.85)	80.5 (± 160.09)	31.8 (± 32.28)
LDH; Week5; n=0,0,3,1,1	99999 (± 99999)	99999 (± 99999)	45 (± 82.02)	43 (± 99999)
LDH; Week6; n=7,10,7,10,8	18.7 (± 49.19)	10.1 (± 20.43)	21.3 (± 31.78)	36.8 (± 36.43)
LDH; Week8; n=9,7,9,9,9	-11.8 (± 36.81)	3.7 (± 18.59)	14.8 (± 21.62)	40.4 (± 25.95)
LDH; Week10; n=7,8,4,7,8	-3.7 (± 25.92)	22.4 (± 25.05)	23.8 (± 22.91)	41.3 (± 31.37)
LDH; Week12; n=7,7,7,8,7	0.6 (± 27.16)	18.4 (± 16.92)	9.7 (± 32.91)	46 (± 34.33)
LDH; Week16; n=5,6,3,6,6	-2.2 (± 28.59)	9.3 (± 18.91)	4.3 (± 14.05)	17.7 (± 18.11)

Notes:

[65] - ITT Population. "Not available (NA)" data is presented as "99999"

[66] - ITT Population. "Not available (NA)" data is presented as "99999"

[67] - ITT Population. "Not available (NA)" data is presented as "99999"

[68] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[69]			
Units: International units per liter				
arithmetic mean (standard deviation)				
ALP; Week2; n=9,9,9,9,10	-3.7 (± 9.33)			
ALP; Week3; n=1,1,1,0,0	99999 (± 99999)			
ALP; Week4; n=8,9,8,9,9	0.3 (± 20.46)			
ALP; Week5; n=0,0,3,1,1	4 (± 99999)			
ALP; Week6; n=7,10,7,10,8	-2 (± 10.94)			
ALP; Week8; n=9,7,9,9,9	-3.3 (± 10.7)			
ALP; Week10; n=7,8,4,7,8	0.6 (± 13.32)			
ALP; Week12; n=7,7,7,8,7	-3.6 (± 8.14)			
ALP; Week16; n=5,6,3,6,6	11.7 (± 37.75)			
ALT; Week2; n=9,9,9,9,10	1.4 (± 4.06)			
ALT; Week3; n=1,1,1,0,0	99999 (± 99999)			
ALT; Week4; n=8,9,8,9,9	1.1 (± 6.83)			
ALT; Week5; n=0,0,3,1,1	0 (± 99999)			
ALT; Week6; n=7,10,7,10,8	0.3 (± 4.65)			
ALT; Week8; n=9,7,9,9,9	1 (± 5.63)			
ALT; Week10; n=7,8,4,7,8	-1.9 (± 4.94)			
ALT; Week12; n=7,7,7,8,7	-0.9 (± 3.85)			
ALT; Week16; n=5,6,3,6,6	-0.7 (± 3.67)			
AST; Week2; n=9,9,9,9,10	2 (± 3.02)			
AST; Week3; n=1,1,1,0,0	99999 (± 99999)			
AST; Week4; n=8,9,8,9,9	0.8 (± 4.74)			
AST; Week5; n=0,0,3,1,1	0 (± 99999)			
AST; Week6; n=7,10,7,10,8	-0.5 (± 2)			
AST; Week8; n=9,7,9,9,9	0.3 (± 4.12)			
AST; Week10; n=7,8,4,7,8	-0.6 (± 4.57)			
AST; Week12; n=7,7,7,8,7	0 (± 2.31)			
AST; Week16; n=5,6,3,6,6	0.7 (± 2.58)			
CK; Week2; n=9,9,9,9,10	0.3 (± 6.58)			
CK; Week3; n=1,1,1,0,0	99999 (± 99999)			

CK; Week4; n=8,9,8,9,9	4.7 (± 13.72)			
CK; Week5; n=0,0,3,1,1	-5 (± 99999)			
CK; Week6; n=7,10,7,10,8	7.6 (± 22.19)			
CK; Week8; n=9,7,9,9,9	4.9 (± 13.36)			
CK; Week10; n=7,8,4,7,8	9.6 (± 34.85)			
CK; Week12; n=7,7,7,8,7	24.9 (± 52.2)			
CK; Week16; n=5,6,3,6,6	-1.8 (± 18.45)			
GGT; Week2; n=9,9,9,9,10	-0.6 (± 7.26)			
GGT; Week3; n=1,1,1,0,0	99999 (± 99999)			
GGT; Week4; n=8,9,8,9,9	4 (± 16.12)			
GGT; Week5; n=0,0,3,1,1	-2 (± 99999)			
GGT; Week6; n=7,10,7,10,8	-0.1 (± 7.3)			
GGT; Week8; n=9,7,9,9,9	-0.7 (± 6.26)			
GGT; Week10; n=7,8,4,7,8	-1.9 (± 6.38)			
GGT; Week12; n=7,7,7,8,7	-2.6 (± 4.79)			
GGT; Week16; n=5,6,3,6,6	6.3 (± 20.55)			
LDH; Week2; n=9,9,9,9,10	5.9 (± 20.62)			
LDH; Week3; n=1,1,1,0,0	99999 (± 99999)			
LDH; Week4; n=8,9,8,9,9	-7.7 (± 17.93)			
LDH; Week5; n=0,0,3,1,1	-1 (± 99999)			
LDH; Week6; n=7,10,7,10,8	-5.4 (± 15.68)			
LDH; Week8; n=9,7,9,9,9	-1.6 (± 20.43)			
LDH; Week10; n=7,8,4,7,8	-1.1 (± 11.92)			
LDH; Week12; n=7,7,7,8,7	3.9 (± 22.3)			
LDH; Week16; n=5,6,3,6,6	-1.5 (± 30.33)			

Notes:

[69] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in anion gap, calcium, cholesterol, chloride, carbon dioxide, glucose, HDL cholesterol, potassium, LDL cholesterol, magnesium, phosphate, sodium, triglycerides, urea, VLDL cholesterol at the indicated time points up to Week 16.

End point title	Change from Baseline in anion gap, calcium, cholesterol, chloride, carbon dioxide, glucose, HDL cholesterol, potassium, LDL cholesterol, magnesium, phosphate, sodium, triglycerides, urea, VLDL cholesterol at the indicated time points up to Week 16.[70]

End point description:

Change from Baseline in the anion gap, calcium, ionised calcium, cholesterol, chloride, carbon dioxide, glucose, high density lipoprotein (HDL) cholesterol (fasted and not fasted), potassium, low density lipoprotein (LDL) cholesterol (fasted and not fasted), magnesium, phosphate, sodium, triglycerides (fasted and not fasted), urea and very low density lipoprotein (VLDL) cholesterol values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (n=X,X,X,X,X). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[70] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[71]	10[72]	10[73]	10[74]
Units: Millimoles per liter				
arithmetic mean (standard deviation)				
Anion Gap; Week2; n=9,9,9,9,10	-1.8 (± 2.49)	-0.8 (± 2.39)	-1 (± 3.71)	-0.1 (± 2.37)
Anion Gap; Week3; n=1,1,1,0,0	-3 (± 99999)	-3 (± 99999)	-5 (± 99999)	99999 (± 99999)
Anion Gap; Week4; n=8,9,8,9,9	0 (± 3.55)	-0.8 (± 3.15)	-0.6 (± 4.57)	-1 (± 4.06)
Anion Gap; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	-9 (± 99999)	-3 (± 99999)
Anion Gap; Week6; n=6,10,6,9,7	0 (± 1.67)	-1 (± 3.09)	-1.7 (± 2.66)	-1.7 (± 2.5)
Anion Gap; Week8; n=8,7,8,9,9	-0.5 (± 2.56)	-0.9 (± 3.93)	-0.5 (± 3.93)	-0.3 (± 3.87)
Anion Gap; Week10; n=7,8,4,7,8	0 (± 2.94)	-1.3 (± 3.62)	-1.3 (± 2.5)	0 (± 2.08)
Anion Gap; Week12; n=6,7,7,8,7	2.3 (± 2.5)	-0.9 (± 3.08)	-1.3 (± 4.54)	-0.3 (± 2.82)
Anion Gap; Week16; n=5,6,3,6,6	-0.8 (± 2.77)	0.8 (± 3.19)	-2.3 (± 3.06)	-0.3 (± 2.88)
Calcium; Week2; n=9,9,9,9,10	-0.036 (± 0.0654)	-0.011 (± 0.0842)	-0.029 (± 0.0985)	-0.034 (± 0.0814)
Calcium; Week3; n=1,1,1,0,0	-0.12 (± 99999)	-0.06 (± 99999)	0.01 (± 99999)	99999 (± 99999)
Calcium; Week4; n=8,9,8,9,9	-0.001 (± 0.0517)	-0.007 (± 0.0667)	-0.01 (± 0.0404)	-0.02 (± 0.061)
Calcium; Week5; n=0,0,3,1,1	99999 (± 99999)	99999 (± 99999)	0.08 (± 99999)	0.19 (± 99999)
Calcium; Week6; n=7,10,7,10,8	-0.033 (± 0.0596)	0.023 (± 0.0952)	0.043 (± 0.1108)	-0.02 (± 0.0833)
Calcium; Week8; n=9,7,9,9,9	-0.051 (± 0.1109)	-0.02 (± 0.0728)	0.028 (± 0.0992)	0.002 (± 0.0856)
Calcium; Week10; n=7,8,4,7,8	-0.053 (± 0.0692)	-0.032 (± 0.0794)	0 (± 0.0606)	-0.013 (± 0.0685)
Calcium; Week12; n=7,7,7,8,7	-0.053 (± 0.0783)	-0.023 (± 0.105)	0.003 (± 0.0665)	-0.055 (± 0.0644)
Calcium; Week16; n=5,6,3,6,6	-0.02 (± 0.1288)	-0.065 (± 0.0779)	-0.03 (± 0.0755)	-0.04 (± 0.0654)
Calcium ionised; Week2; n=9,9,9,9,10	0.003 (± 0.032)	0.001 (± 0.0448)	-0.011 (± 0.0183)	-0.011 (± 0.0306)
Calcium ionised; Week3; n=1,1,1,0,0	-0.05 (± 99999)	0.01 (± 99999)	0.04 (± 99999)	99999 (± 99999)
Calcium ionised; Week4; n=8,9,8,9,9	0.009 (± 0.0314)	-0.002 (± 0.0268)	0.011 (± 0.0217)	0.001 (± 0.0392)
Calcium ionised; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	0.08 (± 99999)	0.14 (± 99999)
Calcium ionised; Week6; n=6,10,6,9,7	0.007 (± 0.0356)	0.004 (± 0.0357)	0.013 (± 0.0327)	0.01 (± 0.0456)
Calcium ionised; Week8; n=8,7,8,9,9	-0.019 (± 0.0491)	0.009 (± 0.0302)	0.03 (± 0.0283)	0.009 (± 0.0293)
Calcium ionised; Week10; n=7,8,4,7,8	0.003 (± 0.0359)	-0.01 (± 0.0351)	0.01 (± 0.0216)	0.006 (± 0.0315)
Calcium ionised; Week12; n=7,7,7,8,7	-0.016 (± 0.0506)	-0.013 (± 0.0427)	0.011 (± 0.0334)	-0.021 (± 0.0348)
Calcium ionised; Week16; n=5,6,3,6,6	0.012 (± 0.0396)	-0.018 (± 0.0382)	0.017 (± 0.0379)	-0.007 (± 0.0398)

Cholesterol; Week2; n=9,9,9,9,10	-0.126 (± 0.5514)	0.167 (± 0.4644)	-0.039 (± 0.4517)	0.316 (± 0.6995)
Cholesterol; Week3; n=1,1,1,0,0	-0.56 (± 99999)	-0.15 (± 99999)	1.51 (± 99999)	99999 (± 99999)
Cholesterol; Week4; n=8,9,8,9,9	0.197 (± 0.8224)	0.197 (± 0.7258)	0.519 (± 0.9386)	0.322 (± 0.6854)
Cholesterol; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	0.98 (± 99999)	-0.55 (± 99999)
Cholesterol; Week6; n=7,10,6,10,8	-0.023 (± 0.7105)	0.325 (± 0.5219)	0.472 (± 0.8739)	0.559 (± 0.7808)
Cholesterol; Week8; n=8,7,9,9,9	0.146 (± 0.5702)	-0.039 (± 0.3315)	0.466 (± 0.5557)	0.688 (± 0.8384)
Cholesterol; Week10; n=7,8,4,7,8	-0.061 (± 0.5494)	0.26 (± 0.5641)	0.195 (± 0.3747)	0.551 (± 0.6929)
Cholesterol; Week12; n=7,7,7,8,7	0.173 (± 0.5702)	0.147 (± 0.384)	0.119 (± 0.3293)	0.601 (± 0.5253)
Cholesterol; Week16; n=5,6,3,6,6	-0.472 (± 0.4219)	0.04 (± 0.3043)	0.133 (± 0.0569)	0.223 (± 0.4871)
Chloride; Week2; n=9,9,9,9,10	0.3 (± 2.6)	1 (± 1.73)	0.1 (± 3.22)	-1.3 (± 2.12)
Chloride; Week3; n=1,1,1,0,0	3 (± 99999)	-1 (± 99999)	-3 (± 99999)	99999 (± 99999)
Chloride; Week4; n=8,9,8,9,9	99999 (± 99999)	0.7 (± 1.94)	-0.9 (± 2.3)	-0.4 (± 2.4)
Chloride; Week5; n=0,0,1,1,1	-1.3 (± 1.39)	99999 (± 99999)	-1 (± 99999)	-3 (± 99999)
Chloride; Week6; n=7,10,6,10,8	-0.3 (± 1.11)	-0.8 (± 2.53)	-0.3 (± 1.51)	-0.3 (± 2.06)
Chloride; Week8; n=8,7,9,9,9	-0.5 (± 2.33)	1.6 (± 2.15)	0.1 (± 1.96)	-1.1 (± 3.06)
Chloride; Week10; n=7,8,4,7,8	0.9 (± 2.41)	0.9 (± 2.42)	0.3 (± 1.71)	-0.7 (± 1.25)
Chloride; Week12; n=7,7,7,8,7	0.3 (± 2.14)	1.4 (± 2.76)	0.3 (± 1.98)	-0.5 (± 2.88)
Chloride; Week16; n=5,6,3,6,6	-0.4 (± 2.19)	1.5 (± 2.35)	-0.7 (± 2.08)	-1.5 (± 2.66)
Carbon Dioxide; Week2; n=9,9,9,9,10	0 (± 1.8)	-1 (± 1.32)	-0.4 (± 3)	-0.1 (± 1.62)
Carbon Dioxide; Week3; n=1,1,1,0,0	-1 (± 99999)	3 (± 99999)	5 (± 99999)	99999 (± 99999)
Carbon Dioxide; Week4; n=8,9,8,9,9	-0.4 (± 2.77)	-1.3 (± 2.45)	0.4 (± 3.29)	0.2 (± 1.64)
Carbon Dioxide; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	7 (± 99999)	4 (± 99999)
Carbon Dioxide; Week6; n=7,10,6,10,8	-0.9 (± 2.19)	0.5 (± 2.17)	0.3 (± 1.51)	0.9 (± 2.69)
Carbon Dioxide; Week8; n=8,7,9,9,9	0.3 (± 1.98)	-1 (± 2.45)	-1.1 (± 3.59)	-0.1 (± 2.71)
Carbon Dioxide; Week10; n=7,8,4,7,8	-1.6 (± 2.88)	-0.1 (± 1.81)	0.3 (± 2.99)	0.6 (± 2.15)
Carbon Dioxide; Week12; n=7,7,7,8,7	-2.1 (± 2.34)	-1.3 (± 1.38)	-0.6 (± 3.64)	0.1 (± 2.42)
Carbon Dioxide; Week16; n=5,6,3,6,6	-0.2 (± 0.84)	-1.8 (± 1.83)	1.7 (± 1.53)	0.8 (± 2.23)
Glucose; Week2; n=9,9,9,9,10	0.2 (± 0.304)	0.04 (± 0.384)	0.27 (± 1.302)	0.03 (± 0.779)
Glucose; Week3; n=1,1,1,0,0	1.7 (± 99999)	-0.1 (± 99999)	-1.3 (± 99999)	99999 (± 99999)
Glucose; Week4; n=8,9,8,9,9	0.11 (± 0.348)	0.11 (± 0.276)	-0.14 (± 0.403)	0.12 (± 0.851)
Glucose; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	-0.5 (± 99999)	0.7 (± 99999)
Glucose; Week6; n=7,10,6,10,8	0.46 (± 0.506)	0.09 (± 0.428)	0.53 (± 1.813)	-0.08 (± 1.191)
Glucose; Week8; n=8,7,9,9,9	0.06 (± 0.444)	-0.01 (± 0.186)	0.26 (± 0.646)	0.11 (± 0.796)
Glucose; Week10; n=7,8,4,7,8	0.21 (± 0.334)	0.03 (± 0.271)	0 (± 0.356)	-0.2 (± 0.889)
Glucose; Week12; n=7,7,7,8,7	0.16 (± 0.613)	0.16 (± 0.424)	-0.31 (± 0.414)	-0.19 (± 0.559)
Glucose; Week16; n=5,6,3,6,6	0.12 (± 0.383)	0.13 (± 0.207)	-0.07 (± 0.289)	1.48 (± 4.014)
HDL Cholesterol, Fasted; Week2; n=0,1,0,0,1	99999 (± 99999)	-0.3 (± 99999)	99999 (± 99999)	99999 (± 99999)

HDL Cholesterol, Fasted; Week3; n=1,1,0,0,0	-0.18 (± 99999)	-0.27 (± 99999)	99999 (± 99999)	99999 (± 99999)
HDL Cholesterol, Fasted; Week4; n=1,1,2,0,1	0.66 (± 99999)	0.4 (± 99999)	0.225 (± 0.0354)	99999 (± 99999)
HDL Cholesterol, Fasted; Week6; n=0,1,0,1,0	99999 (± 99999)	0.1 (± 99999)	99999 (± 99999)	0.08 (± 99999)
HDL Cholesterol, Fasted; Week8; n=0,0,3,01	99999 (± 99999)	99999 (± 99999)	-0.013 (± 0.3664)	99999 (± 99999)
HDL Cholesterol, Fasted; Week10; n=2,1,0,0,0	0.125 (± 0.0354)	-0.2 (± 99999)	99999 (± 99999)	99999 (± 99999)
HDL Cholesterol, Fasted; Week12; n=5,6,4,6,5	0.06 (± 0.1925)	0.06 (± 0.1637)	0.098 (± 0.3063)	0.487 (± 0.3847)
HDL Cholesterol, Not fasted; Week2; n=9,8,9,9,9	-0.013 (± 0.1655)	0.145 (± 0.1305)	-0.24 (± 0.3226)	0.107 (± 0.4241)
HDL Cholesterol, Not fasted; Week3; n=0,0,1,0,0	99999 (± 99999)	99999 (± 99999)	-0.09 (± 99999)	99999 (± 99999)
HDL Cholesterol, Not fasted; Week4; n=7,8,6,9,8	-0.029 (± 0.1046)	0.16 (± 0.1336)	-0.145 (± 0.125)	0.294 (± 0.2932)
HDL Cholesterol, Not fasted; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	0.05 (± 99999)	0.05 (± 99999)
HDL Cholesterol, Not fasted; Week6; n=7,9,6,9,8	-0.05 (± 0.1751)	0.159 (± 0.309)	0.073 (± 0.207)	0.322 (± 0.2712)
HDL Cholesterol, Not fasted; Week8; n=8,7,6,8,8	0.066 (± 0.0639)	0.11 (± 0.2728)	0.033 (± 0.2309)	0.543 (± 0.4174)
HDL Cholesterol, Not fasted; Week10; n=5,7,4,7,7	-0.138 (± 0.1397)	0.136 (± 0.0969)	0.058 (± 0.2804)	0.464 (± 0.2531)
HDL Cholesterol, Not fasted; Week12; n=2,1,4,2,2	-0.165 (± 0.1909)	-0.1 (± 99999)	0.12 (± 0.1581)	0.175 (± 0.0212)
HDL Cholesterol, Not fasted; Week16; n=5,6,3,6,6	-0.278 (± 0.2805)	-0.003 (± 0.2211)	-0.2 (± 0.2931)	0.137 (± 0.1875)
Potassium; Week2; n=9,9,9,9,10	-0.18 (± 0.299)	0.01 (± 0.196)	-0.13 (± 0.312)	-0.18 (± 0.367)
Potassium; Week3; n=1,1,1,0,0	0 (± 99999)	0.2 (± 99999)	0.2 (± 99999)	99999 (± 99999)
Potassium; Week4; n=8,9,8,9,9	-0.06 (± 0.141)	0.07 (± 0.461)	-0.15 (± 0.421)	-0.16 (± 0.34)
Potassium; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	-0.4 (± 99999)	0 (± 99999)
Potassium; Week6; n=7,10,6,10,8	0.03 (± 0.214)	0.15 (± 0.403)	0.03 (± 0.197)	-0.18 (± 0.371)
Potassium; Week8; n=8,7,9,9,9	-0.06 (± 0.338)	0.03 (± 0.315)	0 (± 0.418)	-0.06 (± 0.283)
Potassium; Week10; n=7,8,4,7,8	-0.26 (± 0.223)	0.05 (± 0.382)	-0.03 (± 0.222)	-0.14 (± 0.42)
Potassium; Week12; n=7,7,7,8,7	-0.06 (± 0.113)	-0.04 (± 0.369)	0.04 (± 0.341)	-0.11 (± 0.383)
Potassium; Week16; n=5,6,3,6,6	-0.2 (± 0.292)	-0.08 (± 0.371)	0.07 (± 0.321)	-0.12 (± 0.286)
LDL Cholesterol, Fasted; Week2; n=0,1,0,0,1	99999 (± 99999)	-0.38 (± 99999)	99999 (± 99999)	99999 (± 99999)
LDL Cholesterol, Fasted; Week3; n=1,1,0,0,0	-0.62 (± 99999)	-0.34 (± 99999)	99999 (± 99999)	99999 (± 99999)
LDL Cholesterol, Fasted; Week4; n=1,1,2,0,1	1.5 (± 99999)	1.3 (± 99999)	0.52 (± 1.3576)	99999 (± 99999)
LDL Cholesterol, Fasted; Week6; n=0,1,0,1,0	99999 (± 99999)	-0.21 (± 99999)	99999 (± 99999)	-1 (± 99999)
LDL Cholesterol, Fasted; Week8; n=0,0,3,01	99999 (± 99999)	99999 (± 99999)	0.37 (± 0.2946)	99999 (± 99999)
LDL Cholesterol, Fasted; Week10; n=2,1,0,0,0	0.01 (± 0.396)	0.14 (± 99999)	99999 (± 99999)	99999 (± 99999)
LDL Cholesterol, Fasted; Week12; n=4,5,4,6,5	0.147 (± 0.287)	0 (± 0.3272)	0.105 (± 0.2464)	0.187 (± 0.283)

