



Clinical trial results:

An Open-Label Extension Study to Assess the Safety of GSK1605786A in Subjects with Crohn's Disease

Summary

EudraCT number	2010-022384-35
Trial protocol	DE BE SE GB CZ DK HU GR AT PL ES PT EE IT SK BG
Global end of trial date	29 October 2013

Results information

Result version number	v1
This version publication date	26 February 2016
First version publication date	05 June 2015

Trial information

Trial identification

Sponsor protocol code	CCX114644
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01318993
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 March 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 October 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of long-term treatment with GSK1605786A in subjects with Crohn's disease.

Protection of trial subjects:

Women of child-bearing potential were excluded unless they agreed to take adequate contraceptive measures.

Subjects with known hepatic disease and / or biliary dysfunction were excluded.

Liver chemistry stopping criteria were implemented in alignment with premarketing clinical liver safety guidance.

Withdrawal criteria were implemented for those developing prolongation of the QTc interval.

Background medications to manage Crohn's Disease were permitted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 April 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Estonia: 1
Country: Number of subjects enrolled	Denmark: 13
Country: Number of subjects enrolled	France: 22
Country: Number of subjects enrolled	Germany: 32
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Japan: 23
Country: Number of subjects enrolled	Korea, Republic of: 9
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	Slovakia: 4
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	South Africa: 4
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Ukraine: 1

Country: Number of subjects enrolled	United Kingdom: 16
Country: Number of subjects enrolled	United States: 107
Country: Number of subjects enrolled	Australia: 23
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Belgium: 24
Country: Number of subjects enrolled	Canada: 53
Country: Number of subjects enrolled	Czech Republic: 29
Worldwide total number of subjects	398
EEA total number of subjects	166

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)	391
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were eligible to enter the study if they completed the placebo-controlled induction study CCX114151; completed the maintenance study CCX114157 at Week 52; or withdrew from the maintenance study CCX114157.

Pre-assignment

Screening details:

All participants entered the study at a Baseline visit, Week 0, and received GSK1605786A 500 milligrams (mg), twice daily (BID) for 216 weeks.

Period 1

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

Arms

Arm title	GSK1605786A 500 mg BID
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Arm description:

Participants received two GSK1605786A 250 milligram (mg), oral capsules twice daily (BID), once in the morning and once in the evening, for 216 weeks.

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

Dosage and administration details:

500 mg twice daily, oral administration

Number of subjects in period 1	GSK1605786A 500 mg BID
Started	398
Completed	174
Not completed	224
Physician decision	13
Consent withdrawn by subject	24
Protocol Defined Stopping Criteria	6
Adverse event, non-fatal	53
Lost to follow-up	4
Lack of efficacy	121
Protocol deviation	3

Baseline characteristics

Reporting groups

Reporting group title	Overall Study
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Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	398	398	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	36.5		
standard deviation	± 11.99	-	
Gender categorical			
Units: Subjects			
Female	213	213	
Male	185	185	
Race, Customized			
Units: Subjects			
White- Caucasian/European	341	341	
White- Arabic/North African	10	10	
Black	7	7	
Asian- Central/South	4	4	
Asian- East	9	9	
Asian- South East	1	1	
Asian- Japanese	24	24	
American Indian/native Alaskan	1	1	
Multiple Race	1	1	

End points

End points reporting groups

Reporting group title	GSK1605786A 500 mg BID
Reporting group description:	
Participants received two GSK1605786A 250 milligram (mg), oral capsules twice daily (BID), once in the morning and once in the evening, for 216 weeks.	

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

End point title	Number of participants with any adverse event (AE) and any serious adverse event (SAE) ^[1]
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End point description:

An AE is defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. A SAE is defined as any untoward medical occurrence that, at any dose, results in death; was life threatening; required hospitalization or prolongation of existing hospitalization; resulted in disability/incapacity; was a congenital anomaly/birth defect. The Safety population consisted of all participants who enrolled in the study except those who did not take ≥ 1 dose of investigational product.