LDL Cholesterol, Not fasted; Week2; n=9,7,9,9,9	-0.271 (± 0.6127)	0.157 (± 0.5447)	-0.212 (± 0.3942)	0.144 (± 0.6862)
LDL Cholesterol, Not fasted; Week3; n=0,0,1,0,0	99999 (± 99999)	99999 (± 99999)	0.19 (± 99999)	99999 (± 99999)
LDL Cholesterol, Not fasted; Week4; n=7,7,6,9,8	-0.104 (± 0.4535)	-0.089 (± 0.3488)	-0.03 (± 0.3504)	0.086 (± 0.6037)
LDL Cholesterol, Not fasted; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	0.1 (± 99999)	-0.62 (± 99999)
LDL Cholesterol, Not fasted; Week6; n=7,8,6,9,8	-0.301 (± 0.6443)	0.349 (± 0.578)	0.052 (± 0.5242)	0.25 (± 0.5119)
LDL Cholesterol, Not fasted; Week8; n=8,6,6,8,8	0.143 (± 0.635)	0.085 (± 0.6563)	0.102 (± 0.4613)	0.166 (± 0.663)
LDL Cholesterol, Not fasted; Week10; n=5,6,4,7,7	-0.492 (± 0.2993)	0.385 (± 0.6471)	-0.198 (± 0.3826)	0.121 (± 0.6339)
LDL Cholesterol, Not fasted; Week12; n=2,1,4,2,2	-0.105 (± 0.8839)	0.43 (± 99999)	-0.253 (± 0.3269)	0.54 (± 0.3111)
LDL Cholesterol, Not fasted; Week16; n=5,5,3,6,6	-0.48 (± 0.6055)	0.294 (± 0.6993)	-0.267 (± 0.2479)	-0.055 (± 0.542)
Magnesium; Week2; n=9,9,9,9,10	-0.02 (± 0.0548)	0.023 (± 0.0904)	0.011 (± 0.0766)	0.019 (± 0.0417)
Magnesium; Week3; n=1,1,1,0,0	0.07 (± 99999)	0.13 (± 99999)	0.14 (± 99999)	99999 (± 99999)
Magnesium; Week4; n=8,9,8,9,9	0.015 (± 0.0207)	0.006 (± 0.0841)	0.025 (± 0.0573)	0.004 (± 0.0557)
Magnesium; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	0.08 (± 99999)	0 (± 99999)
Magnesium; Week6; n=7,10,6,10,8	-0.016 (± 0.0493)	0.009 (± 0.0745)	0.03 (± 0.0978)	0.007 (± 0.0675)
Magnesium; Week8; n=8,7,9,9,9	0.001 (± 0.0391)	0.013 (± 0.0909)	0.023 (± 0.063)	0 (± 0.0524)
Magnesium; Week10; n=7,8,4,7,8	-0.021 (± 0.0641)	0.023 (± 0.1057)	-0.06 (± 0.0572)	-0.013 (± 0.0468)
Magnesium; Week12; n=7,7,7,8,7	-0.007 (± 0.0509)	0.013 (± 0.0789)	-0.016 (± 0.0808)	-0.005 (± 0.0396)
Magnesium; Week16; n=5,6,3,6,6	-0.024 (± 0.0152)	0.032 (± 0.1005)	-0.05 (± 0.11)	-0.023 (± 0.0509)
Phosphate; Week2; n=9,9,9,9,10	-0.073 (± 0.1103)	-0.032 (± 0.2049)	-0.148 (± 0.1866)	-0.114 (± 0.2266)
Phosphate; Week3; n=1,1,1,0,0	-0.03 (± 99999)	0.03 (± 99999)	0.1 (± 99999)	99999 (± 99999)
Phosphate; Week4; n=8,9,8,9,9	-0.045 (± 0.1683)	-0.043 (± 0.114)	-0.134 (± 0.1987)	-0.197 (± 0.1091)
Phosphate; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	0.05 (± 99999)	-0.02 (± 99999)
Phosphate; Week6; n=7,10,6,10,8	0.004 (± 0.0704)	0.014 (± 0.1047)	0.095 (± 0.119)	-0.12 (± 0.1595)
Phosphate; Week8; n=8,7,9,9,9	-0.032 (± 0.3227)	0.026 (± 0.136)	0.059 (± 0.1365)	-0.09 (± 0.1179)
Phosphate; Week10; n=7,8,4,7,8	-0.051 (± 0.1788)	-0.054 (± 0.2326)	0.085 (± 0.2089)	-0.144 (± 0.1929)
Phosphate; Week12; n=7,7,7,8,7	-0.116 (± 0.2435)	-0.131 (± 0.2291)	0.071 (± 0.1065)	-0.105 (± 0.1775)
Phosphate; Week16; n=5,6,3,6,6	0.008 (± 0.1232)	-0.118 (± 0.1614)	-0.01 (± 0.1473)	-0.133 (± 0.2058)
Sodium; Week2; n=9,9,9,9,10	-1.1 (± 1.83)	-0.9 (± 1.45)	-1.3 (± 2.74)	-1.4 (± 1.01)
Sodium; Week3; n=1,1,1,0,0	-1 (± 99999)	-1 (± 99999)	-3 (± 99999)	99999 (± 99999)
Sodium; Week4; n=8,9,8,9,9	-1.6 (± 2)	-1.6 (± 1.13)	-1 (± 2.39)	-1.2 (± 2.22)
Sodium; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	-3 (± 99999)	-2 (± 99999)
Sodium; Week6; n=7,10,6,10,8	-0.7 (± 1.25)	-1.4 (± 1.71)	-1.7 (± 1.63)	-0.7 (± 1.57)

Sodium; Week8; n=8,7,9,9,9	-0.6 (± 2.26)	-0.4 (± 2.07)	-1.1 (± 2.76)	-1.6 (± 2.74)
Sodium; Week10; n=7,8,4,7,8	-0.4 (± 2.44)	-0.5 (± 1.07)	-0.5 (± 3)	-0.1 (± 1.46)
Sodium; Week12; n=7,7,7,8,7	-0.4 (± 1.13)	-0.9 (± 1.57)	-1.6 (± 2.99)	-0.6 (± 1.85)
Sodium; Week16; n=5,6,3,6,6	-1 (± 2)	0.3 (± 1.86)	-1.3 (± 3.21)	-1.2 (± 1.72)
Triglycerides, Fasted; Week2; n=0,1,0,0,1	99999 (± 99999)	2.68 (± 99999)	99999 (± 99999)	99999 (± 99999)
Triglycerides, Fasted; Week3; n=1,1,0,0,0	0.51 (± 99999)	1.01 (± 99999)	99999 (± 99999)	99999 (± 99999)
Triglycerides, Fasted; Week4; n=1,1,2,0,1	-1.25 (± 99999)	0.2 (± 99999)	0.55 (± 0.495)	99999 (± 99999)
Triglycerides, Fasted; Week6; n=0,1,0,1,0	99999 (± 99999)	0 (± 99999)	99999 (± 99999)	0.16 (± 99999)
Triglycerides, Fasted; Week8; n=0,0,3,01	99999 (± 99999)	99999 (± 99999)	0.29 (± 0.27)	99999 (± 99999)
Triglycerides, Fasted; Week10; n=2,1,0,0,0	0.44 (± 0.6788)	0.56 (± 99999)	99999 (± 99999)	99999 (± 99999)
Triglycerides, Fasted; Week12; n=5,6,4,6,5	0.474 (± 1.4676)	-0.252 (± 0.6544)	-0.072 (± 0.4272)	-0.232 (± 0.5087)
Triglycerides, Not Fasted; Week2; n=9,8,9,9,9	0.142 (± 0.6915)	-0.358 (± 0.783)	0.224 (± 0.6196)	-0.118 (± 0.397)
Triglycerides, Not Fasted; Week3; n=0,0,1,0,0	99999 (± 99999)	99999 (± 99999)	1.61 (± 99999)	99999 (± 99999)
Triglycerides, Not Fasted; Week4; n=7,8,6,9,8	-0.116 (± 0.533)	-0.208 (± 0.7373)	0.218 (± 0.3916)	-0.388 (± 0.3914)
Triglycerides, Not Fasted; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	0.36 (± 99999)	0.05 (± 99999)
Triglycerides, Not Fasted; Week6; n=7,9,6,9,8	0.316 (± 0.9129)	-0.239 (± 0.4658)	0.145 (± 0.2891)	0.05 (± 0.7227)
Triglycerides, Not Fasted; Week8; n=8,7,6,8,8	-0.182 (± 0.7551)	-0.299 (± 0.737)	0.093 (± 0.2452)	-0.314 (± 0.3539)
Triglycerides, Not Fasted; Week10; n=5,7,4,7,7	0.354 (± 0.441)	-0.38 (± 0.6995)	-0.03 (± 0.0622)	-0.259 (± 0.4313)
Triglycerides, Not Fasted; Week12; n=2,1,4,2,2	-0.065 (± 0.1344)	0.04 (± 99999)	-0.03 (± 0.1842)	-0.555 (± 0.7566)
Triglycerides, Not Fasted; Week16; n=5,6,3,6,6	0.082 (± 0.7262)	-0.235 (± 0.8101)	0.257 (± 0.3683)	-0.107 (± 0.4525)
Urea; Week2; n=9,9,9,9,10	0.6 (± 1.017)	0.7 (± 1.595)	-0.28 (± 1.28)	-0.08 (± 0.736)
Urea; Week3; n=1,1,1,0,0	-0.4 (± 99999)	1.2 (± 99999)	2.4 (± 99999)	99999 (± 99999)
Urea; Week4; n=8,9,8,9,9	0.56 (± 1.581)	-0.53 (± 0.957)	-0.33 (± 1.243)	0.21 (± 1.014)
Urea; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	1 (± 99999)	-1.6 (± 99999)
Urea; Week6; n=7,10,6,10,8	0.09 (± 1.224)	-0.05 (± 1.178)	0.32 (± 0.9)	0.14 (± 1.372)
Urea; Week8; n=8,7,9,9,9	-0.3 (± 1.331)	-1 (± 1.021)	0.09 (± 1.447)	0.37 (± 0.866)
Urea; Week10; n=7,8,4,7,8	0 (± 1.954)	-0.93 (± 1.077)	1.03 (± 1.615)	0.39 (± 1.804)
Urea; Week12; n=7,7,7,8,7	-0.51 (± 1.548)	-0.47 (± 1.889)	-0.11 (± 1.199)	0.41 (± 1.988)
Urea; Week16; n=5,6,3,6,6	-0.32 (± 1.069)	-0.68 (± 2.282)	-0.17 (± 0.666)	-0.03 (± 1.546)
VLDL Cholesterol; Week2; n=9,8,9,9,10	-0.014 (± 0.3899)	0.16 (± 0.4416)	0.081 (± 0.2732)	-0.008 (± 0.2493)
VLDL Cholesterol; Week3; n=1,1,1,0,0	0.24 (± 99999)	0.46 (± 99999)	0.75 (± 99999)	99999 (± 99999)
VLDL Cholesterol; Week4; n=8,8,8,9,9	-0.18 (± 0.2344)	0.065 (± 0.2066)	0.136 (± 0.1591)	-0.13 (± 0.1935)
VLDL Cholesterol; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	0.17 (± 99999)	0.02 (± 99999)

VLDL Cholesterol; Week6; n=7,9,6,10,8	0.073 (± 0.4708)	-0.004 (± 0.0879)	0.007 (± 0.1586)	0.071 (± 0.3474)
VLDL Cholesterol; Week8; n=8,6,9,9,9	-0.151 (± 0.4333)	0.003 (± 0.1986)	0.024 (± 0.1483)	-0.126 (± 0.1764)
VLDL Cholesterol; Week10; n=7,7,4,7,8	0.11 (± 0.2424)	0.01 (± 0.1751)	-0.098 (± 0.1531)	-0.064 (± 0.2046)
VLDL Cholesterol; Week12; n=6,6,7,8,7	-0.075 (± 0.0914)	0.018 (± 0.1486)	0.031 (± 0.1247)	-0.138 (± 0.251)
VLDL Cholesterol; Week16; n=5,5,3,6,6	-0.05 (± 0.2547)	0.038 (± 0.1659)	0.027 (± 0.2801)	0.012 (± 0.2164)

Notes:

[71] - ITT Population. "Not available (NA)" data is presented as "99999"

[72] - ITT Population. "Not available (NA)" data is presented as "99999"

[73] - ITT Population. "Not available (NA)" data is presented as "99999"

[74] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[75]			
Units: Millimoles per liter				
arithmetic mean (standard deviation)				
Anion Gap; Week2; n=9,9,9,9,10	-1.1 (± 3.48)			
Anion Gap; Week3; n=1,1,1,0,0	99999 (± 99999)			
Anion Gap; Week4; n=8,9,8,9,9	-0.7 (± 2.69)			
Anion Gap; Week5; n=0,0,1,1,1	-2 (± 99999)			
Anion Gap; Week6; n=6,10,6,9,7	0 (± 1)			
Anion Gap; Week8; n=8,7,8,9,9	-1.4 (± 1.51)			
Anion Gap; Week10; n=7,8,4,7,8	-1 (± 1.51)			
Anion Gap; Week12; n=6,7,7,8,7	-2.4 (± 3.1)			
Anion Gap; Week16; n=5,6,3,6,6	-0.7 (± 3.5)			
Calcium; Week2; n=9,9,9,9,10	-0.03 (± 0.1111)			
Calcium; Week3; n=1,1,1,0,0	99999 (± 99999)			
Calcium; Week4; n=8,9,8,9,9	-0.006 (± 0.0843)			
Calcium; Week5; n=0,0,3,1,1	0.11 (± 99999)			
Calcium; Week6; n=7,10,7,10,8	-0.049 (± 0.1166)			
Calcium; Week8; n=9,7,9,9,9	-0.059 (± 0.1125)			
Calcium; Week10; n=7,8,4,7,8	-0.046 (± 0.0825)			
Calcium; Week12; n=7,7,7,8,7	-0.027 (± 0.072)			
Calcium; Week16; n=5,6,3,6,6	-0.027 (± 0.1046)			
Calcium ionised; Week2; n=9,9,9,9,10	-0.012 (± 0.0326)			
Calcium ionised; Week3; n=1,1,1,0,0	99999 (± 99999)			
Calcium ionised; Week4; n=8,9,8,9,9	0.003 (± 0.0274)			
Calcium ionised; Week5; n=0,0,1,1,1	0 (± 99999)			
Calcium ionised; Week6; n=6,10,6,9,7	-0.023 (± 0.0446)			

Calcium ionised; Week8; n=8,7,8,9,9	-0.003 (± 0.0433)			
Calcium ionised; Week10; n=7,8,4,7,8	-0.001 (± 0.0356)			
Calcium ionised; Week12; n=7,7,7,8,7	0.013 (± 0.039)			
Calcium ionised; Week16; n=5,6,3,6,6	0.007 (± 0.0372)			
Cholesterol; Week2; n=9,9,9,9,10	0.079 (± 0.3626)			
Cholesterol; Week3; n=1,1,1,0,0	99999 (± 99999)			
Cholesterol; Week4; n=8,9,8,9,9	-0.023 (± 0.3443)			
Cholesterol; Week5; n=0,0,1,1,1	0.92 (± 99999)			
Cholesterol; Week6; n=7,10,6,10,8	-0.103 (± 0.5727)			
Cholesterol; Week8; n=8,7,9,9,9	-0.171 (± 0.3699)			
Cholesterol; Week10; n=7,8,4,7,8	-0.549 (± 0.2554)			
Cholesterol; Week12; n=7,7,7,8,7	-0.176 (± 0.348)			
Cholesterol; Week16; n=5,6,3,6,6	-0.26 (± 0.3636)			
Chloride; Week2; n=9,9,9,9,10	0.1 (± 2.42)			
Chloride; Week3; n=1,1,1,0,0	99999 (± 99999)			
Chloride; Week4; n=8,9,8,9,9	0.7 (± 1.73)			
Chloride; Week5; n=0,0,1,1,1	-6 (± 99999)			
Chloride; Week6; n=7,10,6,10,8	0.3 (± 1.67)			
Chloride; Week8; n=8,7,9,9,9	0.6 (± 1.67)			
Chloride; Week10; n=7,8,4,7,8	0.9 (± 2.1)			
Chloride; Week12; n=7,7,7,8,7	0.6 (± 1.13)			
Chloride; Week16; n=5,6,3,6,6	1.2 (± 1.33)			
Carbon Dioxide; Week2; n=9,9,9,9,10	1.1 (± 2.38)			
Carbon Dioxide; Week3; n=1,1,1,0,0	99999 (± 99999)			
Carbon Dioxide; Week4; n=8,9,8,9,9	0.9 (± 2.03)			
Carbon Dioxide; Week5; n=0,0,1,1,1	4 (± 99999)			
Carbon Dioxide; Week6; n=7,10,6,10,8	0.4 (± 1.6)			
Carbon Dioxide; Week8; n=8,7,9,9,9	0.9 (± 2.26)			
Carbon Dioxide; Week10; n=7,8,4,7,8	0.5 (± 1.77)			
Carbon Dioxide; Week12; n=7,7,7,8,7	1.7 (± 2.56)			
Carbon Dioxide; Week16; n=5,6,3,6,6	0 (± 3.69)			
Glucose; Week2; n=9,9,9,9,10	0.07 (± 0.368)			
Glucose; Week3; n=1,1,1,0,0	99999 (± 99999)			
Glucose; Week4; n=8,9,8,9,9	0.32 (± 0.338)			
Glucose; Week5; n=0,0,1,1,1	0.4 (± 99999)			
Glucose; Week6; n=7,10,6,10,8	0.69 (± 1.106)			
Glucose; Week8; n=8,7,9,9,9	0 (± 0.403)			
Glucose; Week10; n=7,8,4,7,8	0.05 (± 0.487)			
Glucose; Week12; n=7,7,7,8,7	-0.03 (± 0.386)			
Glucose; Week16; n=5,6,3,6,6	-0.02 (± 0.271)			

HDL Cholesterol, Fasted; Week2; n=0,1,0,0,1	0.25 (± 99999)			
HDL Cholesterol, Fasted; Week3; n=1,1,0,0,0	99999 (± 99999)			
HDL Cholesterol, Fasted; Week4; n=1,1,2,0,1	-0.09 (± 99999)			
HDL Cholesterol, Fasted; Week6; n=0,1,0,1,0	99999 (± 99999)			
HDL Cholesterol, Fasted; Week8; n=0,0,3,01	-0.08 (± 99999)			
HDL Cholesterol, Fasted; Week10; n=2,1,0,0,0	0.03 (± 99999)			
HDL Cholesterol, Fasted; Week12; n=5,6,4,6,5	-0.158 (± 0.177)			
HDL Cholesterol, Not fasted; Week2; n=9,8,9,9,9	0.046 (± 0.2051)			
HDL Cholesterol, Not fasted; Week3; n=0,0,1,0,0	99999 (± 99999)			
HDL Cholesterol, Not fasted; Week4; n=7,8,6,9,8	0.017 (± 0.1951)			
HDL Cholesterol, Not fasted; Week5; n=0,0,1,1,1	0.06 (± 99999)			
HDL Cholesterol, Not fasted; Week6; n=7,9,6,9,8	0.04 (± 0.3704)			
HDL Cholesterol, Not fasted; Week8; n=8,7,6,8,8	-0.05 (± 0.2594)			
HDL Cholesterol, Not fasted; Week10; n=5,7,4,7,7	-0.151 (± 0.2769)			
HDL Cholesterol, Not fasted; Week12; n=2,1,4,2,2	0.045 (± 0.1344)			
HDL Cholesterol, Not fasted; Week16; n=5,6,3,6,6	-0.103 (± 0.2808)			
Potassium; Week2; n=9,9,9,9,10	0.1 (± 0.447)			
Potassium; Week3; n=1,1,1,0,0	99999 (± 99999)			
Potassium; Week4; n=8,9,8,9,9	0.13 (± 0.367)			
Potassium; Week5; n=0,0,1,1,1	0.2 (± 99999)			
Potassium; Week6; n=7,10,6,10,8	0.13 (± 0.392)			
Potassium; Week8; n=8,7,9,9,9	-0.08 (± 0.399)			
Potassium; Week10; n=7,8,4,7,8	0.04 (± 0.207)			
Potassium; Week12; n=7,7,7,8,7	-0.09 (± 0.334)			
Potassium; Week16; n=5,6,3,6,6	0 (± 0.363)			
LDL Cholesterol, Fasted; Week2; n=0,1,0,0,1	0.4 (± 99999)			
LDL Cholesterol, Fasted; Week3; n=1,1,0,0,0	99999 (± 99999)			
LDL Cholesterol, Fasted; Week4; n=1,1,2,0,1	0.07 (± 99999)			
LDL Cholesterol, Fasted; Week6; n=0,1,0,1,0	99999 (± 99999)			
LDL Cholesterol, Fasted; Week8; n=0,0,3,01	-0.35 (± 99999)			
LDL Cholesterol, Fasted; Week10; n=2,1,0,0,0	-0.18 (± 99999)			
LDL Cholesterol, Fasted; Week12; n=4,5,4,6,5	0.096 (± 0.3396)			
LDL Cholesterol, Not fasted; Week2; n=9,7,9,9,9	-0.016 (± 0.2168)			

LDL Cholesterol, Not fasted; Week3; n=0,0,1,0,0	99999 (± 99999)			
LDL Cholesterol, Not fasted; Week4; n=7,7,6,9,8	-0.023 (± 0.5208)			
LDL Cholesterol, Not fasted; Week5; n=0,0,1,1,1	0.55 (± 99999)			
LDL Cholesterol, Not fasted; Week6; n=7,8,6,9,8	-0.101 (± 0.428)			
LDL Cholesterol, Not fasted; Week8; n=8,6,6,8,8	0.091 (± 0.3331)			
LDL Cholesterol, Not fasted; Week10; n=5,6,4,7,7	-0.424 (± 0.2717)			
LDL Cholesterol, Not fasted; Week12; n=2,1,4,2,2	0.105 (± 0.0919)			
LDL Cholesterol, Not fasted; Week16; n=5,5,3,6,6	-0.082 (± 0.3476)			
Magnesium; Week2; n=9,9,9,9,10	-0.003 (± 0.046)			
Magnesium; Week3; n=1,1,1,0,0	99999 (± 99999)			
Magnesium; Week4; n=8,9,8,9,9	-0.013 (± 0.0433)			
Magnesium; Week5; n=0,0,1,1,1	0.05 (± 99999)			
Magnesium; Week6; n=7,10,6,10,8	0.004 (± 0.0555)			
Magnesium; Week8; n=8,7,9,9,9	-0.019 (± 0.0523)			
Magnesium; Week10; n=7,8,4,7,8	-0.009 (± 0.0562)			
Magnesium; Week12; n=7,7,7,8,7	-0.019 (± 0.0521)			
Magnesium; Week16; n=5,6,3,6,6	-0.018 (± 0.0571)			
Phosphate; Week2; n=9,9,9,9,10	0.009 (± 0.193)			
Phosphate; Week3; n=1,1,1,0,0	99999 (± 99999)			
Phosphate; Week4; n=8,9,8,9,9	-0.074 (± 0.1664)			
Phosphate; Week5; n=0,0,1,1,1	0.22 (± 99999)			
Phosphate; Week6; n=7,10,6,10,8	-0.028 (± 0.2064)			
Phosphate; Week8; n=8,7,9,9,9	-0.1 (± 0.2302)			
Phosphate; Week10; n=7,8,4,7,8	-0.039 (± 0.1174)			
Phosphate; Week12; n=7,7,7,8,7	0.026 (± 0.1439)			
Phosphate; Week16; n=5,6,3,6,6	0.023 (± 0.0816)			
Sodium; Week2; n=9,9,9,9,10	0.1 (± 1.6)			
Sodium; Week3; n=1,1,1,0,0	99999 (± 99999)			
Sodium; Week4; n=8,9,8,9,9	0.7 (± 2.24)			
Sodium; Week5; n=0,0,1,1,1	-4 (± 99999)			
Sodium; Week6; n=7,10,6,10,8	0.5 (± 2.39)			
Sodium; Week8; n=8,7,9,9,9	0 (± 1.73)			
Sodium; Week10; n=7,8,4,7,8	0.4 (± 1.69)			
Sodium; Week12; n=7,7,7,8,7	0 (± 1.29)			
Sodium; Week16; n=5,6,3,6,6	0.7 (± 1.51)			

Triglycerides, Fasted; Week2; n=0,1,0,0,1	0.06 (± 99999)			
Triglycerides, Fasted; Week3; n=1,1,0,0,0	99999 (± 99999)			
Triglycerides, Fasted; Week4; n=1,1,2,0,1	0.46 (± 99999)			
Triglycerides, Fasted; Week6; n=0,1,0,1,0	99999 (± 99999)			
Triglycerides, Fasted; Week8; n=0,0,3,01	-0.45 (± 99999)			
Triglycerides, Fasted; Week10; n=2,1,0,0,0	-0.53 (± 99999)			
Triglycerides, Fasted; Week12; n=5,6,4,6,5	-0.394 (± 0.4215)			
Triglycerides, Not Fasted; Week2; n=9,8,9,9,9	0.146 (± 0.3789)			
Triglycerides, Not Fasted; Week3; n=0,0,1,0,0	99999 (± 99999)			
Triglycerides, Not Fasted; Week4; n=7,8,6,9,8	0.099 (± 0.3549)			
Triglycerides, Not Fasted; Week5; n=0,0,1,1,1	-0.1 (± 99999)			
Triglycerides, Not Fasted; Week6; n=7,9,6,9,8	0.105 (± 0.3932)			
Triglycerides, Not Fasted; Week8; n=8,7,6,8,8	-0.02 (± 0.2491)			
Triglycerides, Not Fasted; Week10; n=5,7,4,7,7	0.199 (± 0.4482)			
Triglycerides, Not Fasted; Week12; n=2,1,4,2,2	-0.015 (± 0.3748)			
Triglycerides, Not Fasted; Week16; n=5,6,3,6,6	0.2 (± 0.2739)			
Urea; Week2; n=9,9,9,9,10	-0.1 (± 1.357)			
Urea; Week3; n=1,1,1,0,0	99999 (± 99999)			
Urea; Week4; n=8,9,8,9,9	0.08 (± 1.352)			
Urea; Week5; n=0,0,1,1,1	-0.1 (± 99999)			
Urea; Week6; n=7,10,6,10,8	0.56 (± 0.877)			
Urea; Week8; n=8,7,9,9,9	0.16 (± 1.014)			
Urea; Week10; n=7,8,4,7,8	-0.06 (± 1.158)			
Urea; Week12; n=7,7,7,8,7	0.29 (± 0.501)			
Urea; Week16; n=5,6,3,6,6	-0.18 (± 1.085)			
VLDL Cholesterol; Week2; n=9,8,9,9,10	0.009 (± 0.0681)			
VLDL Cholesterol; Week3; n=1,1,1,0,0	99999 (± 99999)			
VLDL Cholesterol; Week4; n=8,8,8,9,9	0.01 (± 0.1916)			
VLDL Cholesterol; Week5; n=0,0,1,1,1	0.12 (± 99999)			
VLDL Cholesterol; Week6; n=7,9,6,10,8	-0.011 (± 0.176)			
VLDL Cholesterol; Week8; n=8,6,9,9,9	-0.104 (± 0.1613)			
VLDL Cholesterol; Week10; n=7,7,4,7,8	-0.014 (± 0.2629)			
VLDL Cholesterol; Week12; n=6,6,7,8,7	-0.116 (± 0.2032)			
VLDL Cholesterol; Week16; n=5,5,3,6,6	-0.012 (± 0.1447)			

Notes:

[75] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in bilirubin, creatinine, iron binding capacity, iron and uric acid at the indicated time points up to Week 16

End point title	Change from Baseline in bilirubin, creatinine, iron binding capacity, iron and uric acid at the indicated time points up to Week 16[76]

End point description:

Change from Baseline in the bilirubin, direct and indirect bilirubin, creatinine, total iron binding capacity (TIBC), unsaturated iron binding capacity (UIBC), iron and uric acid values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[76] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[77]	10[78]	10[79]	10[80]
Units: Micromoles per liter				
arithmetic mean (standard deviation)				
Direct Bilirubin; Week2; n=9,9,9,9,10	-0.1 (± 1.17)	0.2 (± 0.83)	-0.1 (± 0.93)	-0.1 (± 0.33)
Direct Bilirubin; Week3; n=1,1,1,0,0	0 (± 99999)	-1 (± 99999)	1 (± 99999)	99999 (± 99999)
Direct Bilirubin; Week4; n=8,9,8,9,9	0.1 (± 0.99)	0.6 (± 0.88)	0.6 (± 1.19)	0.4 (± 0.53)
Direct Bilirubin; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	2 (± 99999)	1 (± 99999)
Direct Bilirubin; Week6; n=7,10,6,10,8	0.3 (± 0.95)	-0.1 (± 1.1)	0.8 (± 1.17)	0 (± 0.47)
Direct Bilirubin; Week8; n=8,7,9,9,9	0.3 (± 1.04)	0.6 (± 1.13)	0.2 (± 1.3)	0 (± 0.87)
Direct Bilirubin; Week10; n=7,8,4,7,8	0.3 (± 0.76)	0.3 (± 0.71)	0.8 (± 0.96)	0.6 (± 0.53)
Direct Bilirubin; Week12; n=7,7,7,8,7	0.4 (± 0.79)	0.4 (± 0.79)	0.4 (± 0.98)	-0.1 (± 0.83)
Direct Bilirubin; Week16; n=5,6,3,6,6	-0.4 (± 0.89)	0.3 (± 0.82)	1 (± 1.73)	0.2 (± 0.41)
Bilirubin; Week2; n=9,9,9,9,10	0.8 (± 1.99)	0.8 (± 2.44)	-0.4 (± 1.42)	0.6 (± 1.94)
Bilirubin; Week3; n=1,1,1,0,0	0 (± 99999)	-2 (± 99999)	6 (± 99999)	99999 (± 99999)
Bilirubin; Week4; n=8,9,8,9,9	0.5 (± 2.27)	1.9 (± 2.52)	2.9 (± 4.16)	1.6 (± 1.33)
Bilirubin; Week5; n=0,0,3,1,1	99999 (± 99999)	99999 (± 99999)	4.3 (± 2.52)	0 (± 99999)
Bilirubin; Week6; n=7,10,7,10,8	1.9 (± 3.02)	-0.2 (± 2.15)	2.9 (± 3.29)	0.3 (± 1.57)
Bilirubin; Week8; n=8,7,9,9,9	1.4 (± 2.01)	-0.7 (± 3.4)	0.9 (± 4.34)	0.4 (± 1.13)

Bilirubin; Week10; n=7,8,4,7,8	0.4 (± 2.7)	0 (± 3.02)	1.8 (± 4.57)	1.4 (± 1.99)
Bilirubin; Week12; n=7,7,7,8,7	0.3 (± 2.63)	0.6 (± 3.64)	2 (± 3.92)	0.1 (± 2.47)
Bilirubin; Week16; n=5,6,3,6,6	-0.4 (± 2.7)	0.2 (± 2.79)	4 (± 6.93)	1 (± 2.1)
Indirect Bilirubin; Week2; n=9,9,9,9,10	0.9 (± 1.83)	0.6 (± 2.24)	-0.3 (± 0.87)	0.7 (± 1.66)
Indirect Bilirubin; Week3; n=1,1,1,0,0	0 (± 99999)	-1 (± 99999)	5 (± 99999)	99999 (± 99999)
Indirect Bilirubin; Week4; n=8,9,8,9,9	0.4 (± 2.13)	1.3 (± 2.35)	2.3 (± 3.65)	1.1 (± 1.05)
Indirect Bilirubin; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	5 (± 99999)	-1 (± 99999)
Indirect Bilirubin; Week6; n=7,10,6,10,8	1.6 (± 2.57)	-0.1 (± 2.18)	1.5 (± 2.59)	0.3 (± 1.34)
Indirect Bilirubin; Week8; n=8,7,9,9,9	1.4 (± 2.07)	-1.3 (± 3.04)	0.7 (± 3.57)	0.4 (± 0.73)
Indirect Bilirubin; Week10; n=7,8,4,7,8	0.1 (± 2.85)	-0.3 (± 3.11)	1 (± 3.92)	0.9 (± 1.57)
Indirect Bilirubin; Week12; n=7,7,7,8,7	-0.1 (± 2.48)	0.1 (± 3.34)	1.6 (± 3.41)	0.3 (± 1.83)
Indirect Bilirubin; Week16; n=5,6,3,6,6	0 (± 2.92)	-0.2 (± 2.93)	3 (± 5.2)	0.8 (± 1.72)
Creatinine; Week2; n=9,9,9,9,10	2.31 (± 9.124)	1.79 (± 3.958)	3.34 (± 5.611)	6.09 (± 6.748)
Creatinine; Week3; n=1,1,1,0,0	8.5 (± 99999)	-3.4 (± 99999)	3.5 (± 99999)	99999 (± 99999)
Creatinine; Week4; n=8,9,8,9,9	2.4 (± 5.475)	1.34 (± 6.522)	1.71 (± 5.713)	5.72 (± 5.253)
Creatinine; Week5; n=0,0,3,1,1	99999 (± 99999)	99999 (± 99999)	9.8 (± 99999)	2.8 (± 99999)
Creatinine; Week6; n=6,9,7,9,8	0.67 (± 5.167)	1.22 (± 3.868)	2.17 (± 3.472)	5.87 (± 7.206)
Creatinine; Week8; n=9,7,9,9,9	4.66 (± 4.364)	6.19 (± 6.258)	3.49 (± 7.516)	8.14 (± 6.011)
Creatinine; Week10; n=7,8,4,7,8	2.3 (± 4.974)	3.03 (± 6.911)	5.3 (± 3.997)	10.19 (± 5.328)
Creatinine; Week12; n=7,7,7,8,7	-0.29 (± 3.402)	1.49 (± 6.839)	2.26 (± 7.047)	5.97 (± 6.331)
Creatinine; Week16; n=5,6,3,6,6	-0.26 (± 3.259)	0.5 (± 4.944)	1.33 (± 3.781)	-0.03 (± 5.32)
TIBC; Week2; n=9,9,9,9,10	-1.6 (± 4.33)	1.2 (± 2.99)	1 (± 4.5)	3.8 (± 4.74)
TIBC; Week3; n=1,1,1,0,0	5 (± 99999)	-8 (± 99999)	0 (± 99999)	99999 (± 99999)
TIBC; Week4; n=8,9,8,9,9	1.1 (± 5.46)	2.7 (± 4.66)	4 (± 6.5)	3.4 (± 4.67)
TIBC; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	-4 (± 99999)	3 (± 99999)
TIBC; Week6; n=7,10,6,10,8	0.3 (± 2.21)	0.5 (± 5.66)	4 (± 2.76)	3.9 (± 8.2)
TIBC; Week8; n=8,7,9,9,8	1.3 (± 6.8)	-0.7 (± 5.06)	2.9 (± 5.09)	4.2 (± 9.82)
TIBC; Week10; n=7,8,4,7,8	0.1 (± 4.06)	2 (± 4.14)	0.8 (± 5.68)	7 (± 8.94)
TIBC; Week12; n=7,7,7,8,7	1.1 (± 5.27)	3.4 (± 3.99)	2.3 (± 6.6)	7.1 (± 9.78)
TIBC; Week16; n=5,6,3,6,6	-1.2 (± 2.86)	3.7 (± 4.32)	0.3 (± 5.86)	3.7 (± 6.31)
UIBC; Week2; n=9,9,9,9,10	-3.2 (± 9.24)	-2.4 (± 11.39)	0.4 (± 9.46)	3 (± 9.8)
UIBC; Week3; n=1,1,1,0,0	5 (± 99999)	-13 (± 99999)	-31 (± 99999)	99999 (± 99999)
UIBC; Week4; n=8,9,8,9,9	3.8 (± 7.25)	-1.6 (± 10.09)	0.5 (± 10.98)	1.3 (± 6.4)
UIBC; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	-4 (± 99999)	12 (± 99999)
UIBC; Week6; n=7,10,6,10,8	-3.1 (± 8.07)	-0.8 (± 5.31)	6 (± 8.15)	4.5 (± 11.31)
UIBC; Week8; n=8,7,9,9,9	3.3 (± 8.21)	1.3 (± 8.85)	4.3 (± 5.96)	5.4 (± 9.96)
UIBC; Week10; n=7,8,4,7,8	0.7 (± 8.01)	4.8 (± 7.92)	-1.3 (± 9.74)	3.6 (± 10.18)
UIBC; Week12; n=7,7,7,8,7	1 (± 6)	4.7 (± 6.78)	1.4 (± 10.81)	5.8 (± 7.65)
UIBC; Week16; n=5,6,3,6,6	2 (± 6)	3.8 (± 7.19)	0 (± 7.55)	3.8 (± 10.03)
Iron; Week2; n=9,9,9,9,10	1.7 (± 6.32)	3.7 (± 11.43)	0.6 (± 9.03)	0.8 (± 9.02)
Iron; Week3; n=1,1,1,0,0	0 (± 99999)	5 (± 99999)	31 (± 99999)	99999 (± 99999)
Iron; Week4; n=8,9,8,9,9	-2.6 (± 3.38)	4.2 (± 11.04)	3.5 (± 7.98)	2.1 (± 7.29)

Iron; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	0 (± 99999)	-9 (± 99999)
Iron; Week6; n=7,10,6,10,8	3.4 (± 9.47)	1.3 (± 2.16)	-2 (± 6.45)	-0.6 (± 6.02)
Iron; Week8; n=8,7,9,9,9	-2 (± 7.45)	-2 (± 6.06)	-1.4 (± 4.8)	-1.2 (± 6.14)
Iron; Week10; n=7,8,4,7,8	-0.6 (± 4.96)	-2.8 (± 4.8)	2 (± 9.2)	3.4 (± 4.89)
Iron; Week12; n=7,7,7,8,7	0.1 (± 6.41)	-1.3 (± 6.18)	0.9 (± 9.99)	1.4 (± 11.15)
Iron; Week16; n=5,6,3,6,6	-3.2 (± 6.06)	-0.2 (± 5.34)	0.3 (± 4.16)	-0.2 (± 4.36)
Uric acid; Week2; n=9,9,9,9,10	-5.7 (± 34.67)	5.8 (± 50.46)	-14.4 (± 24.81)	-13.4 (± 14.48)
Uric acid; Week3; n=1,1,1,0,0	-8 (± 99999)	37 (± 99999)	-73 (± 99999)	99999 (± 99999)
Uric acid; Week4; n=8,9,8,9,9	-4.6 (± 49.4)	0.4 (± 57.21)	-16.8 (± 26.38)	-15.9 (± 32.94)
Uric acid; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	-14 (± 99999)	-45 (± 99999)
Uric acid; Week6; n=7,10,6,10,8	-11.3 (± 29.83)	1.7 (± 54.57)	-14.5 (± 16.84)	-15.8 (± 25.33)
Uric acid; Week8; n=8,7,9,9,9	2.4 (± 30.83)	-2 (± 62.41)	-16.2 (± 40.28)	-6.1 (± 46.93)
Uric acid; Week10; n=7,8,4,7,8	-4.7 (± 35.92)	-5.1 (± 53.14)	-8.8 (± 33.18)	-14.9 (± 41.09)
Uric acid; Week12; n=7,7,7,8,7	-14.9 (± 19.07)	2.3 (± 75.78)	-23.3 (± 28.6)	-12.3 (± 36.1)
Uric acid; Week16; n=5,6,3,6,6	-13 (± 31.1)	-9.5 (± 60.18)	-13 (± 19.47)	-23.7 (± 28.89)

Notes:

[77] - ITT Population. "Not available (NA)" data is presented as "99999"

[78] - ITT Population. "Not available (NA)" data is presented as "99999"

[79] - ITT Population. "Not available (NA)" data is presented as "99999"

[80] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[81]			
Units: Micromoles per liter				
arithmetic mean (standard deviation)				
Direct Bilirubin; Week2; n=9,9,9,9,10	-0.1 (± 0.74)			
Direct Bilirubin; Week3; n=1,1,1,0,0	99999 (± 99999)			
Direct Bilirubin; Week4; n=8,9,8,9,9	0.1 (± 0.33)			
Direct Bilirubin; Week5; n=0,0,1,1,1	0 (± 99999)			
Direct Bilirubin; Week6; n=7,10,6,10,8	-0.5 (± 0.93)			
Direct Bilirubin; Week8; n=8,7,9,9,9	0.1 (± 0.33)			
Direct Bilirubin; Week10; n=7,8,4,7,8	-0.4 (± 0.74)			
Direct Bilirubin; Week12; n=7,7,7,8,7	0 (± 0)			
Direct Bilirubin; Week16; n=5,6,3,6,6	0 (± 0.63)			
Bilirubin; Week2; n=9,9,9,9,10	-1.1 (± 2.47)			
Bilirubin; Week3; n=1,1,1,0,0	99999 (± 99999)			
Bilirubin; Week4; n=8,9,8,9,9	-1.6 (± 1.33)			
Bilirubin; Week5; n=0,0,3,1,1	0 (± 99999)			
Bilirubin; Week6; n=7,10,7,10,8	-1.9 (± 2.8)			
Bilirubin; Week8; n=8,7,9,9,9	-1.8 (± 1.72)			
Bilirubin; Week10; n=7,8,4,7,8	-2.4 (± 1.77)			
Bilirubin; Week12; n=7,7,7,8,7	-2.1 (± 1.77)			

Bilirubin; Week16; n=5,6,3,6,6	-2.3 (± 2.07)			
Indirect Bilirubin; Week2; n=9,9,9,9,10	-1.2 (± 2.2)			
Indirect Bilirubin; Week3; n=1,1,1,0,0	99999 (± 99999)			
Indirect Bilirubin; Week4; n=8,9,8,9,9	-1.4 (± 1.42)			
Indirect Bilirubin; Week5; n=0,0,1,1,1	0 (± 99999)			
Indirect Bilirubin; Week6; n=7,10,6,10,8	-1.4 (± 2.83)			
Indirect Bilirubin; Week8; n=8,7,9,9,9	-1.9 (± 1.69)			
Indirect Bilirubin; Week10; n=7,8,4,7,8	-2 (± 1.77)			
Indirect Bilirubin; Week12; n=7,7,7,8,7	-2.1 (± 1.77)			
Indirect Bilirubin; Week16; n=5,6,3,6,6	-2.3 (± 1.86)			
Creatinine; Week2; n=9,9,9,9,10	-0.53 (± 4.592)			
Creatinine; Week3; n=1,1,1,0,0	99999 (± 99999)			
Creatinine; Week4; n=8,9,8,9,9	-2.76 (± 3.749)			
Creatinine; Week5; n=0,0,3,1,1	3.1 (± 99999)			
Creatinine; Week6; n=6,9,7,9,8	-2.66 (± 2.67)			
Creatinine; Week8; n=9,7,9,9,9	-2.99 (± 4.281)			
Creatinine; Week10; n=7,8,4,7,8	-0.8 (± 4.798)			
Creatinine; Week12; n=7,7,7,8,7	-3.3 (± 2.796)			
Creatinine; Week16; n=5,6,3,6,6	-4.62 (± 3.779)			
TIBC; Week2; n=9,9,9,9,10	-1.8 (± 6)			
TIBC; Week3; n=1,1,1,0,0	99999 (± 99999)			
TIBC; Week4; n=8,9,8,9,9	-1 (± 4.66)			
TIBC; Week5; n=0,0,1,1,1	3 (± 99999)			
TIBC; Week6; n=7,10,6,10,8	1 (± 4.81)			
TIBC; Week8; n=8,7,9,9,8	-1.9 (± 8.89)			
TIBC; Week10; n=7,8,4,7,8	-2 (± 6.19)			
TIBC; Week12; n=7,7,7,8,7	-2.3 (± 3.9)			
TIBC; Week16; n=5,6,3,6,6	-4.2 (± 6.97)			
UIBC; Week2; n=9,9,9,9,10	-1.2 (± 9.13)			
UIBC; Week3; n=1,1,1,0,0	99999 (± 99999)			
UIBC; Week4; n=8,9,8,9,9	0.4 (± 7.23)			
UIBC; Week5; n=0,0,1,1,1	12 (± 99999)			
UIBC; Week6; n=7,10,6,10,8	5.6 (± 8.05)			
UIBC; Week8; n=8,7,9,9,9	-0.4 (± 11.08)			
UIBC; Week10; n=7,8,4,7,8	0.5 (± 9.1)			
UIBC; Week12; n=7,7,7,8,7	2.1 (± 5.01)			
UIBC; Week16; n=5,6,3,6,6	-2.2 (± 5.78)			
Iron; Week2; n=9,9,9,9,10	-0.6 (± 7.09)			
Iron; Week3; n=1,1,1,0,0	99999 (± 99999)			
Iron; Week4; n=8,9,8,9,9	-1.4 (± 4.13)			
Iron; Week5; n=0,0,1,1,1	-9 (± 99999)			
Iron; Week6; n=7,10,6,10,8	-4.6 (± 6.8)			
Iron; Week8; n=8,7,9,9,9	-1.6 (± 3.91)			
Iron; Week10; n=7,8,4,7,8	-2.5 (± 5.13)			
Iron; Week12; n=7,7,7,8,7	-4.4 (± 3.36)			

Iron; Week16; n=5,6,3,6,6	-2 (± 2.9)			
Uric acid; Week2; n=9,9,9,9,10	2.2 (± 35.59)			
Uric acid; Week3; n=1,1,1,0,0	99999 (± 99999)			
Uric acid; Week4; n=8,9,8,9,9	-7.2 (± 31.58)			
Uric acid; Week5; n=0,0,1,1,1	9 (± 99999)			
Uric acid; Week6; n=7,10,6,10,8	-2.1 (± 30.02)			
Uric acid; Week8; n=8,7,9,9,9	0.7 (± 35.19)			
Uric acid; Week10; n=7,8,4,7,8	-1.9 (± 29.46)			
Uric acid; Week12; n=7,7,7,8,7	-7.1 (± 18.25)			
Uric acid; Week16; n=5,6,3,6,6	-4.7 (± 25.45)			

Notes:

[81] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in albumin/globulin, BUN/creatinine and transferrin saturation at the indicated time points up to Week 16

End point title	Change from Baseline in albumin/globulin, BUN/creatinine and transferrin saturation at the indicated time points up to Week 16[82]

End point description:

Change from baseline in the albumin/globulin, blood urea nitrogen (BUN)/creatinine and transferrin saturation values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[82] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[83]	10[84]	10[85]	10[86]
Units: Ratio				
arithmetic mean (standard deviation)				
Albumin/Globulin; Week2; n=9,9,9,9,10	0.07 (± 0.173)	0.03 (± 0.122)	-0.04 (± 0.133)	0.09 (± 0.117)
Albumin/Globulin; Week3; n=1,1,1,0,0	-0.1 (± 99999)	-0.1 (± 99999)	0.4 (± 99999)	99999 (± 99999)
Albumin/Globulin; Week4; n=8,9,8,9,9	0.13 (± 0.149)	0.07 (± 0.166)	0.05 (± 0.207)	0.17 (± 0.087)
Albumin/Globulin; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	0.5 (± 99999)	0 (± 99999)
Albumin/Globulin; Week6; n=7,10,6,10,8	0.01 (± 0.107)	0.03 (± 0.142)	0.15 (± 0.266)	0.21 (± 0.129)
Albumin/Globulin; Week8; n=8,7,9,9,9	0.09 (± 0.189)	0.11 (± 0.146)	0.12 (± 0.164)	0.18 (± 0.139)
Albumin/Globulin; Week10; n=7,8,4,7,8	0.11 (± 0.168)	0.05 (± 0.193)	0.03 (± 0.096)	0.21 (± 0.107)

Albumin/Globulin; Week12; n=7,7,7,8,7	0.03 (± 0.125)	0.09 (± 0.297)	0.03 (± 0.309)	0.1 (± 0.227)
Albumin/Globulin; Week16; n=5,6,3,6,6	-0.04 (± 0.055)	-0.05 (± 0.176)	-0.07 (± 0.153)	0.07 (± 0.25)
BUN/Creatinine; Week2; n=9,9,9,9,10	8.8 (± 18.91)	8.9 (± 27.81)	-9.1 (± 22.05)	-7.4 (± 15.45)
BUN/Creatinine; Week3; n=1,1,1,0,0	-15 (± 99999)	21 (± 99999)	40 (± 99999)	99999 (± 99999)
BUN/Creatinine; Week4; n=8,9,8,9,9	4 (± 19.27)	-10.2 (± 22.94)	-7.3 (± 20.95)	-3.7 (± 15.7)
BUN/Creatinine; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	1 (± 99999)	-36 (± 99999)
BUN/Creatinine; Week6; n=6,9,6,9,8	-0.7 (± 16.49)	-1 (± 17.48)	2 (± 15.05)	-5.8 (± 20.52)
BUN/Creatinine; Week8; n=8,7,9,9,9	-11.8 (± 21.42)	-23.9 (± 21.14)	-4 (± 16.48)	-5.2 (± 12.78)
BUN/Creatinine; Week10; n=7,8,4,7,8	-2.6 (± 29.07)	-17.8 (± 22.25)	9.8 (± 22.9)	-7.4 (± 34.32)
BUN/Creatinine; Week12; n=7,7,7,8,7	-8.7 (± 23.14)	-9.3 (± 35.49)	-4.3 (± 16.2)	-1 (± 28.24)
BUN/Creatinine; Week16; n=5,6,3,6,6	-5.2 (± 15.99)	-11.8 (± 43.73)	-5.7 (± 6.66)	0.2 (± 33.39)
Transferrin saturation; Week2; n=9,9,9,9,10	0.036 (± 0.1093)	0.05 (± 0.1577)	0.002 (± 0.1242)	0.004 (± 0.1599)
Transferrin saturation; Week3; n=1,1,1,0,0	0 (± 99999)	0.13 (± 99999)	0.46 (± 99999)	99999 (± 99999)
Transferrin saturation; Week4; n=8,9,8,9,9	-0.05 (± 0.0763)	0.04 (± 0.1459)	0.043 (± 0.1172)	0.018 (± 0.111)
Transferrin saturation; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	0.01 (± 99999)	-0.17 (± 99999)
Transferrin saturation; Week6; n=7,10,6,10,8	0.049 (± 0.1297)	0.016 (± 0.0317)	-0.033 (± 0.0905)	-0.011 (± 0.1343)
Transferrin saturation; Week8; n=8,7,9,9,8	-0.039 (± 0.1246)	-0.029 (± 0.0888)	-0.03 (± 0.0758)	-0.031 (± 0.1046)
Transferrin saturation; Week10; n=7,8,4,7,8	-0.01 (± 0.0906)	-0.048 (± 0.0742)	0.045 (± 0.1392)	0.031 (± 0.084)
Transferrin saturation; Week12; n=7,7,7,8,7	-0.007 (± 0.1013)	-0.024 (± 0.0856)	0.01 (± 0.1502)	-0.013 (± 0.1659)
Transferrin saturation; Week16; n=5,6,3,6,6	-0.054 (± 0.1095)	-0.01 (± 0.078)	0.017 (± 0.0723)	-0.015 (± 0.0922)

Notes:

[83] - ITT Population. "Not available (NA)" data is presented as "99999"

[84] - ITT Population. "Not available (NA)" data is presented as "99999"

[85] - ITT Population. "Not available (NA)" data is presented as "99999"

[86] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[87]			
Units: Ratio				
arithmetic mean (standard deviation)				
Albumin/Globulin; Week2; n=9,9,9,9,10	-0.12 (± 0.132)			
Albumin/Globulin; Week3; n=1,1,1,0,0	99999 (± 99999)			
Albumin/Globulin; Week4; n=8,9,8,9,9	-0.06 (± 0.194)			
Albumin/Globulin; Week5; n=0,0,1,1,1	-0.1 (± 99999)			
Albumin/Globulin; Week6; n=7,10,6,10,8	-0.11 (± 0.196)			
Albumin/Globulin; Week8; n=8,7,9,9,9	-0.02 (± 0.139)			

Albumin/Globulin; Week10; n=7,8,4,7,8	-0.1 (± 0.131)			
Albumin/Globulin; Week12; n=7,7,7,8,7	-0.04 (± 0.151)			
Albumin/Globulin; Week16; n=5,6,3,6,6	-0.13 (± 0.186)			
BUN/Creatinine; Week2; n=9,9,9,9,10	0.3 (± 21.19)			
BUN/Creatinine; Week3; n=1,1,1,0,0	99999 (± 99999)			
BUN/Creatinine; Week4; n=8,9,8,9,9	7.8 (± 23.2)			
BUN/Creatinine; Week5; n=0,0,1,1,1	-4 (± 99999)			
BUN/Creatinine; Week6; n=6,9,6,9,8	15.4 (± 14.92)			
BUN/Creatinine; Week8; n=8,7,9,9,9	8.7 (± 19.92)			
BUN/Creatinine; Week10; n=7,8,4,7,8	3 (± 20.73)			
BUN/Creatinine; Week12; n=7,7,7,8,7	10.9 (± 7.6)			
BUN/Creatinine; Week16; n=5,6,3,6,6	6.8 (± 25.88)			
Transferrin saturation; Week2; n=9,9,9,9,10	0 (± 0.1036)			
Transferrin saturation; Week3; n=1,1,1,0,0	99999 (± 99999)			
Transferrin saturation; Week4; n=8,9,8,9,9	-0.024 (± 0.0641)			
Transferrin saturation; Week5; n=0,0,1,1,1	-0.2 (± 99999)			
Transferrin saturation; Week6; n=7,10,6,10,8	-0.08 (± 0.1251)			
Transferrin saturation; Week8; n=8,7,9,9,8	-0.026 (± 0.0847)			
Transferrin saturation; Week10; n=7,8,4,7,8	-0.036 (± 0.0868)			
Transferrin saturation; Week12; n=7,7,7,8,7	-0.071 (± 0.0549)			
Transferrin saturation; Week16; n=5,6,3,6,6	-0.028 (± 0.044)			

Notes:

[87] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in creatinine clearance at the indicated time points up to Week 16

End point title	Change from Baseline in creatinine clearance at the indicated time points up to Week 16[88]

End point description:

Change from Baseline in the Creatinine Clearance values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[88] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[89]	10[90]	10[91]	10[92]
Units: Milliliter per minute (mL/min)				
arithmetic mean (standard deviation)				
Creatinine clearance; Week2; n=9,9,9,9,10	-1.8 (± 27.86)	-5.6 (± 9.34)	-5.9 (± 11.89)	-13.2 (± 16.84)
Creatinine clearance; Week3; n=1,1,0,0,0	-13 (± 99999)	4 (± 99999)	99999 (± 99999)	99999 (± 99999)
Creatinine clearance; Week4; n=8,9,8,9,9	-7.1 (± 16.25)	-3.2 (± 11.2)	-6.8 (± 13.66)	-13.2 (± 13.55)
Creatinine clearance; Week5; n=0,0,1,1,1	99999 (± 99999)	99999 (± 99999)	-36 (± 99999)	-13 (± 99999)
Creatinine clearance; Week6; n=0,3,1,2,0	99999 (± 99999)	3.7 (± 1.53)	5 (± 99999)	-9.5 (± 99999)
Creatinine clearance; Week8; n=8,7,8,9,9	-10.6 (± 11.19)	-12.1 (± 14.58)	-10.9 (± 17.21)	-18.3 (± 18.83)
Creatinine clearance; Week10; n=2,2,1,1,2	-10 (± 14.14)	7.5 (± 4.95)	-6 (± 99999)	-29 (± 99999)
Creatinine clearance; Week12; n=7,7,7,8,7	-2.1 (± 17.03)	-3 (± 14.41)	-3 (± 23.79)	-14.6 (± 18.07)
Creatinine clearance; Week16; n=5,6,3,6,6	-3.6 (± 17.81)	-1 (± 10.53)	-1 (± 3.46)	-1.7 (± 10.61)

Notes:

[89] - ITT Population. "Not available (NA)" data is presented as "99999"

[90] - ITT Population. "Not available (NA)" data is presented as "99999"

[91] - ITT Population. "Not available (NA)" data is presented as "99999"

[92] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[93]			
Units: Milliliter per minute (mL/min)				
arithmetic mean (standard deviation)				
Creatinine clearance; Week2; n=9,9,9,9,10	1.7 (± 8.03)			
Creatinine clearance; Week3; n=1,1,0,0,0	99999 (± 99999)			
Creatinine clearance; Week4; n=8,9,8,9,9	7.7 (± 10.78)			
Creatinine clearance; Week5; n=0,0,1,1,1	-5 (± 99999)			
Creatinine clearance; Week6; n=0,3,1,2,0	99999 (± 99999)			
Creatinine clearance; Week8; n=8,7,8,9,9	10.1 (± 13.91)			
Creatinine clearance; Week10; n=2,2,1,1,2	-10.5 (± 10.61)			
Creatinine clearance; Week12; n=7,7,7,8,7	9.6 (± 10.28)			
Creatinine clearance; Week16; n=5,6,3,6,6	14.8 (± 14.8)			

Notes:

[93] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, neutrophils, neutrophils SG, platelets and leukocytes at the indicated time points up to Week 16

End point title	Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, neutrophils, neutrophils SG, platelets and leukocytes at the indicated time points up to Week 16[94]

End point description:

Change from Baseline in the basophils, eosinophils, lymphocytes, monocytes, neutrophils, neutrophils segmented (SG), platelets and leukocytes values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 1, 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[94] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[95]	10[96]	10[97]	10[98]
Units: Billions per liter				
arithmetic mean (standard deviation)				
Basophils, Week1, n=9,10,9,10,11	-0.002 (± 0.0335)	0.002 (± 0.0114)	-0.004 (± 0.0219)	0.004 (± 0.0178)
Basophils, Week2, n=9,9,10,9,9	0.001 (± 0.0271)	-0.004 (± 0.0133)	-0.008 (± 0.014)	0.004 (± 0.0088)
Basophils, Week3, n=9,7,9,6,7	-0.002 (± 0.0468)	0 (± 0.0141)	0.004 (± 0.03)	0.01 (± 0.0261)
Basophils, Week4, n=6,9,9,9,9	0 (± 0.0469)	0.002 (± 0.013)	-0.001 (± 0.0176)	0.002 (± 0.0164)
Basophils, Week5, n=7,6,6,9,7	-0.011 (± 0.0449)	0.012 (± 0.0147)	0.002 (± 0.0354)	0 (± 0.015)
Basophils, Week6, n=7,10,6,10,7	-0.023 (± 0.0399)	0.003 (± 0.0106)	-0.013 (± 0.0137)	0 (± 0.0082)
Basophils, Week8, n=8,7,9,9,9	-0.011 (± 0.0458)	0.001 (± 0.0146)	0.019 (± 0.047)	0.003 (± 0.015)
Basophils, Week10, n=7,8,4,7,8	-0.011 (± 0.0324)	0 (± 0.0076)	-0.018 (± 0.0096)	0.001 (± 0.0069)
Basophils, Week12, n=7,7,7,8,7	-0.014 (± 0.0264)	0.006 (± 0.0215)	-0.01 (± 0.0058)	-0.005 (± 0.0093)
Basophils, Week16, n=5,6,3,6,6	-0.006 (± 0.0207)	-0.003 (± 0.0121)	-0.007 (± 0.0115)	0.008 (± 0.0214)

Eosinophils, Week1, n=9,10,9,10,11	0.006 (± 0.0515)	-0.027 (± 0.0707)	-0.051 (± 0.1523)	0.035 (± 0.0665)
Eosinophils, Week2, n=9,9,10,9,9	0.137 (± 0.2082)	-0.023 (± 0.1009)	0.003 (± 0.2005)	0.03 (± 0.0705)
Eosinophils, Week3, n=9,7,9,6,7	0.072 (± 0.1225)	-0.02 (± 0.1071)	-0.05 (± 0.1396)	0.023 (± 0.0288)
Eosinophils, Week4, n=6,9,9,9,9	-0.002 (± 0.0523)	-0.044 (± 0.0879)	-0.027 (± 0.1622)	-0.027 (± 0.0534)
Eosinophils, Week5, n=7,6,6,9,7	0.019 (± 0.0752)	-0.035 (± 0.1009)	0.008 (± 0.0449)	-0.017 (± 0.0585)
Eosinophils, Week6, n=7,10,6,10,7	-0.017 (± 0.0499)	-0.05 (± 0.101)	-0.023 (± 0.0186)	-0.028 (± 0.0711)
Eosinophils, Week8, n=8,7,9,9,9	0.016 (± 0.0437)	-0.04 (± 0.0935)	-0.029 (± 0.1039)	-0.017 (± 0.043)
Eosinophils, Week10, n=7,8,4,7,8	0.039 (± 0.0917)	0.001 (± 0.126)	-0.033 (± 0.0299)	-0.019 (± 0.1125)
Eosinophils, Week12, n=7,7,7,8,7	0.021 (± 0.0767)	-0.009 (± 0.126)	-0.014 (± 0.0351)	-0.008 (± 0.0504)
Eosinophils, Week16, n=5,6,3,6,6	0.002 (± 0.0295)	-0.048 (± 0.1034)	0.053 (± 0.1274)	-0.052 (± 0.0773)
Lymphocytes, Week1, n=9,10,9,10,11	0.763 (± 1.5656)	0.115 (± 0.701)	-0.127 (± 0.4761)	0.148 (± 0.5696)
Lymphocytes, Week2, n=9,9,10,9,9	0.407 (± 1.0582)	0.043 (± 0.2932)	-0.36 (± 0.3286)	-0.258 (± 0.7151)
Lymphocytes, Week3, n=9,7,9,6,7	0.754 (± 1.2905)	0.151 (± 0.2727)	0.139 (± 0.6525)	0.173 (± 0.5052)
Lymphocytes, Week4, n=6,9,9,9,9	0.813 (± 1.4774)	0.033 (± 0.292)	0.308 (± 0.8582)	-0.151 (± 0.4103)
Lymphocytes, Week5, n=7,6,6,9,7	0.286 (± 0.5651)	0.142 (± 0.1136)	0.332 (± 1.2818)	-0.017 (± 0.5348)
Lymphocytes, Week6, n=7,10,6,10,7	0.246 (± 0.4796)	-0.136 (± 0.2762)	0.297 (± 0.832)	-0.059 (± 0.5509)
Lymphocytes, Week8, n=8,7,9,9,9	0.519 (± 1.2726)	0.131 (± 0.93)	0.227 (± 0.8526)	0 (± 0.6471)
Lymphocytes, Week10, n=7,8,4,7,8	0.127 (± 0.3555)	0.128 (± 0.4077)	-0.19 (± 0.1206)	-0.161 (± 0.4008)
Lymphocytes, Week12, n=7,7,7,8,7	-0.06 (± 0.3709)	-0.05 (± 0.0887)	0.221 (± 0.5321)	-0.328 (± 0.4631)
Lymphocytes, Week16, n=5,6,3,6,6	0.064 (± 0.4868)	0.163 (± 0.5223)	0.117 (± 0.0833)	0.01 (± 0.6658)
Monocytes, Week1, n=9,10,9,10,11	-0.066 (± 0.349)	-0.006 (± 0.1543)	0.056 (± 0.2089)	0.02 (± 0.1585)
Monocytes, Week2, n=9,9,10,9,9	-0.149 (± 0.4253)	0.042 (± 0.1965)	-0.034 (± 0.1685)	-0.116 (± 0.1068)
Monocytes, Week3, n=9,7,9,6,7	-0.153 (± 0.3728)	0.024 (± 0.139)	0.163 (± 0.2259)	-0.02 (± 0.1682)
Monocytes, Week4, n=6,9,9,9,9	-0.165 (± 0.4373)	0.038 (± 0.1776)	0.167 (± 0.5101)	-0.043 (± 0.2149)
Monocytes, Week5, n=7,6,6,9,7	0.006 (± 0.1131)	0.058 (± 0.1425)	0.062 (± 0.1843)	-0.02 (± 0.1912)
Monocytes, Week6, n=7,10,6,10,7	-0.074 (± 0.1254)	-0.057 (± 0.1542)	0.038 (± 0.1209)	-0.117 (± 0.1517)
Monocytes, Week8, n=8,7,9,9,9	-0.129 (± 0.3993)	0.041 (± 0.1325)	0.008 (± 0.1173)	-0.047 (± 0.0843)
Monocytes, Week10, n=7,8,4,7,8	0.01 (± 0.0995)	-0.006 (± 0.1413)	-0.015 (± 0.1234)	-0.08 (± 0.1743)
Monocytes, Week12, n=7,7,7,8,7	-0.004 (± 0.119)	0.006 (± 0.1001)	0.094 (± 0.2385)	-0.049 (± 0.1195)
Monocytes, Week16, n=5,6,3,6,6	-0.004 (± 0.0378)	-0.047 (± 0.1565)	-0.01 (± 0.0964)	-0.14 (± 0.1296)
Neutrophils, Week1, n=9,10,9,10,11	-0.192 (± 1.4294)	1.638 (± 3.9206)	1.422 (± 0.8979)	0.092 (± 2.6648)

Neutrophils, Week2, n=9,9,10,9,9	-1.231 (± 1.6188)	0.247 (± 1.7058)	0.14 (± 0.8193)	-1.291 (± 2.8048)
Neutrophils, Week3, n=9,7,9,6,7	0.069 (± 1.3707)	0.327 (± 2.4038)	0.912 (± 1.4991)	-2.055 (± 2.4167)
Neutrophils, Week4, n=6,9,9,9,9	-0.033 (± 1.6415)	0.052 (± 1.8589)	0.606 (± 0.6448)	-1.423 (± 2.1838)
Neutrophils, Week5, n=7,6,6,9,7	-0.153 (± 1.3439)	0.09 (± 2.0247)	1.387 (± 2.6017)	-1.407 (± 3.1341)
Neutrophils, Week6, n=7,9,6,10,7	-0.054 (± 1.6672)	-0.031 (± 2.3978)	0.927 (± 2.0966)	-0.445 (± 2.4812)
Neutrophils, Week8, n=8,7,9,9,9	-0.629 (± 1.6773)	-0.216 (± 2.159)	0.46 (± 1.1872)	-1.619 (± 3.3418)
Neutrophils, Week10, n=7,8,4,7,8	-1.124 (± 1.257)	0.189 (± 1.5403)	0.798 (± 0.9581)	-1.474 (± 4.2315)
Neutrophils, Week12, n=7,7,7,8,7	-0.087 (± 1.3356)	0.196 (± 0.8878)	0.164 (± 1.1213)	-1.576 (± 3.7465)
Neutrophils, Week16, n=5,6,3,6,6	-1.25 (± 1.8168)	-0.693 (± 1.52)	0.233 (± 0.9611)	-0.938 (± 2.3948)
Neutrophils SG, Week1, n=9,10,9,10,11	-0.192 (± 1.4294)	1.638 (± 3.9206)	1.422 (± 0.8979)	0.092 (± 2.6648)
Neutrophils SG, Week2, n=9,9,10,9,9	-1.231 (± 1.6188)	0.247 (± 1.7058)	0.14 (± 0.8193)	-1.291 (± 2.8048)
Neutrophils SG, Week3, n=9,7,9,6,7	0.069 (± 1.3707)	0.327 (± 2.4038)	0.912 (± 1.4991)	-2.055 (± 2.4167)
Neutrophils SG, Week4, n=6,9,9,9,9	-0.033 (± 1.6415)	0.052 (± 1.8589)	0.606 (± 0.6448)	-1.423 (± 2.1838)
Neutrophils SG, Week5, n=7,6,6,9,7	-0.153 (± 1.3439)	0.09 (± 2.0247)	1.387 (± 2.6017)	-1.407 (± 3.1341)
Neutrophils SG, Week6, n=7,10,6,10,7	-0.054 (± 1.6672)	0.119 (± 2.31)	0.927 (± 2.0966)	-0.445 (± 2.4812)
Neutrophils SG, Week8, n=8,7,9,9,9	-0.629 (± 1.6773)	-0.216 (± 2.159)	0.46 (± 1.1872)	-1.619 (± 3.3418)
Neutrophils SG, Week10, n=7,8,4,7,8	-1.124 (± 1.257)	0.189 (± 1.5403)	0.798 (± 0.9581)	-1.474 (± 4.2315)
Neutrophils SG, Week12, n=7,7,7,8,7	-0.087 (± 1.3356)	0.196 (± 0.8878)	0.164 (± 1.1213)	-1.576 (± 3.7465)
Neutrophils SG, Week16, n=5,6,3,6,6	-1.25 (± 1.8168)	-0.693 (± 1.52)	0.233 (± 0.9611)	-0.938 (± 2.3948)
Platelets, Week1, n=9,10,9,10,11	-2.3 (± 24.32)	-4.7 (± 30.15)	13.8 (± 41.28)	23.8 (± 26.09)
Platelets, Week2, n=9,9,10,9,9	-31.3 (± 48.71)	-48.4 (± 50.31)	-45.2 (± 44.47)	-32.2 (± 33.25)
Platelets, Week3, n=9,7,9,6,7	2.4 (± 25.74)	-36.7 (± 39.77)	0 (± 29.29)	-39.2 (± 58.51)
Platelets, Week4, n=6,9,9,9,9	-10.8 (± 22.74)	-32.2 (± 45.34)	-0.1 (± 47.01)	-19.1 (± 17.52)
Platelets, Week5, n=7,6,7,9,7	3.1 (± 30.99)	-35.7 (± 57.01)	12.1 (± 66.55)	-15.6 (± 38.46)
Platelets, Week6, n=7,10,5,10,8	7.7 (± 38.77)	-18.9 (± 36.06)	-9.6 (± 20.48)	1.8 (± 43.42)
Platelets, Week8, n=8,7,9,9,9	-11.3 (± 51.49)	-33 (± 29.68)	-6.9 (± 34.56)	-1.9 (± 65.75)
Platelets, Week10, n=7,8,4,7,8	2.4 (± 25.1)	-19.5 (± 30.8)	-16.5 (± 23.95)	-12.4 (± 67.01)
Platelets, Week12, n=7,7,7,8,7	13.6 (± 26.69)	-29.7 (± 57.09)	-3 (± 19.08)	-14.4 (± 43.84)
Platelets, Week16, n=5,6,3,6,6	7.8 (± 31.88)	-35.2 (± 40.04)	9 (± 16.52)	10.8 (± 54.17)
Leukocytes, Week1, n=9,10,9,10,11	0.53 (± 2.076)	1.73 (± 3.604)	1.3 (± 0.763)	0.3 (± 2.489)
Leukocytes, Week2, n=9,9,10,9,9	-0.81 (± 1.548)	0.3 (± 1.938)	-0.27 (± 1.033)	-1.62 (± 2.984)
Leukocytes, Week3, n=9,7,9,6,7	0.77 (± 1.942)	0.47 (± 2.404)	1.16 (± 1.998)	-1.88 (± 2.283)

Leukocytes, Week4, n=6,9,9,9,9	0.62 (± 1.321)	0.06 (± 1.902)	1.03 (± 1.464)	-1.62 (± 2.411)
Leukocytes, Week5, n=7,6,6,9,7	0.17 (± 0.75)	0.27 (± 2.201)	1.78 (± 3.843)	-1.46 (± 2.985)
Leukocytes, Week6, n=7,10,6,10,7	0.1 (± 1.398)	-0.15 (± 2.314)	1.25 (± 1.712)	-0.65 (± 2.911)
Leukocytes, Week8, n=8,7,9,9,9	-0.2 (± 1.098)	-0.09 (± 2.126)	0.7 (± 1.795)	-1.68 (± 3.515)
Leukocytes, Week10, n=7,8,4,7,8	-0.94 (± 0.964)	0.31 (± 1.49)	0.53 (± 1.097)	-1.73 (± 4.375)
Leukocytes, Week12, n=7,7,7,8,7	-0.14 (± 1.33)	0.16 (± 0.913)	0.44 (± 1.533)	-1.95 (± 3.777)
Leukocytes, Week16, n=5,6,3,6,6	-1.2 (± 1.678)	-0.65 (± 1.15)	0.4 (± 1.153)	-1.1 (± 2.45)

Notes:

[95] - ITT Population

[96] - ITT Population

[97] - ITT Population

[98] - ITT Population

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[99]			
Units: Billions per liter				
arithmetic mean (standard deviation)				
Basophils, Week1, n=9,10,9,10,11	-0.003 (± 0.0195)			
Basophils, Week2, n=9,9,10,9,9	-0.003 (± 0.0122)			
Basophils, Week3, n=9,7,9,6,7	0.001 (± 0.0135)			
Basophils, Week4, n=6,9,9,9,9	-0.007 (± 0.01)			
Basophils, Week5, n=7,6,6,9,7	-0.004 (± 0.019)			
Basophils, Week6, n=7,10,6,10,7	-0.006 (± 0.0127)			
Basophils, Week8, n=8,7,9,9,9	-0.002 (± 0.0164)			
Basophils, Week10, n=7,8,4,7,8	0.001 (± 0.0083)			
Basophils, Week12, n=7,7,7,8,7	-0.001 (± 0.0285)			
Basophils, Week16, n=5,6,3,6,6	-0.005 (± 0.0105)			
Eosinophils, Week1, n=9,10,9,10,11	-0.003 (± 0.0631)			
Eosinophils, Week2, n=9,9,10,9,9	-0.003 (± 0.0332)			
Eosinophils, Week3, n=9,7,9,6,7	0.064 (± 0.0981)			
Eosinophils, Week4, n=6,9,9,9,9	-0.009 (± 0.0267)			
Eosinophils, Week5, n=7,6,6,9,7	-0.014 (± 0.0162)			
Eosinophils, Week6, n=7,10,6,10,7	-0.011 (± 0.0212)			
Eosinophils, Week8, n=8,7,9,9,9	0 (± 0.0265)			
Eosinophils, Week10, n=7,8,4,7,8	0.008 (± 0.0459)			

Eosinophils, Week12, n=7,7,7,8,7	0.047 (± 0.0682)			
Eosinophils, Week16, n=5,6,3,6,6	0.032 (± 0.0504)			
Lymphocytes, Week1, n=9,10,9,10,11	-0.1 (± 0.41)			
Lymphocytes, Week2, n=9,9,10,9,9	-0.086 (± 0.3673)			
Lymphocytes, Week3, n=9,7,9,6,7	0.193 (± 0.6479)			
Lymphocytes, Week4, n=6,9,9,9,9	-0.02 (± 0.5295)			
Lymphocytes, Week5, n=7,6,6,9,7	0.054 (± 0.5757)			
Lymphocytes, Week6, n=7,10,6,10,7	-0.183 (± 0.4596)			
Lymphocytes, Week8, n=8,7,9,9,9	-0.084 (± 0.3248)			
Lymphocytes, Week10, n=7,8,4,7,8	-0.011 (± 0.5503)			
Lymphocytes, Week12, n=7,7,7,8,7	0.081 (± 0.6077)			
Lymphocytes, Week16, n=5,6,3,6,6	0.075 (± 0.4366)			
Monocytes, Week1, n=9,10,9,10,11	-0.055 (± 0.1408)			
Monocytes, Week2, n=9,9,10,9,9	-0.009 (± 0.1291)			
Monocytes, Week3, n=9,7,9,6,7	-0.017 (± 0.0673)			
Monocytes, Week4, n=6,9,9,9,9	-0.038 (± 0.1102)			
Monocytes, Week5, n=7,6,6,9,7	-0.001 (± 0.1272)			
Monocytes, Week6, n=7,10,6,10,7	-0.076 (± 0.0783)			
Monocytes, Week8, n=8,7,9,9,9	-0.013 (± 0.091)			
Monocytes, Week10, n=7,8,4,7,8	-0.054 (± 0.0803)			
Monocytes, Week12, n=7,7,7,8,7	-0.036 (± 0.0675)			
Monocytes, Week16, n=5,6,3,6,6	0.043 (± 0.1293)			
Neutrophils, Week1, n=9,10,9,10,11	0.439 (± 1.5593)			
Neutrophils, Week2, n=9,9,10,9,9	-0.023 (± 0.512)			
Neutrophils, Week3, n=9,7,9,6,7	0.206 (± 1.6235)			
Neutrophils, Week4, n=6,9,9,9,9	-0.241 (± 0.8247)			
Neutrophils, Week5, n=7,6,6,9,7	0.893 (± 0.7082)			
Neutrophils, Week6, n=7,9,6,10,7	0.151 (± 1.2003)			
Neutrophils, Week8, n=8,7,9,9,9	-0.177 (± 0.7237)			
Neutrophils, Week10, n=7,8,4,7,8	-0.356 (± 1.144)			
Neutrophils, Week12, n=7,7,7,8,7	-0.563 (± 0.4907)			

Neutrophils, Week16, n=5,6,3,6,6	0.332 (± 0.4296)			
Neutrophils SG, Week1, n=9,10,9,10,11	0.439 (± 1.5593)			
Neutrophils SG, Week2, n=9,9,10,9,9	-0.023 (± 0.512)			
Neutrophils SG, Week3, n=9,7,9,6,7	0.206 (± 1.6235)			
Neutrophils SG, Week4, n=6,9,9,9,9	-0.241 (± 0.8247)			
Neutrophils SG, Week5, n=7,6,6,9,7	0.893 (± 0.7082)			
Neutrophils SG, Week6, n=7,10,6,10,7	0.151 (± 1.2003)			
Neutrophils SG, Week8, n=8,7,9,9,9	-0.177 (± 0.7237)			
Neutrophils SG, Week10, n=7,8,4,7,8	-0.356 (± 1.144)			
Neutrophils SG, Week12, n=7,7,7,8,7	-0.563 (± 0.4907)			
Neutrophils SG, Week16, n=5,6,3,6,6	0.332 (± 0.4296)			
Platelets, Week1, n=9,10,9,10,11	10.6 (± 21.81)			
Platelets, Week2, n=9,9,10,9,9	2.6 (± 17.08)			
Platelets, Week3, n=9,7,9,6,7	16.9 (± 29.04)			
Platelets, Week4, n=6,9,9,9,9	18.9 (± 30.53)			
Platelets, Week5, n=7,6,7,9,7	41.4 (± 35.64)			
Platelets, Week6, n=7,10,5,10,8	29 (± 36.18)			
Platelets, Week8, n=8,7,9,9,9	15.8 (± 28.31)			
Platelets, Week10, n=7,8,4,7,8	24.4 (± 42.88)			
Platelets, Week12, n=7,7,7,8,7	25.1 (± 34.12)			
Platelets, Week16, n=5,6,3,6,6	16.5 (± 23.71)			
Leukocytes, Week1, n=9,10,9,10,11	0.29 (± 1.575)			
Leukocytes, Week2, n=9,9,10,9,9	-0.12 (± 0.634)			
Leukocytes, Week3, n=9,7,9,6,7	0.44 (± 1.212)			
Leukocytes, Week4, n=6,9,9,9,9	-0.31 (± 1.029)			
Leukocytes, Week5, n=7,6,6,9,7	0.93 (± 0.986)			
Leukocytes, Week6, n=7,10,6,10,7	-0.11 (± 1.295)			
Leukocytes, Week8, n=8,7,9,9,9	-0.28 (± 1.003)			
Leukocytes, Week10, n=7,8,4,7,8	-0.41 (± 1.331)			
Leukocytes, Week12, n=7,7,7,8,7	-0.47 (± 0.73)			
Leukocytes, Week16, n=5,6,3,6,6	0.5 (± 0.839)			

Notes:

[99] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in basophils/leukocytes, eosinophils/leukocytes, lymphocytes/leukocytes, monocytes/leukocytes, neutrophils/leukocytes, neutrophils SG/leukocytes and EDW at the indicated time points up to Week 16

End point title	Change from Baseline in basophils/leukocytes, eosinophils/leukocytes, lymphocytes/leukocytes, monocytes/leukocytes, neutrophils/leukocytes, neutrophils SG/leukocytes and EDW at the indicated time points up to Week 16[100]

End point description:

Change from Baseline in the basophils/leukocytes, eosinophils/leukocytes, lymphocytes/leukocytes, monocytes/leukocytes, neutrophils/leukocytes, neutrophils segmented (SG)/leukocytes and erythrocyte distribution width (EDW) values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (n=X,X,X,X,X). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 1, 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[100] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[101]	10[102]	10[103]	10[104]
Units: Percentage				
arithmetic mean (standard deviation)				
Basophils/Leukocytes, Week1, n=9,10,9,10,11	-0.02 (± 0.367)	-0.03 (± 0.149)	-0.08 (± 0.441)	-0.01 (± 0.242)
Basophils/Leukocytes, Week2, n=9,9,10,9,9	0.12 (± 0.373)	-0.09 (± 0.145)	-0.14 (± 0.272)	0.07 (± 0.173)
Basophils/Leukocytes, Week3, n=9,7,9,6,7	-0.04 (± 0.416)	-0.04 (± 0.251)	0.18 (± 0.595)	0.18 (± 0.431)
Basophils/Leukocytes, Week4, n=6,9,9,9,9	0.02 (± 0.462)	-0.02 (± 0.244)	-0.07 (± 0.357)	0.03 (± 0.26)
Basophils/Leukocytes, Week5, n=7,6,6,9,7	-0.11 (± 0.449)	0.18 (± 0.248)	-0.13 (± 0.344)	-0.03 (± 0.229)
Basophils/Leukocytes, Week6, n=7,10,6,10,7	-0.24 (± 0.387)	0.05 (± 0.196)	-0.28 (± 0.299)	-0.03 (± 0.106)
Basophils/Leukocytes, Week8, n=8,7,9,9,9	-0.09 (± 0.455)	0.03 (± 0.214)	0.4 (± 0.941)	0.11 (± 0.203)
Basophils/Leukocytes, Week10, n=7,8,4,7,8	-0.07 (± 0.35)	-0.01 (± 0.21)	-0.35 (± 0.173)	0.06 (± 0.172)
Basophils/Leukocytes, Week12, n=7,7,7,8,7	-0.17 (± 0.243)	0.03 (± 0.298)	-0.17 (± 0.138)	-0.05 (± 0.214)
Basophils/Leukocytes, Week16, n=5,6,3,6,6	0 (± 0.308)	-0.08 (± 0.172)	-0.1 (± 0.3)	0.12 (± 0.279)
Eosinophils/Leukocytes, Week1, n=9,10,9,10,11	0.11 (± 1.054)	-0.69 (± 1.501)	-2.21 (± 5.829)	0.49 (± 0.716)
Eosinophils/Leukocytes, Week2, n=9,9,10,9,9	2.1 (± 2.264)	-0.39 (± 1.394)	-0.64 (± 7.039)	1.29 (± 2.389)
Eosinophils/Leukocytes, Week3, n=9,7,9,6,7	0.61 (± 1.114)	-0.73 (± 1.947)	-2.08 (± 5.652)	0.87 (± 0.437)
Eosinophils/Leukocytes, Week4, n=6,9,9,9,9	-0.37 (± 0.958)	-0.89 (± 1.578)	-1.7 (± 5.803)	-0.04 (± 0.642)
Eosinophils/Leukocytes, Week5, n=7,6,6,9,7	0.2 (± 1.405)	-0.73 (± 1.188)	0.15 (± 0.997)	0.12 (± 0.574)
Eosinophils/Leukocytes, Week6, n=7,10,6,10,7	-0.43 (± 1.048)	-0.86 (± 1.581)	-0.58 (± 0.496)	-0.16 (± 0.662)

Eosinophils/Leukocytes, Week8, n=8,7,9,9,9	0.1 (± 0.678)	-0.74 (± 1.259)	-1.2 (± 3.844)	0.29 (± 0.695)
Eosinophils/Leukocytes, Week10, n=7,8,4,7,8	0.87 (± 2.131)	-0.19 (± 2.307)	-0.8 (± 0.757)	0.51 (± 2.343)
Eosinophils/Leukocytes, Week12, n=7,7,7,8,7	0.06 (± 1.212)	-0.34 (± 2.167)	-0.37 (± 0.848)	0.75 (± 1.449)
Eosinophils/Leukocytes, Week16, n=5,6,3,6,6	0.24 (± 0.77)	-0.87 (± 1.742)	1.33 (± 2.829)	-0.55 (± 0.718)
Lymphocytes/Leukocytes, Week1, n=9,10,9,10,11	7.37 (± 10.9)	-2.44 (± 11.9)	-7.27 (± 7.597)	-0.18 (± 8.646)
Lymphocytes/Leukocytes, Week2, n=9,9,10,9,9	5.57 (± 11.455)	-0.09 (± 5.623)	-6.49 (± 6.821)	1.56 (± 9.714)
Lymphocytes/Leukocytes, Week3, n=9,7,9,6,7	6.17 (± 12.256)	0.64 (± 8.374)	-2.63 (± 7.333)	9.45 (± 6.77)
Lymphocytes/Leukocytes, Week4, n=6,9,9,9,9	8.02 (± 12.199)	0.27 (± 8.848)	-1.2 (± 5.79)	4.68 (± 8.387)
Lymphocytes/Leukocytes, Week5, n=7,6,6,9,7	1.93 (± 9.353)	1.87 (± 7.289)	-3.7 (± 8.298)	6.59 (± 10.764)
Lymphocytes/Leukocytes, Week6, n=7,10,6,10,7	4.07 (± 10.43)	-0.84 (± 7.714)	0.73 (± 15.625)	1.79 (± 5.275)
Lymphocytes/Leukocytes, Week8, n=8,7,9,9,9	6.49 (± 13.921)	0.89 (± 10.618)	-0.08 (± 11.076)	7.33 (± 12.026)
Lymphocytes/Leukocytes, Week10, n=7,8,4,7,8	4.69 (± 8.153)	0.04 (± 7.789)	-6.05 (± 4.08)	3.69 (± 10.497)
Lymphocytes/Leukocytes, Week12, n=7,7,7,8,7	-0.41 (± 6.828)	-1.86 (± 3.134)	3.1 (± 9.892)	2.74 (± 11.547)
Lymphocytes/Leukocytes, Week16, n=5,6,3,6,6	4.58 (± 10.518)	4.75 (± 11.131)	0.67 (± 5.311)	3.5 (± 10.198)
Monocytes/Leukocytes, Week1, n=9,10,9,10,11	-0.23 (± 4.618)	-1.44 (± 1.851)	-0.26 (± 4.954)	-0.1 (± 3.053)
Monocytes/Leukocytes, Week2, n=9,9,10,9,9	-0.78 (± 4.229)	-0.01 (± 2.606)	-0.66 (± 3.168)	-0.78 (± 2.485)
Monocytes/Leukocytes, Week3, n=9,7,9,6,7	-1.96 (± 4.246)	-0.19 (± 2.83)	1.66 (± 5.079)	0.63 (± 3.533)
Monocytes/Leukocytes, Week4, n=6,9,9,9,9	-2.05 (± 4.077)	0.12 (± 2.8)	0.34 (± 3.968)	0.8 (± 5.071)
Monocytes/Leukocytes, Week5, n=7,6,6,9,7	-0.27 (± 2.188)	0.72 (± 1.309)	0.37 (± 4.712)	0.68 (± 4.668)
Monocytes/Leukocytes, Week6, n=7,10,6,10,7	-1 (± 1.69)	-0.51 (± 2.682)	-0.97 (± 4.149)	-1.82 (± 2.439)
Monocytes/Leukocytes, Week8, n=8,7,9,9,9	-1.24 (± 2.856)	1.34 (± 4.065)	-0.17 (± 2.401)	0.69 (± 2.816)
Monocytes/Leukocytes, Week10, n=7,8,4,7,8	0.59 (± 1.416)	-0.65 (± 2.519)	-0.98 (± 3.645)	0.03 (± 3.539)
Monocytes/Leukocytes, Week12, n=7,7,7,8,7	0.04 (± 2.326)	-0.2 (± 1.882)	1.34 (± 3.38)	0.95 (± 3.746)
Monocytes/Leukocytes, Week16, n=5,6,3,6,6	0.94 (± 1.358)	-0.43 (± 2.207)	-0.83 (± 0.569)	-1.62 (± 2.091)
Neutrophils/Leukocytes, Week1, n=8,10,9,10,11	-6.89 (± 10.974)	4.6 (± 14.042)	9.81 (± 9.751)	-0.2 (± 11.49)
Neutrophils/Leukocytes, Week2, n=8,9,10,9,9	-6.95 (± 10.766)	0.58 (± 7.422)	7.93 (± 8.472)	-2.13 (± 10.553)
Neutrophils/Leukocytes, Week3, n=8,7,9,6,7	-4.61 (± 12.278)	0.31 (± 11.97)	2.88 (± 10.999)	-11.13 (± 8.861)
Neutrophils/Leukocytes, Week4, n=5,9,9,9,9	-6.88 (± 11.033)	0.52 (± 12.138)	2.62 (± 9.988)	-5.47 (± 9.665)
Neutrophils/Leukocytes, Week5, n=6,6,6,9,7	-1.67 (± 11.661)	-2.03 (± 7.169)	3.32 (± 12.056)	-7.36 (± 13.85)
Neutrophils/Leukocytes, Week6, n=6,10,6,10,7	-2.7 (± 13)	2.16 (± 9.334)	1.1 (± 16.691)	0.22 (± 5.022)
Neutrophils/Leukocytes, Week8, n=7,7,9,9,9	-5.21 (± 13.064)	-1.51 (± 13.268)	1.04 (± 10.843)	-8.42 (± 13.702)

Neutrophils/Leukocytes, Week10, n=6,8,4,7,8	-5.93 (± 11.454)	0.81 (± 11.653)	8.18 (± 5.705)	-4.29 (± 12.505)
Neutrophils/Leukocytes, Week12, n=6,7,7,8,7	0.68 (± 7.055)	2.37 (± 5.459)	-3.9 (± 10.99)	-4.39 (± 14.892)
Neutrophils/Leukocytes, Week16, n=4,6,3,6,6	-5.38 (± 13.405)	-3.37 (± 12.751)	-1.07 (± 4.007)	-1.45 (± 11.237)
Neutrophils SG/Leukocytes, Week1, n=9,10,9,10,11	-7.22 (± 10.314)	4.6 (± 14.042)	9.81 (± 9.751)	-0.2 (± 11.49)
Neutrophils SG/Leukocytes, Week2, n=9,9,10,9,9	-6.98 (± 10.071)	0.58 (± 7.422)	7.93 (± 8.472)	-2.13 (± 10.553)
Neutrophils SG/Leukocytes, Week3, n=9,7,9,6,7	-4.78 (± 11.496)	0.31 (± 11.97)	2.88 (± 10.999)	-11.13 (± 8.861)
Neutrophils SG/Leukocytes, Week4, n=6,9,9,9,9	-5.62 (± 10.342)	0.52 (± 12.138)	2.62 (± 9.988)	-5.47 (± 9.665)
Neutrophils SG/Leukocytes, Week5, n=7,6,6,9,7	-1.74 (± 10.647)	-2.03 (± 7.169)	3.32 (± 12.056)	-7.36 (± 13.85)
Neutrophils SG/Leukocytes, Week6, n=7,10,6,10,7	-2.4 (± 11.894)	2.16 (± 9.334)	1.1 (± 16.691)	0.22 (± 5.022)
Neutrophils SG/Leukocytes, Week8, n=8,7,9,9,9	-5.26 (± 12.096)	-1.51 (± 13.268)	1.04 (± 10.843)	-8.42 (± 13.702)
Neutrophils SG/Leukocytes, Week10, n=7,8,4,7,8	-6.07 (± 10.462)	0.81 (± 11.653)	8.18 (± 5.705)	-4.29 (± 12.505)
Neutrophils SG/Leukocytes, Week12, n=7,7,7,8,7	0.49 (± 6.462)	2.37 (± 5.459)	-3.9 (± 10.99)	-4.39 (± 14.892)
Neutrophils SG/Leukocytes, Week16, n=5,6,3,6,6	-5.76 (± 11.641)	-3.37 (± 12.751)	-1.07 (± 4.007)	-1.45 (± 11.237)
EDW, Week1, n=9,10,9,10,11	0.07 (± 0.447)	0.03 (± 0.523)	-0.26 (± 0.75)	-0.25 (± 0.472)
EDW, Week2, n=9,9,10,9,9	0.28 (± 0.387)	0.22 (± 0.545)	0.08 (± 0.594)	-0.33 (± 0.654)
EDW, Week3, n=9,7,9,7,7	0.14 (± 0.691)	0.37 (± 0.206)	0.44 (± 0.918)	-0.2 (± 0.936)
EDW, Week4, n=6,9,9,9,9	0.85 (± 0.864)	0.1 (± 0.51)	0.54 (± 0.644)	-0.08 (± 1.099)
EDW, Week5, n=7,6,6,9,7	0.59 (± 0.96)	0.43 (± 0.833)	1.2 (± 1.131)	0.39 (± 1.237)
EDW, Week6, n=7,10,6,10,8	0.43 (± 1.268)	0.06 (± 0.744)	0.55 (± 1.544)	0.46 (± 0.987)
EDW, Week8, n=8,7,9,9,9	0.31 (± 1.169)	0.01 (± 0.773)	1.02 (± 1.498)	0.77 (± 0.97)
EDW, Week10, n=7,8,4,7,8	0.23 (± 0.945)	0.06 (± 1.187)	0.5 (± 1.538)	0.91 (± 1.129)
EDW, Week12, n=7,7,7,8,7	0.51 (± 1.794)	0.11 (± 1.275)	0.51 (± 1.235)	0.94 (± 1.25)
EDW, Week16, n=5,6,3,6,6	0.7 (± 1.377)	0.57 (± 1.341)	0.5 (± 0.265)	0.52 (± 1.16)

Notes:

[101] - ITT Population

[102] - ITT Population

[103] - ITT Population

[104] - ITT Population

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[105]			
Units: Percentage				
arithmetic mean (standard deviation)				
Basophils/Leukocytes, Week1, n=9,10,9,10,11	-0.09 (± 0.266)			
Basophils/Leukocytes, Week2, n=9,9,10,9,9	-0.12 (± 0.244)			
Basophils/Leukocytes, Week3, n=9,7,9,6,7	0.01 (± 0.277)			
Basophils/Leukocytes, Week4, n=6,9,9,9,9	-0.12 (± 0.179)			

Basophils/Leukocytes, Week5, n=7,6,6,9,7	-0.14 (± 0.288)			
Basophils/Leukocytes, Week6, n=7,10,6,10,7	-0.09 (± 0.234)			
Basophils/Leukocytes, Week8, n=8,7,9,9,9	-0.07 (± 0.296)			
Basophils/Leukocytes, Week10, n=7,8,4,7,8	0.03 (± 0.139)			
Basophils/Leukocytes, Week12, n=7,7,7,8,7	-0.06 (± 0.369)			
Basophils/Leukocytes, Week16, n=5,6,3,6,6	-0.1 (± 0.228)			
Eosinophils/Leukocytes, Week1, n=9,10,9,10,11	0.1 (± 1.052)			
Eosinophils/Leukocytes, Week2, n=9,9,10,9,9	-0.07 (± 0.515)			
Eosinophils/Leukocytes, Week3, n=9,7,9,6,7	1.59 (± 2.26)			
Eosinophils/Leukocytes, Week4, n=6,9,9,9,9	-0.07 (± 0.57)			
Eosinophils/Leukocytes, Week5, n=7,6,6,9,7	-0.24 (± 0.31)			
Eosinophils/Leukocytes, Week6, n=7,10,6,10,7	-0.04 (± 0.42)			
Eosinophils/Leukocytes, Week8, n=8,7,9,9,9	0.12 (± 0.67)			
Eosinophils/Leukocytes, Week10, n=7,8,4,7,8	0.46 (± 1.234)			
Eosinophils/Leukocytes, Week12, n=7,7,7,8,7	1.14 (± 1.408)			
Eosinophils/Leukocytes, Week16, n=5,6,3,6,6	0.53 (± 0.763)			
Lymphocytes/Leukocytes, Week1, n=9,10,9,10,11	-1.85 (± 7.021)			
Lymphocytes/Leukocytes, Week2, n=9,9,10,9,9	-1.49 (± 6.214)			
Lymphocytes/Leukocytes, Week3, n=9,7,9,6,7	3.99 (± 14.729)			
Lymphocytes/Leukocytes, Week4, n=6,9,9,9,9	-0.31 (± 6.648)			
Lymphocytes/Leukocytes, Week5, n=7,6,6,9,7	-2.39 (± 4.963)			
Lymphocytes/Leukocytes, Week6, n=7,10,6,10,7	-2.81 (± 8.409)			
Lymphocytes/Leukocytes, Week8, n=8,7,9,9,9	-0.62 (± 3.987)			
Lymphocytes/Leukocytes, Week10, n=7,8,4,7,8	0.77 (± 7.583)			
Lymphocytes/Leukocytes, Week12, n=7,7,7,8,7	2.83 (± 9.272)			
Lymphocytes/Leukocytes, Week16, n=5,6,3,6,6	-1.2 (± 4.572)			
Monocytes/Leukocytes, Week1, n=9,10,9,10,11	-0.86 (± 2.037)			
Monocytes/Leukocytes, Week2, n=9,9,10,9,9	-0.12 (± 2.164)			
Monocytes/Leukocytes, Week3, n=9,7,9,6,7	-0.51 (± 1.142)			
Monocytes/Leukocytes, Week4, n=6,9,9,9,9	-0.51 (± 1.722)			
Monocytes/Leukocytes, Week5, n=7,6,6,9,7	-0.87 (± 1.863)			

Monocytes/Leukocytes, Week6, n=7,10,6,10,7	-1.13 (± 0.972)			
Monocytes/Leukocytes, Week8, n=8,7,9,9,9	0.29 (± 1.642)			
Monocytes/Leukocytes, Week10, n=7,8,4,7,8	-0.45 (± 1.448)			
Monocytes/Leukocytes, Week12, n=7,7,7,8,7	-0.04 (± 0.986)			
Monocytes/Leukocytes, Week16, n=5,6,3,6,6	0.3 (± 1.74)			
Neutrophils/Leukocytes, Week1, n=8,10,9,10,11	2.71 (± 8.625)			
Neutrophils/Leukocytes, Week2, n=8,9,10,9,9	1.8 (± 8.24)			
Neutrophils/Leukocytes, Week3, n=8,7,9,6,7	-5.07 (± 16.55)			
Neutrophils/Leukocytes, Week4, n=5,9,9,9,9	1.01 (± 7.743)			
Neutrophils/Leukocytes, Week5, n=6,6,6,9,7	3.64 (± 5.422)			
Neutrophils/Leukocytes, Week6, n=6,10,6,10,7	4.07 (± 8.798)			
Neutrophils/Leukocytes, Week8, n=7,7,9,9,9	0.28 (± 5.261)			
Neutrophils/Leukocytes, Week10, n=6,8,4,7,8	-0.81 (± 8.921)			
Neutrophils/Leukocytes, Week12, n=6,7,7,8,7	-3.87 (± 8.832)			
Neutrophils/Leukocytes, Week16, n=4,6,3,6,6	0.47 (± 5.895)			
Neutrophils SG/Leukocytes, Week1, n=9,10,9,10,11	2.71 (± 8.625)			
Neutrophils SG/Leukocytes, Week2, n=9,9,10,9,9	1.8 (± 8.24)			
Neutrophils SG/Leukocytes, Week3, n=9,7,9,6,7	-5.07 (± 16.55)			
Neutrophils SG/Leukocytes, Week4, n=6,9,9,9,9	1.01 (± 7.743)			
Neutrophils SG/Leukocytes, Week5, n=7,6,6,9,7	3.64 (± 5.422)			
Neutrophils SG/Leukocytes, Week6, n=7,10,6,10,7	4.07 (± 8.798)			
Neutrophils SG/Leukocytes, Week8, n=8,7,9,9,9	0.28 (± 5.261)			
Neutrophils SG/Leukocytes, Week10, n=7,8,4,7,8	-0.81 (± 8.921)			
Neutrophils SG/Leukocytes, Week12, n=7,7,7,8,7	-3.87 (± 8.832)			
Neutrophils SG/Leukocytes, Week16, n=5,6,3,6,6	0.47 (± 5.895)			
EDW, Week1, n=9,10,9,10,11	-0.17 (± 0.427)			
EDW, Week2, n=9,9,10,9,9	0.08 (± 0.672)			
EDW, Week3, n=9,7,9,7,7	0.1 (± 0.847)			
EDW, Week4, n=6,9,9,9,9	0.31 (± 1.288)			
EDW, Week5, n=7,6,6,9,7	0.41 (± 1.489)			
EDW, Week6, n=7,10,6,10,8	-0.02 (± 1.635)			
EDW, Week8, n=8,7,9,9,9	0.37 (± 1.907)			
EDW, Week10, n=7,8,4,7,8	0.91 (± 2.906)			
EDW, Week12, n=7,7,7,8,7	1.57 (± 2.715)			

EDW, Week16, n=5,6,3,6,6	1.72 (± 3.98)			

Notes:

[105] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in erythrocytes and reticulocytes at the indicated time points up to Week 16

End point title	Change from Baseline in erythrocytes and reticulocytes at the indicated time points up to Week 16[106]

End point description:

Change from Baseline in the erythrocyte and reticulocyte values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 1, 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[106] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[107]	10[108]	10[109]	10[110]
Units: Trillion per liter				
arithmetic mean (standard deviation)				
Erythrocytes, Week1, n=9,10,9,10,11	-0.07 (± 0.187)	-0.08 (± 0.162)	0.01 (± 0.226)	-0.06 (± 0.178)
Erythrocytes, Week2, n=9,9,10,9,9	-0.1 (± 0.166)	0.02 (± 0.277)	0.07 (± 0.226)	-0.07 (± 0.2)
Erythrocytes, Week3, n=9,7,9,7,7	-0.12 (± 0.172)	0.03 (± 0.263)	0.04 (± 0.201)	-0.04 (± 0.27)
Erythrocytes, Week4, n=6,9,9,9,9	-0.05 (± 0.207)	-0.07 (± 0.2)	0.04 (± 0.151)	-0.13 (± 0.283)
Erythrocytes, Week5, n=7,6,7,9,7	-0.27 (± 0.17)	0 (± 0.29)	0 (± 0.141)	-0.19 (± 0.176)
Erythrocytes, Week6, n=7,10,6,10,8	-0.17 (± 0.25)	0.08 (± 0.377)	0.08 (± 0.279)	-0.08 (± 0.204)
Erythrocytes, Week8, n=8,7,9,9,9	0.04 (± 0.302)	-0.06 (± 0.151)	-0.06 (± 0.207)	-0.09 (± 0.341)
Erythrocytes, Week10, n=7,8,4,7,8	-0.13 (± 0.214)	-0.03 (± 0.296)	-0.05 (± 0.129)	-0.21 (± 0.146)
Erythrocytes, Week12, n=7,7,7,8,7	-0.11 (± 0.227)	-0.01 (± 0.204)	0.01 (± 0.107)	-0.04 (± 0.311)
Erythrocytes, Week16, n=5,6,3,6,6	-0.02 (± 0.327)	-0.1 (± 0.21)	-0.17 (± 0.058)	-0.03 (± 0.32)
Reticulocytes, Week1, n=9,10,9,10,11	0.01023 (± 0.013577)	-0.00241 (± 0.016591)	0.00822 (± 0.014942)	0.00233 (± 0.01305)

Reticulocytes, Week2, n=9,9,10,9,9	0.01356 (± 0.014036)	-0.00686 (± 0.020924)	-0.0008 (± 0.014329)	-0.0026 (± 0.017417)
Reticulocytes, Week3, n=9,7,9,7,7	0.02272 (± 0.022383)	0.00693 (± 0.032031)	0.01006 (± 0.011791)	0.00519 (± 0.022769)
Reticulocytes, Week4, n=6,9,9,9,9	0.01822 (± 0.008272)	0.00904 (± 0.039946)	0.00202 (± 0.018841)	0.00278 (± 0.020853)
Reticulocytes, Week5, n=7,6,7,9,7	0.01267 (± 0.015672)	0.00122 (± 0.015623)	0.01227 (± 0.019674)	0.00874 (± 0.022087)
Reticulocytes, Week6, n=7,10,6,10,8	0.00827 (± 0.018538)	0.00131 (± 0.020422)	-0.00193 (± 0.01615)	0.00872 (± 0.019709)
Reticulocytes, Week8, n=8,7,9,9,9	0.00609 (± 0.01307)	0.00561 (± 0.02537)	0.01772 (± 0.026266)	0.01912 (± 0.046264)
Reticulocytes, Week10, n=7,8,4,7,8	0.01343 (± 0.005743)	-0.00155 (± 0.024259)	-0.00227 (± 0.010259)	0.01686 (± 0.027415)
Reticulocytes, Week12, n=7,7,7,8,7	0.00839 (± 0.01347)	0.00454 (± 0.019287)	0.00017 (± 0.011061)	0.00011 (± 0.025521)
Reticulocytes, Week16, n=5,6,3,6,6	0.00778 (± 0.01031)	-0.00515 (± 0.012694)	0.00853 (± 0.013776)	0.00412 (± 0.023629)

Notes:

[107] - ITT Population

[108] - ITT Population

[109] - ITT Population

[110] - ITT Population

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[111]			
Units: Trillion per liter				
arithmetic mean (standard deviation)				
Erythrocytes, Week1, n=9,10,9,10,11	-0.13 (± 0.127)			
Erythrocytes, Week2, n=9,9,10,9,9	-0.14 (± 0.088)			
Erythrocytes, Week3, n=9,7,9,7,7	-0.13 (± 0.221)			
Erythrocytes, Week4, n=6,9,9,9,9	-0.09 (± 0.22)			
Erythrocytes, Week5, n=7,6,7,9,7	-0.07 (± 0.198)			
Erythrocytes, Week6, n=7,10,6,10,8	0.05 (± 0.12)			
Erythrocytes, Week8, n=8,7,9,9,9	-0.04 (± 0.219)			
Erythrocytes, Week10, n=7,8,4,7,8	0.04 (± 0.256)			
Erythrocytes, Week12, n=7,7,7,8,7	-0.04 (± 0.331)			
Erythrocytes, Week16, n=5,6,3,6,6	0.03 (± 0.28)			
Reticulocytes, Week1, n=9,10,9,10,11	-0.00318 (± 0.015587)			
Reticulocytes, Week2, n=9,9,10,9,9	-0.00031 (± 0.024158)			
Reticulocytes, Week3, n=9,7,9,7,7	-0.00409 (± 0.022753)			
Reticulocytes, Week4, n=6,9,9,9,9	0.00083 (± 0.025744)			
Reticulocytes, Week5, n=7,6,7,9,7	0.00009 (± 0.031287)			
Reticulocytes, Week6, n=7,10,6,10,8	-0.00243 (± 0.023781)			
Reticulocytes, Week8, n=8,7,9,9,9	0.00214 (± 0.025027)			

Reticulocytes, Week10, n=7,8,4,7,8	0.00125 (± 0.035393)			
Reticulocytes, Week12, n=7,7,7,8,7	0.00859 (± 0.009494)			
Reticulocytes, Week16, n=5,6,3,6,6	0.00195 (± 0.008808)			

Notes:

[111] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in hemoglobin and EMCHC at the indicated time points up to Week 16

End point title	Change from Baseline in hemoglobin and EMCHC at the indicated time points up to Week 16[112]

End point description:

Change from Baseline in the hemoglobin and erythrocyte mean corpuscular hemoglobin concentration (EMCHC) values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 1, 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[112] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[113]	10[114]	10[115]	10[116]
Units: Grams per liter				
arithmetic mean (standard deviation)				
Hemoglobin, Week1, n=9,10,9,10,11	-2.4 (± 5.61)	-2.5 (± 4.14)	0.2 (± 6.46)	-0.7 (± 6.07)
Hemoglobin, Week2, n=9,9,10,9,9	-2.6 (± 4.42)	-0.3 (± 7.48)	1.6 (± 6.47)	-1 (± 6.52)
Hemoglobin, Week3, n=9,7,9,7,7	-3.6 (± 4.75)	0.9 (± 5.46)	1 (± 5.63)	-0.9 (± 6.67)
Hemoglobin, Week4, n=6,9,9,9,9	-1.8 (± 7.14)	-1.6 (± 6.56)	1.8 (± 4.74)	-3.1 (± 8.91)
Hemoglobin, Week5, n=7,6,7,9,7	-8.6 (± 3.99)	-0.5 (± 7.97)	2.1 (± 4.45)	-3.9 (± 7.15)
Hemoglobin, Week6, n=7,10,6,10,8	-6.3 (± 5.68)	2.4 (± 11.46)	3.8 (± 7)	-1.7 (± 6.85)
Hemoglobin, Week8, n=8,7,9,9,9	0.3 (± 8.94)	-3.1 (± 5.24)	-0.1 (± 5.82)	-3.3 (± 9.33)
Hemoglobin, Week10, n=7,8,4,7,8	-4.9 (± 5.21)	-2.1 (± 9)	1.5 (± 3.7)	-3.6 (± 7.37)
Hemoglobin, Week12, n=7,7,7,8,7	-6 (± 6.58)	-3.7 (± 5.35)	1.4 (± 1.72)	-2.1 (± 8.72)
Hemoglobin, Week16, n=5,6,3,6,6	-6.6 (± 7.67)	-6.2 (± 6.11)	-3 (± 1.73)	-4.2 (± 4.31)
EMCHC, Week1, n=9,10,9,10,11	-4.6 (± 6.52)	-3.9 (± 5.7)	2.4 (± 4.93)	1.4 (± 6.79)
EMCHC, Week2, n=9,9,10,9,9	-2.8 (± 7.28)	-3.3 (± 5.57)	3.8 (± 3.99)	4 (± 5.59)
EMCHC, Week3, n=9,7,9,7,7	1.3 (± 4.64)	-2.4 (± 5.91)	2.3 (± 6.52)	2.9 (± 11.63)
EMCHC, Week4, n=6,9,9,9,9	-1.7 (± 5.89)	1.8 (± 7.53)	2.1 (± 6.39)	6.4 (± 7.99)
EMCHC, Week5, n=7,6,7,9,7	-3.1 (± 7.9)	-3.3 (± 5.85)	1.4 (± 3.41)	3.9 (± 7.99)
EMCHC, Week6, n=7,10,6,10,8	-4.1 (± 9.82)	-0.8 (± 6.66)	3 (± 4.24)	1.8 (± 10.21)

EMCHC, Week8, n=8,7,9,9,9	0.4 (± 5.63)	-1.9 (± 6.04)	2.3 (± 6.2)	1.7 (± 10.69)
EMCHC, Week10, n=7,8,4,7,8	0.6 (± 6.8)	1.4 (± 5.26)	2.3 (± 4.19)	4.3 (± 8.56)
EMCHC, Week12, n=7,7,7,8,7	-3.7 (± 11.79)	-0.9 (± 4.22)	3.1 (± 7.88)	3.4 (± 7.42)
EMCHC, Week16, n=5,6,3,6,6	-6.6 (± 9.96)	0.3 (± 7.26)	5 (± 5.57)	-3.2 (± 13.35)

Notes:

[113] - ITT Population

[114] - ITT Population

[115] - ITT Population

[116] - ITT Population

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[117]			
Units: Grams per liter				
arithmetic mean (standard deviation)				
Hemoglobin, Week1, n=9,10,9,10,11	-4.3 (± 4.47)			
Hemoglobin, Week2, n=9,9,10,9,9	-5.2 (± 3.38)			
Hemoglobin, Week3, n=9,7,9,7,7	-5.1 (± 6.15)			
Hemoglobin, Week4, n=6,9,9,9,9	-4.7 (± 7.16)			
Hemoglobin, Week5, n=7,6,7,9,7	-5.1 (± 7.22)			
Hemoglobin, Week6, n=7,10,6,10,8	-2.4 (± 6.72)			
Hemoglobin, Week8, n=8,7,9,9,9	-5.9 (± 7.54)			
Hemoglobin, Week10, n=7,8,4,7,8	-4.1 (± 7.74)			
Hemoglobin, Week12, n=7,7,7,8,7	-7.7 (± 5.22)			
Hemoglobin, Week16, n=5,6,3,6,6	-4.7 (± 8.12)			
EMCHC, Week1, n=9,10,9,10,11	-0.5 (± 6.33)			
EMCHC, Week2, n=9,9,10,9,9	0.1 (± 5.13)			
EMCHC, Week3, n=9,7,9,7,7	-2.9 (± 4.63)			
EMCHC, Week4, n=6,9,9,9,9	-0.4 (± 5.32)			
EMCHC, Week5, n=7,6,7,9,7	-3.1 (± 9.23)			
EMCHC, Week6, n=7,10,6,10,8	-3.1 (± 10.72)			
EMCHC, Week8, n=8,7,9,9,9	-1.6 (± 9.74)			
EMCHC, Week10, n=7,8,4,7,8	-2.9 (± 7.75)			
EMCHC, Week12, n=7,7,7,8,7	-6 (± 8.33)			
EMCHC, Week16, n=5,6,3,6,6	1.8 (± 15.66)			

Notes:

[117] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in EMCH at the indicated time points up to Week 16

End point title	Change from Baseline in EMCH at the indicated time points up to Week 16[118]

End point description:

Change from Baseline in the hemoglobin and erythrocyte mean corpuscular hemoglobin (EMCH) values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 1, 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[118] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[119]	10[120]	10[121]	10[122]
Units: Picograms				
arithmetic mean (standard deviation)				
EMCH, Week1, n=9,10,9,10,11	-0.17 (± 0.45)	-0.22 (± 0.563)	0.13 (± 0.316)	0.25 (± 0.517)
EMCH, Week2, n=9,9,10,9,9	0.01 (± 0.22)	-0.38 (± 0.58)	0.09 (± 0.348)	0.1 (± 0.532)
EMCH, Week3, n=9,7,9,7,7	0.16 (± 0.553)	-0.11 (± 0.626)	-0.04 (± 0.43)	-0.03 (± 1.029)
EMCH, Week4, n=6,9,9,9,9	0.03 (± 0.869)	0 (± 0.458)	0.1 (± 0.65)	0.14 (± 0.609)
EMCH, Week5, n=7,6,7,9,7	-0.16 (± 0.447)	-0.1 (± 0.4)	0.5 (± 0.216)	0.49 (± 0.747)
EMCH, Week6, n=7,10,6,10,8	-0.23 (± 0.655)	-0.34 (± 0.847)	0.23 (± 0.367)	0.15 (± 0.72)
EMCH, Week8, n=8,7,9,9,9	-0.12 (± 0.907)	-0.46 (± 0.791)	0.28 (± 0.455)	-0.17 (± 1.428)
EMCH, Week10, n=7,8,4,7,8	-0.33 (± 0.668)	-0.35 (± 0.548)	0.52 (± 0.126)	0.54 (± 1.229)
EMCH, Week12, n=7,7,7,8,7	-0.56 (± 0.774)	-0.84 (± 0.914)	0.26 (± 0.675)	-0.15 (± 1.323)
EMCH, Week16, n=5,6,3,6,6	-1.18 (± 1.178)	-0.9 (± 0.957)	0.3 (± 0.5)	-0.88 (± 1.731)

Notes:

[119] - ITT Population.

[120] - ITT Population.

[121] - ITT Population.

[122] - ITT Population.

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[123]			
Units: Picograms				
arithmetic mean (standard deviation)				
EMCH, Week1, n=9,10,9,10,11	-0.13 (± 0.529)			
EMCH, Week2, n=9,9,10,9,9	-0.18 (± 0.62)			
EMCH, Week3, n=9,7,9,7,7	-0.66 (± 0.75)			
EMCH, Week4, n=6,9,9,9,9	-0.49 (± 1.177)			
EMCH, Week5, n=7,6,7,9,7	-0.79 (± 1.442)			
EMCH, Week6, n=7,10,6,10,8	-1 (± 1.504)			
EMCH, Week8, n=8,7,9,9,9	-1.19 (± 1.691)			
EMCH, Week10, n=7,8,4,7,8	-1.37 (± 1.972)			

EMCH, Week12, n=7,7,7,8,7	-1.79 (± 2.323)			
EMCH, Week16, n=5,6,3,6,6	-1.43 (± 2.868)			

Notes:

[123] - ITT Population.

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in EMCV and MPV at the indicated time points up to Week 16

End point title	Change from Baseline in EMCV and MPV at the indicated time points up to Week 16[124]

End point description:

Change from Baseline in the erythrocyte mean corpuscular volume (EMCV) and mean platelet volume (MPV) values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 1, 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[124] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[125]	10[126]	10[127]	10[128]
Units: Femtoliters				
arithmetic mean (standard deviation)				
EMCV, Week1, n=9,10,9,10,11	0.4 (± 1.42)	0.6 (± 1.9)	-0.6 (± 1.13)	0.2 (± 1.32)
EMCV, Week2, n=9,9,10,9,9	0.6 (± 1.74)	-0.3 (± 1.66)	-0.7 (± 0.95)	-1 (± 1.41)
EMCV, Week3, n=9,7,9,7,7	-0.1 (± 1.69)	0.7 (± 1.7)	-0.7 (± 1.66)	-0.9 (± 1.21)
EMCV, Week4, n=6,9,9,9,9	0.3 (± 2.8)	-0.3 (± 2.45)	-0.3 (± 1.73)	-1.7 (± 1.41)
EMCV, Week5, n=7,6,7,9,7	0 (± 1)	0.8 (± 2.64)	1.1 (± 0.9)	0.1 (± 1.96)
EMCV, Week6, n=7,10,6,10,8	0.3 (± 1.98)	-0.8 (± 2.25)	0.2 (± 2.14)	-0.1 (± 2.08)
EMCV, Week8, n=8,7,9,9,9	-0.6 (± 2.83)	-1 (± 2.52)	0.2 (± 2.28)	-1.2 (± 1.99)
EMCV, Week10, n=7,8,4,7,8	-1.6 (± 2.44)	-1.5 (± 1.85)	1 (± 0.82)	0.4 (± 2.3)
EMCV, Week12, n=7,7,7,8,7	-0.9 (± 4.45)	-2.4 (± 2.15)	-0.3 (± 1.7)	-1.6 (± 2.39)
EMCV, Week16, n=5,6,3,6,6	-2.2 (± 5.45)	-3 (± 2.83)	0 (± 0)	-1.7 (± 2.16)
MPV, Week1, n=9,10,9,10,11	0.12 (± 0.273)	-0.04 (± 0.45)	0.06 (± 0.317)	-0.37 (± 0.696)
MPV, Week2, n=9,9,10,9,9	0.1 (± 0.24)	-0.02 (± 0.556)	0.31 (± 0.626)	-0.22 (± 0.821)
MPV, Week3, n=9,7,9,7,7	-0.09 (± 0.352)	-0.01 (± 0.631)	-0.17 (± 0.76)	-0.45 (± 0.829)
MPV, Week4, n=6,9,9,9,9	-0.08 (± 0.248)	-0.02 (± 0.572)	-0.24 (± 0.675)	-0.24 (± 0.805)

MPV, Week5, n=7,6,7,9,7	-0.1 (± 0.416)	0.12 (± 0.595)	-0.1 (± 0.258)	-0.49 (± 0.772)
MPV, Week6, n=7,10,6,10,8	0.2 (± 0.648)	-0.14 (± 0.731)	-0.17 (± 0.388)	-0.56 (± 0.76)
MPV, Week8, n=8,7,9,9,9	-0.17 (± 0.396)	-0.06 (± 0.704)	-0.13 (± 0.557)	-0.39 (± 1.029)
MPV, Week10, n=7,8,4,7,8	-0.16 (± 0.447)	-0.1 (± 0.374)	0.05 (± 0.48)	-0.46 (± 0.832)
MPV, Week12, n=7,7,7,8,7	-0.07 (± 0.736)	0.2 (± 0.569)	0.01 (± 0.689)	-0.24 (± 0.778)
MPV, Week16, n=5,6,3,6,6	0.1 (± 0.566)	-0.08 (± 0.631)	-0.7 (± 0.52)	-0.38 (± 1.003)

Notes:

[125] - ITT Population

[126] - ITT Population

[127] - ITT Population

[128] - ITT Population

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[129]			
Units: Femtoliters				
arithmetic mean (standard deviation)				
EMCV, Week1, n=9,10,9,10,11	-0.3 (± 1.68)			
EMCV, Week2, n=9,9,10,9,9	-0.4 (± 2.7)			
EMCV, Week3, n=9,7,9,7,7	-1 (± 2.24)			
EMCV, Week4, n=6,9,9,9,9	-1.1 (± 2.98)			
EMCV, Week5, n=7,6,7,9,7	-1.6 (± 3.41)			
EMCV, Week6, n=7,10,6,10,8	-2.1 (± 4.22)			
EMCV, Week8, n=8,7,9,9,9	-3.1 (± 4.01)			
EMCV, Week10, n=7,8,4,7,8	-3.5 (± 5.15)			
EMCV, Week12, n=7,7,7,8,7	-3.7 (± 6.34)			
EMCV, Week16, n=5,6,3,6,6	-5.3 (± 6.28)			
MPV, Week1, n=9,10,9,10,11	-0.16 (± 0.32)			
MPV, Week2, n=9,9,10,9,9	-0.08 (± 0.509)			
MPV, Week3, n=9,7,9,7,7	-0.17 (± 0.335)			
MPV, Week4, n=6,9,9,9,9	-0.02 (± 0.421)			
MPV, Week5, n=7,6,7,9,7	-0.07 (± 0.616)			
MPV, Week6, n=7,10,6,10,8	-0.09 (± 0.569)			
MPV, Week8, n=8,7,9,9,9	-0.12 (± 0.663)			
MPV, Week10, n=7,8,4,7,8	0.01 (± 0.579)			
MPV, Week12, n=7,7,7,8,7	-0.03 (± 0.789)			
MPV, Week16, n=5,6,3,6,6	0 (± 0.559)			

Notes:

[129] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in hematocrit and reticulocytes/erythrocytes at the indicated time points up to Week 16

End point title	Change from Baseline in hematocrit and reticulocytes/erythrocytes at the indicated time points up to Week 16[130]

End point description:

Change from Baseline in the hematocrit and reticulocytes/erythrocytes values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 1, 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[130] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[131]	10[132]	10[133]	10[134]
Units: Fraction of 1				
arithmetic mean (standard deviation)				
Hematocrit, Week1, n=9,10,9,10,11	-0.0023 (± 0.01869)	-0.0029 (± 0.01554)	-0.0028 (± 0.02198)	-0.0037 (± 0.01824)
Hematocrit, Week2, n=9,9,10,9,9	-0.0059 (± 0.01841)	0.0036 (± 0.02677)	-0.0001 (± 0.01959)	-0.0086 (± 0.0199)
Hematocrit, Week3, n=9,7,9,7,7	-0.0127 (± 0.01796)	0.0067 (± 0.02298)	-0.0003 (± 0.01761)	-0.0061 (± 0.02975)
Hematocrit, Week4, n=6,9,9,9,9	-0.0037 (± 0.01691)	-0.0067 (± 0.02438)	0.0027 (± 0.01525)	-0.0172 (± 0.02486)
Hematocrit, Week5, n=7,6,7,9,7	-0.0241 (± 0.01661)	0.0038 (± 0.0312)	0.0037 (± 0.0151)	-0.0168 (± 0.02156)
Hematocrit, Week6, n=7,10,6,10,8	-0.0147 (± 0.02043)	0.0069 (± 0.03471)	0.0082 (± 0.01863)	-0.0088 (± 0.01862)
Hematocrit, Week8, n=8,7,9,9,9	-0.0008 (± 0.0306)	-0.0074 (± 0.01758)	-0.0034 (± 0.01955)	-0.0124 (± 0.03152)
Hematocrit, Week10, n=7,8,4,7,8	-0.0173 (± 0.01505)	-0.008 (± 0.03033)	0.0015 (± 0.005)	-0.016 (± 0.01893)
Hematocrit, Week12, n=7,7,7,8,7	-0.0151 (± 0.02123)	-0.0099 (± 0.01541)	-0.0007 (± 0.01132)	-0.011 (± 0.02818)
Hematocrit, Week16, n=5,6,3,6,6	-0.0126 (± 0.0167)	-0.0195 (± 0.0195)	-0.0163 (± 0.00379)	-0.0087 (± 0.02391)
Reticulocytes/Erythrocytes, Week1, n=9,10,9,10,11	0.0026 (± 0.00305)	-0.0004 (± 0.0042)	0.002 (± 0.00339)	0.0009 (± 0.00311)
Reticulocytes/Erythrocytes, Week2, n=9,9,10,9,9	0.0036 (± 0.00357)	-0.0018 (± 0.00502)	-0.0002 (± 0.00346)	-0.0001 (± 0.00392)
Reticulocytes/Erythrocytes, Week3, n=9,7,9,7,7	0.0059 (± 0.00629)	0.002 (± 0.00777)	0.0023 (± 0.0025)	0.0016 (± 0.0055)
Reticulocytes/Erythrocytes, Week4, n=6,9,9,9,9	0.0045 (± 0.00243)	0.0024 (± 0.00961)	0.0002 (± 0.00471)	0.0014 (± 0.00654)
Reticulocytes/Erythrocytes, Week5, n=7,6,7,9,7	0.0037 (± 0.00407)	0.0003 (± 0.00446)	0.0027 (± 0.00461)	0.0031 (± 0.00613)

Reticulocytes/Erythrocytes, Week6, n=7,10,6,10,8	0.0021 (± 0.00418)	-0.0001 (± 0.00461)	-0.0007 (± 0.00413)	0.0025 (± 0.00495)
Reticulocytes/Erythrocytes, Week8, n=8,7,9,9,9	0.0013 (± 0.00337)	0.0017 (± 0.00556)	0.0042 (± 0.00608)	0.0049 (± 0.00957)
Reticulocytes/Erythrocytes, Week10, n=7,8,4,7,8	0.0036 (± 0.00151)	-0.0002 (± 0.00557)	-0.0005 (± 0.00238)	0.0047 (± 0.00582)
Reticulocytes/Erythrocytes, Week12, n=7,7,7,8,7	0.0023 (± 0.00304)	0.0009 (± 0.00418)	-0.0001 (± 0.00219)	0.0004 (± 0.0059)
Reticulocytes/Erythrocytes, Week16, n=5,6,3,6,6	0.002 (± 0.00173)	-0.0007 (± 0.00258)	0.0023 (± 0.00306)	0.0013 (± 0.0048)

Notes:

[131] - ITT Population

[132] - ITT Population

[133] - ITT Population

[134] - ITT Population

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[135]			
Units: Fraction of 1				
arithmetic mean (standard deviation)				
Hematocrit, Week1, n=9,10,9,10,11	-0.0128 (± 0.01308)			
Hematocrit, Week2, n=9,9,10,9,9	-0.0154 (± 0.01507)			
Hematocrit, Week3, n=9,7,9,7,7	-0.0124 (± 0.02204)			
Hematocrit, Week4, n=6,9,9,9,9	-0.0136 (± 0.02166)			
Hematocrit, Week5, n=7,6,7,9,7	-0.0127 (± 0.01685)			
Hematocrit, Week6, n=7,10,6,10,8	-0.0038 (± 0.01552)			
Hematocrit, Week8, n=8,7,9,9,9	-0.0168 (± 0.02049)			
Hematocrit, Week10, n=7,8,4,7,8	-0.0106 (± 0.01983)			
Hematocrit, Week12, n=7,7,7,8,7	-0.0181 (± 0.02038)			
Hematocrit, Week16, n=5,6,3,6,6	-0.019 (± 0.01455)			
Reticulocytes/Erythrocytes, Week1, n=9,10,9,10,11	-0.0004 (± 0.0037)			
Reticulocytes/Erythrocytes, Week2, n=9,9,10,9,9	0.0002 (± 0.0054)			
Reticulocytes/Erythrocytes, Week3, n=9,7,9,7,7	-0.0003 (± 0.00559)			
Reticulocytes/Erythrocytes, Week4, n=6,9,9,9,9	0.0007 (± 0.0061)			
Reticulocytes/Erythrocytes, Week5, n=7,6,7,9,7	0.0006 (± 0.00728)			
Reticulocytes/Erythrocytes, Week6, n=7,10,6,10,8	-0.0006 (± 0.00545)			
Reticulocytes/Erythrocytes, Week8, n=8,7,9,9,9	0.0008 (± 0.00533)			
Reticulocytes/Erythrocytes, Week10, n=7,8,4,7,8	0.0004 (± 0.00821)			
Reticulocytes/Erythrocytes, Week12, n=7,7,7,8,7	0.002 (± 0.00294)			

Reticulocytes/Erythrocytes, Week16, n=5,6,3,6,6	0.0003 (± 0.00197)			

Notes:

[135] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with urinalysis data at the indicated time points up to Week 16

End point title	Number of participants with urinalysis data at the indicated time points up to Week 16[136]

End point description:

Number of participants with negative and positives (trace, +, ++ and +++) data for urine glucose (UGLU), urine ketones (UKET) and urine occult blood (UOB) are summarised for each post-Baseline assesment until Week 16. Urinalysis was performed by dipstick method. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). A value of 99999 indicates no participants were analyzed therefore there is no data for this time point.

End point type	Primary

End point timeframe:

Baseline, Weeks 1, 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[136] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[137]	10[138]	10[139]	10[140]
Units: Participants				
UGLU, Negative, Baseline, n=9,10,10,10,11	9	10	10	10
UGLU, Positive, Baseline, n=9,10,10,10,11	0	0	0	0
UGLU, Negative, Week2, n=9,9,9,9,10	9	9	9	9
UGLU, Positive, Week2, n=9,9,9,9,10	0	0	0	0
UGLU, Negative, Week3, n=1,1,0,0,0	1	1	99999	99999
UGLU, Positive, Week3, n=1,1,0,0,0	0	0	99999	99999
UGLU, Negative, Week4, n=8,9,8,8,9	8	9	8	8
UGLU, Positive, Week4, n=8,9,8,8,9	0	0	0	0
UGLU, Negative, Week5, n=0,0,0,0,2	99999	99999	99999	99999
UGLU, Positive, Week5, n=0,0,0,0,2	99999	99999	99999	99999
UGLU, Negative, Week6, n=7,10,6,9,8	7	10	6	9
UGLU, Positive, Week6, n=7,10,6,9,8	0	0	0	0
UGLU, Negative, Week8, n=8,7,9,9,9	8	7	9	9
UGLU, Positive, Week8, n=8,7,9,9,9	0	0	0	0
UGLU, Negative, Week10, n=7,8,4,7,8	7	8	4	7
UGLU, Positive, Week10, n=7,8,4,7,8	0	0	0	0
UGLU, Negative, Week12, n=7,7,7,8,7	7	7	7	8
UGLU, Positive, Week12, n=7,7,7,8,7	0	0	0	0

UGLU, Negative, Week16, n=5,6,3,6,6	5	6	3	5
UGLU, Positive, Week16, n=5,6,3,6,6	0	0	0	1
UKET, Negative, Baseline, n=9,10,10,10,11	9	10	10	10
UKET, Positive, Baseline, n=9,10,10,10,11	0	0	0	0
UKET, Negative, Week2, n=9,9,9,9,10	9	9	6	7
UKET, Positive, Week2, n=9,9,9,9,10	0	0	3	2
UKET, Negative, Week3, n=1,1,0,0,0	0	1	99999	99999
UKET, Positive, Week3, n=1,1,0,0,0	1	0	99999	99999
UKET, Negative, Week4, n=8,9,8,8,9	8	9	6	7
UKET, Positive, Week4, n=8,9,8,8,9	0	0	2	1
UKET, Negative, Week5, n=0,0,0,0,2	99999	99999	99999	99999
UKET, Positive, Week5, n=0,0,0,0,2	99999	99999	99999	99999
UKET, Negative, Week6, n=7,10,6,9,8	6	9	5	6
UKET, Positive, Week6, n=7,10,6,9,8	1	1	1	3
UKET, Negative, Week8, n=8,7,9,9,9	8	7	8	9
UKET, Positive, Week8, n=8,7,9,9,9	0	0	1	0
UKET, Negative, Week10, n=7,8,4,7,8	7	8	3	7
UKET, Positive, Week10, n=7,8,4,7,8	0	0	1	0
UKET, Negative, Week12, n=7,7,7,8,7	6	7	6	8
UKET, Positive, Week12, n=7,7,7,8,7	1	0	1	0
UKET, Negative, Week16, n=5,6,3,6,6	5	6	3	6
UKET, Positive, Week16, n=5,6,3,6,6	0	0	0	0
UOB, Negative, Baseline, n=9,10,10,10,11	7	10	8	9
UOB, Positive, Baseline, n=9,10,10,10,11	2	0	2	1
UOB, Negative, Week2, n=9,9,9,9,10	7	7	6	7
UOB, Positive, Week2, n=9,9,9,9,10	2	2	3	2
UOB, Negative, Week3, n=1,1,0,0,0	1	1	99999	99999
UOB, Positive, Week3, n=1,1,0,0,0	0	0	99999	99999
UOB, Negative, Week4, n=8,9,8,8,9	5	7	6	6
UOB, Positive, Week4, n=8,9,8,8,9	3	2	2	2
UOB, Negative, Week5, n=0,0,0,0,2	99999	99999	99999	99999
UOB, Positive, Week5, n=0,0,0,0,2	99999	99999	99999	99999
UOB, Negative, Week6, n=7,10,6,9,8	6	10	4	7
UOB, Positive, Week6, n=7,10,6,9,8	1	0	2	2
UOB, Negative, Week8, n=8,7,9,9,9	6	5	6	6
UOB, Positive, Week8, n=8,7,9,9,9	2	2	3	3
UOB, Negative, Week10, n=7,8,4,7,8	4	7	3	6
UOB, Positive, Week10, n=7,8,4,7,8	3	1	1	1
UOB, Negative, Week12, n=7,7,7,8,7	6	5	4	8
UOB, Positive, Week12, n=7,7,7,8,7	1	2	3	0
UOB, Negative, Week16, n=5,6,3,6,6	4	4	2	5
UOB, Positive, Week16, n=5,6,3,6,6	1	2	1	1

Notes:

[137] - ITT Population. "Not available (NA)" data is presented as "99999"

[138] - ITT Population. "Not available (NA)" data is presented as "99999"

[139] - ITT Population. "Not available (NA)" data is presented as "99999"

[140] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			

Subject group type	Reporting group			
Number of subjects analysed	11[141]			
Units: Participants				
UGLU, Negative, Baseline, n=9,10,10,10,11	11			
UGLU, Positive, Baseline, n=9,10,10,10,11	0			
UGLU, Negative, Week2, n=9,9,9,9,10	10			
UGLU, Positive, Week2, n=9,9,9,9,10	0			
UGLU, Negative, Week3, n=1,1,0,0,0	99999			
UGLU, Positive, Week3, n=1,1,0,0,0	99999			
UGLU, Negative, Week4, n=8,9,8,8,9	9			
UGLU, Positive, Week4, n=8,9,8,8,9	0			
UGLU, Negative, Week5, n=0,0,0,0,2	2			
UGLU, Positive, Week5, n=0,0,0,0,2	0			
UGLU, Negative, Week6, n=7,10,6,9,8	8			
UGLU, Positive, Week6, n=7,10,6,9,8	0			
UGLU, Negative, Week8, n=8,7,9,9,9	9			
UGLU, Positive, Week8, n=8,7,9,9,9	0			
UGLU, Negative, Week10, n=7,8,4,7,8	8			
UGLU, Positive, Week10, n=7,8,4,7,8	0			
UGLU, Negative, Week12, n=7,7,7,8,7	7			
UGLU, Positive, Week12, n=7,7,7,8,7	0			
UGLU, Negative, Week16, n=5,6,3,6,6	6			
UGLU, Positive, Week16, n=5,6,3,6,6	0			
UKET, Negative, Baseline, n=9,10,10,10,11	11			
UKET, Positive, Baseline, n=9,10,10,10,11	0			
UKET, Negative, Week2, n=9,9,9,9,10	10			
UKET, Positive, Week2, n=9,9,9,9,10	0			
UKET, Negative, Week3, n=1,1,0,0,0	99999			
UKET, Positive, Week3, n=1,1,0,0,0	99999			
UKET, Negative, Week4, n=8,9,8,8,9	9			
UKET, Positive, Week4, n=8,9,8,8,9	0			
UKET, Negative, Week5, n=0,0,0,0,2	2			
UKET, Positive, Week5, n=0,0,0,0,2	0			
UKET, Negative, Week6, n=7,10,6,9,8	8			
UKET, Positive, Week6, n=7,10,6,9,8	0			
UKET, Negative, Week8, n=8,7,9,9,9	9			
UKET, Positive, Week8, n=8,7,9,9,9	0			
UKET, Negative, Week10, n=7,8,4,7,8	8			
UKET, Positive, Week10, n=7,8,4,7,8	0			
UKET, Negative, Week12, n=7,7,7,8,7	7			
UKET, Positive, Week12, n=7,7,7,8,7	0			
UKET, Negative, Week16, n=5,6,3,6,6	6			
UKET, Positive, Week16, n=5,6,3,6,6	0			
UOB, Negative, Baseline, n=9,10,10,10,11	9			
UOB, Positive, Baseline, n=9,10,10,10,11	2			
UOB, Negative, Week2, n=9,9,9,9,10	4			
UOB, Positive, Week2, n=9,9,9,9,10	6			
UOB, Negative, Week3, n=1,1,0,0,0	99999			

UOB, Positive, Week3, n=1,1,0,0,0	99999			
UOB, Negative, Week4, n=8,9,8,8,9	7			
UOB, Positive, Week4, n=8,9,8,8,9	2			
UOB, Negative, Week5, n=0,0,0,0,2	2			
UOB, Positive, Week5, n=0,0,0,0,2	0			
UOB, Negative, Week6, n=7,10,6,9,8	4			
UOB, Positive, Week6, n=7,10,6,9,8	4			
UOB, Negative, Week8, n=8,7,9,9,9	7			
UOB, Positive, Week8, n=8,7,9,9,9	2			
UOB, Negative, Week10, n=7,8,4,7,8	3			
UOB, Positive, Week10, n=7,8,4,7,8	5			
UOB, Negative, Week12, n=7,7,7,8,7	4			
UOB, Positive, Week12, n=7,7,7,8,7	3			
UOB, Negative, Week16, n=5,6,3,6,6	3			
UOB, Positive, Week16, n=5,6,3,6,6	3			

Notes:

[141] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urine protein at the indicated time points up to Week 16

End point title	Change from Baseline in urine protein at the indicated time points up to Week 16[142]

End point description:

Change from Baseline in the urine protein values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[142] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[143]	10[144]	10[145]	10[146]
Units: Milligrams per liter				
arithmetic mean (standard deviation)				
Protein, Week2, n=9,9,9,9,10	28.3 (± 74.16)	107 (± 273.2)	171.2 (± 368.95)	32.1 (± 79.19)
Protein, Week3, n=1,1,0,0,0	328 (± 99999)	-48 (± 99999)	99999 (± 99999)	99999 (± 99999)
Protein, Week4, n=8,9,8,8,9	-19.8 (± 61.6)	8.3 (± 110.52)	40 (± 155.5)	15.9 (± 47.72)
Protein, Week5, n=0,0,0,0,1	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Protein, Week6, n=7,10,6,9,8	-32.1 (± 46.48)	-26.9 (± 50.61)	16.3 (± 102.91)	32.7 (± 79.87)
Protein, Week8, n=8,7,9,9,9	6.3 (± 42.81)	-19.3 (± 45.15)	-4.9 (± 74.08)	-2.7 (± 43.87)
Protein, Week10, n=7,8,4,6,8	-32 (± 64.44)	11.1 (± 63.62)	2.5 (± 43.81)	15.8 (± 48.02)
Protein, Week12, n=7,7,7,8,7	-1.7 (± 39.77)	6.6 (± 96.54)	-33.7 (± 72.29)	25.1 (± 55.58)
Protein, Week16, n=5,6,3,5,6	2.4 (± 9.61)	62.2 (± 153.9)	-31 (± 19)	33.6 (± 44.18)

Notes:

[143] - ITT Population. "Not available (NA)" data is presented as "99999"

[144] - ITT Population. "Not available (NA)" data is presented as "99999"

[145] - ITT Population. "Not available (NA)" data is presented as "99999"

[146] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[147]			
Units: Milligrams per liter				
arithmetic mean (standard deviation)				
Protein, Week2, n=9,9,9,9,10	-26.2 (± 129.76)			
Protein, Week3, n=1,1,0,0,0	99999 (± 99999)			
Protein, Week4, n=8,9,8,8,9	-56.6 (± 140.52)			
Protein, Week5, n=0,0,0,0,1	-70 (± 99999)			
Protein, Week6, n=7,10,6,9,8	-27.6 (± 65.98)			
Protein, Week8, n=8,7,9,9,9	-14.9 (± 156.33)			
Protein, Week10, n=7,8,4,6,8	46.9 (± 123.75)			
Protein, Week12, n=7,7,7,8,7	33.9 (± 146.43)			
Protein, Week16, n=5,6,3,5,6	-37.3 (± 52.7)			

Notes:

[147] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in urine protein/creatinine at the indicated time points up to Week 16

End point title	Change from Baseline in urine protein/creatinine at the indicated time points up to Week 16[148]

End point description:

Change from Baseline in the urine protein/creatinine values are summarised for each post-Baseline assessment until Week 16. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Primary

End point timeframe:

Baseline, Weeks 2, 3, 4, 5, 6, 8, 10, 12 and 16

Notes:

[148] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[149]	10[150]	10[151]	10[152]
Units: Milligrams per millimole of creatinine				
arithmetic mean (standard deviation)				
Protein/Creatinine, Week2, n=9,9,9,9,10	0.728996 (± 6.069632)	29.8511 (± 94.14456)	9.816302 (± 13.05664)	1.973316 (± 3.402596)
Protein/Creatinine, Week3, n=1,1,0,0,0	1.80992 (± 99999)	-1.6968 (± 99999)	99999 (± 99999)	99999 (± 99999)
Protein/Creatinine, Week4, n=8,9,8,8,9	0.53732 (± 7.831058)	4.235716 (± 12.84549)	4.75104 (± 8.108199)	2.60176 (± 3.212062)
Protein/Creatinine, Week5, n=0,0,0,0,1	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Protein/Creatinine, Week6, n=7,10,6,9,8	-0.95344 (± 3.146321)	-0.83709 (± 7.142045)	3.1108 (± 4.608165)	2.224693 (± 1.939604)
Protein/Creatinine, Week8, n=8,7,9,9,9	-4.76518 (± 5.17726)	-1.30896 (± 3.115669)	-0.55303 (± 3.480368)	2.564053 (± 3.167865)
Protein/Creatinine, Week10, n=7,8,4,6,8	-0.30704 (± 5.187394)	-2.13514 (± 4.764656)	-3.33704 (± 7.572284)	1.036933 (± 1.839954)
Protein/Creatinine, Week12, n=7,7,7,8,7	-3.68448 (± 8.260047)	-0.58176 (± 7.232438)	-1.84224 (± 5.912875)	1.6968 (± 3.279087)
Protein/Creatinine, Week16, n=5,6,3,5,6	-3.25786 (± 3.336944)	4.92072 (± 6.728025)	-1.92304 (± 6.565834)	2.760128 (± 5.543226)

Notes:

[149] - ITT Population. "Not available (NA)" data is presented as "99999"

[150] - ITT Population. "Not available (NA)" data is presented as "99999"

[151] - ITT Population. "Not available (NA)" data is presented as "99999"

[152] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[153]			
Units: Milligrams per millimole of creatinine				
arithmetic mean (standard deviation)				
Protein/Creatinine, Week2, n=9,9,9,9,10	-5.92749 (± 15.42145)			
Protein/Creatinine, Week3, n=1,1,0,0,0	99999 (± 99999)			
Protein/Creatinine, Week4, n=8,9,8,8,9	-9.99227 (± 15.35153)			
Protein/Creatinine, Week5, n=0,0,0,0,1	-3.28048 (± 99999)			
Protein/Creatinine, Week6, n=7,10,6,9,8	-3.33704 (± 16.14217)			
Protein/Creatinine, Week8, n=8,7,9,9,9	-5.54288 (± 13.05642)			
Protein/Creatinine, Week10, n=7,8,4,6,8	-4.75104 (± 10.35333)			
Protein/Creatinine, Week12, n=7,7,7,8,7	-1.616 (± 16.75879)			

Protein/Creatinine, Week16, n=5,6,3,5,6	-8.50285 (± 16.47525)			

Notes:

[153] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any adverse events (AEs) and any serious adverse events (SAEs) up to Week 16

End point title	Number of participants with any adverse events (AEs) and any serious adverse events (SAEs) up to Week 16[154]

End point description:

An AE is defined as any untoward medical occurrence in a participant temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign(including an abnormal laboratory finding), symptom, or disease(new or exacerbated) temporally associated with the use of a medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, a congenital anomaly/birth defect, important medical events that jeopardize the participants or may require medical or surgical intervention to prevent one of the other outcomes listed in the above

End point type	Primary

End point timeframe:

Up to Week 16

Notes:

[154] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[155]	10[156]	10[157]	10[158]
Units: Participants				
Any AE	8	7	7	6
Any SAE	1	2	4	1

Notes:

[155] - ITT Population

[156] - ITT Population

[157] - ITT Population

[158] - ITT Population

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[159]			
Units: Participants				
Any AE	7			
Any SAE	0			

Notes:

[159] - ITT Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with severity Grade 1, 2, 3, 4 and 5 adverse events (AEs)

End point title	Number of participants with severity Grade 1, 2, 3, 4 and 5 adverse events (AEs)[160]

End point description:

The Common Terminology Criteria for Adverse Events (CTCAE, Version 4) has categorised AEs in five grades. Grade refers to the severity of the AE. Grade 1: Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated. Grade 2: Moderate; minimal, local or non-invasive intervention indicated; limiting age-appropriate instrumental activities of daily living. Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care activities of daily living. Grade 4: Life-threatening consequences; urgent intervention indicated. Grade 5: Death related to AE.

End point type	Primary

End point timeframe:

Up to 16 Weeks

Notes:

[160] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[161]	10[162]	10[163]	10[164]
Units: Participants				
Grade 1	3	3	0	3
Grade 2	3	4	4	2
Grade 3	2	0	2	0
Grade 4	0	0	1	1
Grade 5	0	0	0	0

Notes:

[161] - ITT Population

[162] - ITT Population

[163] - ITT Population

[164] - ITT Population

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[165]			
Units: Participants				
Grade 1	3			
Grade 2	4			
Grade 3	0			
Grade 4	0			
Grade 5	0			

Notes:

[165] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: SRI Response Rate at Week 4, 8, 12 and 16

End point title	SRI Response Rate at Week 4, 8, 12 and 16

End point description:

The relationship between dose of GSK2586184 and clinical response was assessed by the SLE Responder Index (SRI). The percentage of participants achieving a response on the composite endpoint are summarised. Response is defined as:>= 4 point reduction from the Baseline in the SELENA SLEDAI score and no worsening (increase of <0.30 points from the Baseline) in Physicians Global Assessment (PGA),and no new British Isles Lupus Assessment Group (BILAG) A organ domain score or 2 new BILAG B organ domain scores compared with the Baseline. Baseline value is defined as the last Pre-treatment value observed.

End point type	Secondary

End point timeframe:

Week 4, 8, 12 and 16

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[166]	10[167]	10[168]	10[169]
Units: Percentage				
Week4	29	13	29	50
Week8	67	14	99999	99999
Week12	25	20	25	40
Week16	99999	99999	11	25

Notes:

[166] - ITT Population. "Not available (NA)" data is presented as "99999"

[167] - ITT Population. "Not available (NA)" data is presented as "99999"

[168] - ITT Population. "Not available (NA)" data is presented as "99999"

[169] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[170]			
Units: Percentage				
Week4	50			
Week8	14			
Week12	99999			
Week16	40			

Notes:

[170] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in SLEDAI-2K score and the S2K RI-50 score over time (up to Week 12).

End point title	Change from baseline in SLEDAI-2K score and the S2K RI-50 score over time (up to Week 12).

End point description:

The relationship between dose of GSK2586184 and clinical response was assessed by Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and SLEDAI-2K Responder Index 50 (S2K RI-50) scores. SLEDAI-2K is a revised version of the SLEDAI in which the persistent active disease in the items rash, alopecia, mucosal ulcers and proteinuria would be scored as opposed to new occurrences as are measured in the SLEDAI. S2K RI-50 detects a minimum 50% improvement in disease manifestations among lupus participants. It covers 9 organ systems, utilising the same 24 descriptors and reflects disease activity over the previous 30 days. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Due to early termination of the study, data for this endpoint was not summarized.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[171]	0[172]	0[173]	0[174]
Units: Scores on a scale				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[171] - ITT Population

[172] - ITT Population

[173] - ITT Population

[174] - ITT Population

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	0[175]			
Units: Scores on a scale				
arithmetic mean (standard deviation)	()			

Notes:

[175] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean GSK2586184 plasma concentrations on Weeks 2, 4, 6, 8, 10 and 12

End point title	Mean GSK2586184 plasma concentrations on Weeks 2, 4, 6, 8, 10 and 12[176]

End point description:

Plasma pharmacokinetic (PK) pre-dose (PRD) samples were collected for all participants at Weeks 2, 4, 8, 10 and 12 prior to the morning dose. At Week 2, additional blood sample were collected at 1hour (hr) and 4 hr post-dose (POD) and at Week 6, additional blood sample were collected, from 6 hr to 10 hr POD. PK Population comprised of all participants randomised to treatment, who have taken at least one dose. Only participants for whom plasma PK samples were obtained were assessed (represented by n=X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the Pharmacokinetic(PK) Population.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 6, 8, 10 and 12

Notes:

[176] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[177]	10[178]	10[179]	10[180]
Units: Nanograms per milliliter				
arithmetic mean (standard deviation)				
Week2, PRD, n=8,8,9,9	6.51 (± 9.581)	30.89 (± 41.553)	17.57 (± 17.588)	281.96 (± 406.519)
Week2, 1 hr POD, n=7,8,8,8	128.53 (± 99.475)	217.44 (± 318.654)	500.29 (± 732.243)	1012.64 (± 679.64)
Week2, 4 hr POD, n=8,8,8,9	55.84 (± 27.093)	309.73 (± 192.275)	614.71 (± 322.065)	1109.96 (± 791.706)
Week4, PRD, n=6,8,7,8	16.78 (± 13.92)	58.28 (± 122.699)	4.61 (± 7.881)	196.74 (± 358.94)
Week6, PRD, n=0,0,0,1	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	70.4 (± 99999)
Week6, 6-10 hr POD, n=7,7,6,7	59.44 (± 43.154)	176.26 (± 101.379)	89.4 (± 90.543)	442.16 (± 310.46)
Week8, PRD, n=6,7,4,7	9.25 (± 7.317)	34.71 (± 51.246)	32.25 (± 28.339)	296.21 (± 421.816)
Week10, PRD, n=4,6,4,6	11.73 (± 9.132)	31.05 (± 28.26)	27.65 (± 3.387)	159.02 (± 156.092)
Week12, PRD, n=4,5,4,5	31.88 (± 38.916)	13.18 (± 13.492)	15.53 (± 15.274)	180.36 (± 118.498)

Notes:

[177] - PK Population. "Not available (NA)" data is presented as "99999"

[178] - PK Population. "Not available (NA)" data is presented as "99999"

[179] - PK Population. "Not available (NA)" data is presented as "99999"

[180] - PK Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the concentration-time curve over the dosing interval (AUC[0-tau]) up to Week 12

End point title	Area under the concentration-time curve over the dosing interval (AUC[0-tau]) up to Week 12[181]

End point description:

Plasma PK PRD samples were collected for all participants at Weeks 2, 4, 8, 10 and 12 prior to the morning dose. At Week 2, additional blood sample were collected at 1hr and 4 hr POD and at Week 6, additional blood sample were collected, from 6 hr to 10 hr POD. AUC(0-tau).is calculated from a population pharmacokinetic model using Non Linear Mixed Effect Model (NONMEM) after log-transformation of PK data. Only participants for whom plasma PK samples were obtained and assessed.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 6, 8, 10 and 12

Notes:

[181] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8[182]	8[183]	8[184]	9[185]
Units: Nanogram per milliliter*hour (ng/mL*h)				
geometric mean (geometric coefficient of variation)	932.4138 (± 25.6)	1815.871 (± 30.4)	3375.907 (± 18)	7656.32 (± 20.1)

Notes:

[182] - PK Population

[183] - PK Population

[184] - PK Population

[185] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent clearance (CL/F) up to Week 12

End point title	Apparent clearance (CL/F) up to Week 12[186]

End point description:

Plasma PK PRD samples were collected for all participants at Weeks 2, 4, 8, 10 and 12 prior to the morning dose. At Week 2, additional blood sample were collected at 1hr and 4 hr POD and at Week 6, additional blood sample were collected, from 6 hr to 10 hr POD. CL/F is calculated, as dose divided by AUC(0-tau), from a population pharmacokinetic model using Non Linear Mixed Effect Model (NONMEM) after log-transformation of PK data. Only participants for whom plasma PK samples were obtained and assessed.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 6, 8, 10 and 12

Notes:

[186] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8[187]	8[188]	8[189]	9[190]
Units: Liter per hour (L/h)				
geometric mean (geometric coefficient of variation)	53.62426 (± 25.6)	55.06999 (± 30.4)	59.24334 (± 18)	52.24442 (± 20.1)

Notes:

[187] - PK Population

[188] - PK Population

[189] - PK Population

[190] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of distribution (Vss) up to Week 12

End point title	Volume of distribution (Vss) up to Week 12[191]

End point description:

Plasma PK PRD samples were collected for all participants at Weeks 2, 4, 8, 10 and 12 prior to the morning dose. At Week 2, additional blood sample were collected at 1hr and 4 hr POD and at Week 6, additional blood sample were collected, from 6 hr to 10 hr POD. Apparent volume of distribution is calculated as dose divided by (AUC[0-tau] lambda z) where lambda z is the terminal phase rate constant. Vss is calculated from a population pharmacokinetic model using Non Linear Mixed Effect Model (NONMEM) after log-transformation of PK data. Only participants for whom plasma PK samples were obtained and assessed.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 6, 8, 10 and 12

Notes:

[191] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There were no statistics for this endpoint.

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8[192]	8[193]	8[194]	9[195]
Units: Liter (L)				
geometric mean (geometric coefficient of variation)	226.0024 (± 20.3)	174.2176 (± 24.1)	178.1342 (± 22.4)	188.2714 (± 30.2)

Notes:

[192] - PK Population

[193] - PK Population

[194] - PK Population

[195] - PK Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in the SF-36 Domain Scores up to Week 16

End point title	Mean change from Baseline in the SF-36 Domain Scores up to Week 16

End point description:

The Short Form (36) Health Survey (SF-36v2) is a participant-reported survey of participant health and measures general health-related quality of life. There are 36 items grouped into nine health domains: Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, Mental Health, Reported health transition (RHT). SF-36v2 gives a score for each of these domains based on the questions as assessed by participants. The lower the score the more disability and the higher the score the less disability. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline, Weeks 12 and 16

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[196]	10[197]	10[198]	10[199]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Physical Functioning, Week12, n=7,7,7,8,7	5.71 (± 8.215)	4.21 (± 13.584)	2.41 (± 7.82)	10.11 (± 11.019)
Physical Functioning, Week16, n=5,6,3,8,6	5.47 (± 8.096)	12.98 (± 8.87)	-0.47 (± 5.358)	10.71 (± 16.17)
Role Physical, Week12, n=7,7,7,8,7	5.95 (± 7.328)	5.6 (± 6.739)	5.95 (± 4.659)	6.12 (± 8.484)
Role Physical, Week16, n=5,6,3,5,6	8.33 (± 5.638)	6.53 (± 5.059)	-0.82 (± 9.272)	2.94 (± 11.142)
Bodily Pain, Week12, n=7,7,7,8,7	4.77 (± 10.497)	6.1 (± 12.968)	8.21 (± 9.106)	8.93 (± 15.33)
Bodily Pain, Week16, n=5,6,3,5,6	1.61 (± 7.068)	7.82 (± 7.814)	8.31 (± 14.396)	2.54 (± 11.578)
General Health, Week12, n=7,7,6,8,7	2.32 (± 7.131)	2.79 (± 4.674)	7.55 (± 6.145)	3.93 (± 9.358)
General Health, Week16, n=5,6,3,5,6	3.91 (± 6.702)	3.26 (± 5.38)	6.2 (± 8.828)	-0.1 (± 4.413)
Vitality, Week12, n=7,7,6,8,7	10.26 (± 16.294)	7.14 (± 9.14)	6.76 (± 9.138)	9.5 (± 11.487)
Vitality, Week16, n=5,6,3,5,6	13.11 (± 14.375)	7.28 (± 4.265)	-1.04 (± 4.769)	4.37 (± 9.261)
Social Functioning, Week12, n=7,7,7,8,7	10.91 (± 13.725)	5.45 (± 7.713)	9.35 (± 5.188)	6.14 (± 11.454)
Social Functioning, Week16, n=5,6,3,5,6	10.91 (± 6.68)	6.36 (± 4.106)	0 (± 10.908)	4.36 (± 10.491)
Role Emotional, Week12, n=7,7,7,8,7	2.22 (± 13.439)	12.22 (± 9.097)	8.89 (± 8.609)	5.83 (± 10.995)
Role Emotional, Week16, n=5,6,3,5,6	3.11 (± 9.281)	9.72 (± 6.387)	-1.3 (± 14.717)	7 (± 12.715)
Mental Health, Week12, n=7,7,6,8,7	12.07 (± 11.578)	7.84 (± 8.75)	12.67 (± 9.037)	1.06 (± 5.619)
Mental Health, Week16, n=5,6,3,5,6	7.88 (± 11.679)	6.57 (± 4.24)	2.5 (± 15.433)	0 (± 7.45)
RHT, Week12, n=7,7,7,8,7	-1 (± 1.155)	-0.71 (± 1.704)	0 (± 0.577)	-1 (± 1.604)
RHT, Week16, n=5,6,3,5,6	-0.6 (± 0.894)	-1.33 (± 1.506)	0.33 (± 0.577)	-1 (± 1.225)
Mental Component Score, Week12, n=7,7,7,8,7	9.63 (± 11.024)	9.96 (± 10.001)	10.36 (± 8.828)	2.92 (± 7.755)
Mental Component Score, Week16, n=5,6,3,5,6	8.7 (± 11.33)	6.23 (± 2.984)	-0.29 (± 14.48)	2.17 (± 7.842)
Physical Component Score, Week12, n=7,7,7,8,7	3.73 (± 5.825)	2.47 (± 9.909)	3.56 (± 5.166)	9.13 (± 10.534)
Physical Component Score, Week16, n=5,6,3,5,6	4.69 (± 4.649)	7.94 (± 5.192)	3.37 (± 4.772)	5.1 (± 10.742)

Notes:

[196] - ITT Population

[197] - ITT Population

[198] - ITT Population

[199] - ITT Population

End point values	Placebo			

Subject group type	Reporting group			
Number of subjects analysed	11[200]			
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Physical Functioning, Week12, n=7,7,7,8,7	-0.3 (± 10.829)			
Physical Functioning, Week16, n=5,6,3,8,6	-1.91 (± 15.312)			
Role Physical, Week12, n=7,7,7,8,7	2.45 (± 9.898)			
Role Physical, Week16, n=5,6,3,5,6	3.27 (± 9.506)			
Bodily Pain, Week12, n=7,7,7,8,7	0.54 (± 13.516)			
Bodily Pain, Week16, n=5,6,3,5,6	0.56 (± 16.192)			
General Health, Week12, n=7,7,6,8,7	2.59 (± 11.34)			
General Health, Week16, n=5,6,3,5,6	-0.56 (± 8.417)			
Vitality, Week12, n=7,7,6,8,7	4.01 (± 9.316)			
Vitality, Week16, n=5,6,3,5,6	7.28 (± 11.956)			
Social Functioning, Week12, n=7,7,7,8,7	2.34 (± 5.323)			
Social Functioning, Week16, n=5,6,3,5,6	0 (± 6.899)			
Role Emotional, Week12, n=7,7,7,8,7	12.22 (± 17.59)			
Role Emotional, Week16, n=5,6,3,5,6	12.31 (± 18.629)			
Mental Health, Week12, n=7,7,6,8,7	7.24 (± 14.619)			
Mental Health, Week16, n=5,6,3,5,6	7.51 (± 15.695)			
RHT, Week12, n=7,7,7,8,7	-0.86 (± 1.215)			
RHT, Week16, n=5,6,3,5,6	-0.83 (± 1.169)			
Mental Component Score, Week12, n=7,7,7,8,7	10.07 (± 12.215)			
Mental Component Score, Week16, n=5,6,3,5,6	10.7 (± 11.68)			
Physical Component Score, Week12, n=7,7,7,8,7	-2.3 (± 11.504)			
Physical Component Score, Week16, n=5,6,3,5,6	-3.43 (± 12.23)			

Notes:

[200] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in the Brief Fatigue Inventory (BFI) Domain Score up to Week 16

End point title	Mean change from Baseline in the Brief Fatigue Inventory (BFI) Domain Score up to Week 16

End point description:

The BFI was developed to quickly measure severity of fatigue in participants as well as its impact on their ability to function over the previous 24 hrs. It consists of nine items that look at fatigue in the past

that are rated on a 0 -10 numeric rating scale where 0 is no fatigue or does not interfere and 10 is bad fatigue or completely interferes with activity. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 6, 8, 10, 12 and 16

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[201]	10[202]	10[203]	10[204]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
BFI Domain Score, Week2, n=9,10,9,8,10	-1.3827 (± 1.63121)	0.6333 (± 1.27124)	-1.2469 (± 2.74187)	-0.75 (± 3.05606)
BFI Domain Score, Week4, n=8,8,8,8,10	-1.625 (± 2.05732)	0.2639 (± 0.74875)	-2.0833 (± 2.14283)	-2.375 (± 3.30033)
BFI Domain Score, Week6, n=7,10,6,9,8	-1.7778 (± 2.19521)	-0.8556 (± 1.3789)	-2.2593 (± 2.87232)	-1.5926 (± 3.33148)
BFI Domain Score, Week8, n=8,7,9,8,9	-2.0972 (± 2.30897)	-1.0794 (± 2.36113)	-2.4198 (± 2.60388)	-2.3889 (± 2.54761)
BFI Domain Score, Week10, n=7,8,4,6,8	-2 (± 1.05604)	-1.1944 (± 2.77857)	-1.7778 (± 2.91865)	-2.3333 (± 2.9523)
BFI Domain Score, Week12, n=7,7,7,8,7	-2.1111 (± 1.41712)	-1.6508 (± 3.00988)	-2.7302 (± 2.23133)	-2 (± 4.02155)
BFI Domain Score, Week16, n=5,6,3,5,6	-2.2667 (± 0.73535)	-1.1667 (± 2.09025)	-1.037 (± 2.31563)	-0.8667 (± 4.33291)

Notes:

[201] - ITT Population

[202] - ITT Population

[203] - ITT Population

[204] - ITT Population

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[205]			
Units: Scores on a scale				
arithmetic mean (standard deviation)				
BFI Domain Score, Week2, n=9,10,9,8,10	-1.1889 (± 1.90951)			
BFI Domain Score, Week4, n=8,8,8,8,10	-1.2778 (± 2.3624)			
BFI Domain Score, Week6, n=7,10,6,9,8	-0.9861 (± 3.02747)			
BFI Domain Score, Week8, n=8,7,9,8,9	-1.0741 (± 1.84759)			
BFI Domain Score, Week10, n=7,8,4,6,8	-0.75 (± 2.26448)			
BFI Domain Score, Week12, n=7,7,7,8,7	-0.4603 (± 2.08209)			
BFI Domain Score, Week16, n=5,6,3,5,6	-2 (± 3.47336)			

Notes:
[205] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in the Brief Pain Inventory (BPI) Domain Score up to Week 16

End point title	Mean change from Baseline in the Brief Pain Inventory (BPI) Domain Score up to Week 16

End point description:

The BPI is a questionnaire used to assess the severity of pain and the impact of pain on daily functioning in the following areas: general activity, mood, walking ability, normal work, including outside the home and housework, relations with other people, enjoyment of life and sleep. Two sub scores are derived from questionnaire: the worst pain score and the interference score. To derive a valid worst pain score, a minimum of 3 (out of 6) non missing values were required versus 4 (out of 7) for the interference score. Change from Baseline was calculated as the individual post-Baseline value minus the Baseline value. Baseline value is defined as the last Pre-treatment value observed. Only those participants available at the specified time points were analysed (represented by n=X,X,X,X,X in category titles). Different participants may have been analysed at different time points, so the overall number of participants analysed reflects everyone in the ITT Population.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2, 4, 6, 8, 10, 12 and 16

End point values	GSK2586184 50 mg BID	GSK2586184 100 mg BID	GSK2586184 200 mg BID	GSK2586184 400 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9[206]	10[207]	10[208]	10[209]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Worst Pain Score, Week2, n=9,10,9,8,10	-1.3333 (± 1.69558)	-0.375 (± 1.43008)	-0.25 (± 2.48433)	-2.2813 (± 2.43647)
Worst Pain Score, Week4, n=8,8,8,8,10	-1.125 (± 2.29518)	-0.3125 (± 1.51628)	-0.125 (± 2.63561)	-2.1563 (± 2.75466)
Worst Pain Score, Week6, n=7,10,6,9,8	-1.6071 (± 2.68816)	-1.4 (± 1.60814)	-0.5417 (± 1.13376)	-1.9688 (± 2.91069)
Worst Pain Score, Week8, n=8,7,9,8,9	-1.7188 (± 1.86336)	-1.7143 (± 2.29777)	-0.6111 (± 1.13376)	-2.2188 (± 2.76275)
Worst Pain Score, Week10, n=7,8,4,6,8	-1.1429 (± 0.85217)	-1.4063 (± 2.6184)	-1 (± 0.79057)	-1.9167 (± 3.1846)
Worst Pain Score, Week12, n=7,7,7,8,7	-1.1786 (± 1.25594)	-2.1429 (± 3.08172)	-1.4643 (± 1.20268)	-2.0313 (± 2.95936)
Worst Pain Score, Week16, n=5,6,3,5,6	-0.75 (± 1.23744)	-3.0417 (± 2.69452)	0.1667 (± 1.75594)	-0.55 (± 3.62888)
Interference Score, Week2, n=9,10,9,8,10	-1.7619 (± 2.76088)	-0.2857 (± 1.34687)	-0.4286 (± 2.75533)	-1.8929 (± 2.27004)
Interference Score, Week4, n=8,8,8,8,10	-1.5179 (± 3.45562)	-0.6607 (± 0.97172)	-0.9643 (± 1.97469)	-2.2679 (± 1.85233)
Interference Score, Week6, n=7,10,6,9,8	-2.4898 (± 3.61578)	-1.8714 (± 2.43784)	-1.7381 (± 1.43261)	-2.127 (± 2.44995)

Interference Score, Week8, n=8,7,9,8,9	-1.7321 (± 3.03088)	-1.1224 (± 2.52932)	-1.6349 (± 2.58144)	-2.125 (± 1.96238)
Interference Score, Week10, n=7,8,4,6,8	-2.1224 (± 1.79839)	-0.5714 (± 3.16872)	-1.75 (± 2.25085)	-1.4762 (± 1.87283)
Interference Score, Week12, n=7,7,7,8,7	-2.5102 (± 2.17884)	-1.4898 (± 3.7169)	-2.3878 (± 1.9927)	-1.4464 (± 2.86269)
Interference Score, Week16, n=5,6,3,5,6	-1.5143 (± 1.19352)	-2.881 (± 2.27572)	-1.381 (± 1.51411)	-0.6286 (± 3.07823)

Notes:

[206] - ITT Population. "Not available (NA)" data is presented as "99999"

[207] - ITT Population. "Not available (NA)" data is presented as "99999"

[208] - ITT Population. "Not available (NA)" data is presented as "99999"

[209] - ITT Population. "Not available (NA)" data is presented as "99999"

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	11[210]			
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Worst Pain Score, Week2, n=9,10,9,8,10	-0.45 (± 0.71492)			
Worst Pain Score, Week4, n=8,8,8,8,10	-0.725 (± 1.88727)			
Worst Pain Score, Week6, n=7,10,6,9,8	-1.0625 (± 2.90858)			
Worst Pain Score, Week8, n=8,7,9,8,9	-0.5833 (± 1.48429)			
Worst Pain Score, Week10, n=7,8,4,6,8	-1.1563 (± 3.31646)			
Worst Pain Score, Week12, n=7,7,7,8,7	-0.0714 (± 2.46523)			
Worst Pain Score, Week16, n=5,6,3,5,6	-0.875 (± 2.41221)			
Interference Score, Week2, n=9,10,9,8,10	-1.1 (± 1.13499)			
Interference Score, Week4, n=8,8,8,8,10	-1.2571 (± 2.12938)			
Interference Score, Week6, n=7,10,6,9,8	-1.375 (± 3.27811)			
Interference Score, Week8, n=8,7,9,8,9	-1.3333 (± 1.58275)			
Interference Score, Week10, n=7,8,4,6,8	-1.6845 (± 3.05462)			
Interference Score, Week12, n=7,7,7,8,7	-0.7143 (± 2.25877)			
Interference Score, Week16, n=5,6,3,5,6	-1.9048 (± 2.40011)			

Notes:

[210] - ITT Population. "Not available (NA)" data is presented as "99999"

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the start of administration of the study drug until the follow-up contact (up to Week 16).

Adverse event reporting additional description:

SAEs and non-serious AEs were reported for members of the ITT population, comprised of all participants who were randomised to treatment, who received at least one dose of study medication and who have at least one valid post dose assessment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	GSK2586184 100 mg BID

Reporting group description:

Participants received a combination of 2 film coated tablets, so that each participant received a total of 100 mg of GSK2586184, BID with food for 12 weeks.

Reporting group title	GSK2586184 50 mg BID

Reporting group description:

Participants received a combination of 2 film coated tablets, so that each participant received a total of 50 milligram (mg) of GSK2586184, twice daily (BID) with food for 12 weeks.

Reporting group title	GSK2586184 400 mg BID

Reporting group description:

Participants received a combination of 2 film coated tablets, so that each participant received a total of 400 mg of GSK2586184, BID with food for 12 weeks.

Reporting group title	Placebo

Reporting group description:

Participants received a combination of 2 film coated tablets of GSK2586184 matching placebo, BID with food for 12 weeks.

Reporting group title	GSK2586184 200 mg BID

Reporting group description:

Participants received a combination of 2 film coated tablets, so that each participant received a total of 200 mg of GSK2586184, BID with food for 12 weeks.

Serious adverse events	GSK2586184 100 mg BID	GSK2586184 50 mg BID	GSK2586184 400 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (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

Transaminases increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Blighted ovum			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug reaction with eosinophilia and systemic symptoms			

subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (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

Serious adverse events	Placebo	GSK2586184 200 mg BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	4 / 10 (40.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Blighted ovum			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Abdominal pain upper			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertransaminasaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver injury			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	GSK2586184 100 mg BID	GSK2586184 50 mg BID	GSK2586184 400 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 10 (60.00%)	8 / 9 (88.89%)	6 / 10 (60.00%)
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Influenza like illness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Local swelling			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dysphonia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Cystatin C increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Transaminases increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Migraine			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tension headache			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Microcytic anaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Aphthous stomatitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Dermatitis contact			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Fibromyalgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Osteochondritis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Periostitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	2 / 10 (20.00%)
occurrences (all)	0	1	2
Upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Pharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	1	1	2
Nasopharyngitis			

subjects affected / exposed	1 / 10 (10.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Vaginal infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vulvovaginitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Herpes simplex			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oral fungal infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Viral infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Viral pharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Non-serious adverse events	Placebo	GSK2586184 200 mg BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 11 (63.64%)	5 / 10 (50.00%)	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	1 / 11 (9.09%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Influenza like illness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Local swelling			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Oedema peripheral			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Dysphonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Cystatin C increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	

Transaminases increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Weight increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Palpitations			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Hypoaesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Migraine			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Tension headache			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	

Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 11 (0.00%)	3 / 10 (30.00%)	
occurrences (all)	0	6	
Leukopenia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	3	
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Microcytic anaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	2	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 11 (9.09%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Aphthous stomatitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	1 / 11 (9.09%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Dermatitis allergic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	1	0	

Dermatitis contact			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Fibromyalgia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Neck pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Osteochondritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Periostitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 11 (27.27%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Pharyngitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Vaginal infection			
subjects affected / exposed	0 / 11 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Vulvovaginitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Herpes simplex			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Oral fungal infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Viral infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Viral pharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 July 2013	Generated to include revisions made in country specific amendments 01, 02, and 03 as well as clarification of assessments, inclusion of a statement regarding a potential temporary pause to recruitment and correction of typographical errors. A detailed list of changes was provided in Appendix 16.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
03 March 2014	Early Termination	-

Notes:

Limitations and caveats

None reported