End point type	Primary
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End point timeframe:

From the start of study medication until the follow-up visit (up to Week 112).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistics for this endpoint.

End point values	GSK1605786A 500 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	398 ^[2]			
Units: Participants				
number (not applicable)				
Any AE	303			
Any SAE	41			

Notes:

[2] - Safety Population

Statistical analyses

No statistical analyses for this end point

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

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

Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) values were obtained as part of vital sign monitoring and measured after the participant was at rest in the supine position for at least 5 minutes. Change from Baseline measurements in SBP and DBP were assessed at Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108 and 4 weeks post-treatment. The Baseline value is defined as the value at Week 0. Change from Baseline was calculated as the post-Baseline value minus the value at Baseline.

End point type	Secondary
End point timeframe:	
Baseline and Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108 and 112	

End point values	GSK1605786A 500 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	398 ^[3]			
Units: millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP, Week 4, n=390	-0.4 (± 11.39)			
SBP, Week 8, n=337	-0.4 (± 11.46)			
SBP, Week 12, n=291	-0.9 (± 13.12)			
SBP, Week 24, n=197	1 (± 12.69)			
SBP, Week 36, n=132	1.3 (± 12.64)			
SBP, Week 48, n=91	-0.5 (± 13.22)			
SBP, Week 60, n=56	1.5 (± 13)			
SBP, Week 72, n=36	-0.1 (± 13.15)			
SBP, Week 84, n=19	5.4 (± 18.65)			
SBP, Week 96, n=13	-5.4 (± 10.72)			
SBP, Week 108, n=6	2.2 (± 13.44)			
SBP, 4 week post treatment, n=298	0.5 (± 13.56)			
DBP, Week 4, n=390	0.1 (± 8.58)			
DBP, Week 8, n=337	0.1 (± 8.18)			
DBP, Week 12, n=291	0.2 (± 9.21)			
DBP, Week 24, n=197	0.1 (± 10.17)			
DBP, Week 36, n=132	1 (± 9.8)			
DBP, Week 48, n=91	0 (± 9.02)			
DBP, Week 60, n=56	1.2 (± 10.59)			
DBP, Week 72, n=36	0 (± 10.03)			
DBP, Week 84, n=19	4.4 (± 11)			
DBP, Week 96, n=13	-1.8 (± 9.33)			
DBP, Week 108, n=6	1.3 (± 9.52)			
DBP, 4 week post treatment, n=298	0.1 (± 9.91)			

Notes:

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

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in heart rate (HR)

End point title	Change from Baseline in heart rate (HR)
End point description:	
Heart Rate (HR) values were obtained as part of vital sign monitoring and measured after the participant was at rest in the supine position for at least 5 minutes. Change from Baseline in HR was assessed at Week 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108 and 4 weeks post-treatment. The Baseline value is defined as the value at Week 0. Change from Baseline was calculated as the post-Baseline value minus the value at Baseline.	
End point type	Secondary

End point timeframe:

Baseline and Weeks 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 108 and 112

End point values	GSK1605786A 500 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	398 ^[4]			
Units: beats per minute				
arithmetic mean (standard deviation)				
HR, Week 4, n=390	1.3 (± 10.92)			
HR, Week 8, n=337	0.1 (± 11.41)			
HR, Week 12, n=291	0.8 (± 11.93)			
HR, Week 24, n=197	-0.5 (± 12.56)			
HR, Week 36, n=132	2.1 (± 12.35)			
HR, Week 48, n=91	-1.2 (± 13.16)			
HR, Week 60, n=56	0.4 (± 12.85)			
HR, Week 72, n=36	-1.2 (± 12.39)			
HR, Week 84, n=19	-0.7 (± 15.44)			
HR, Week 96, n=13	-4.9 (± 17.01)			
HR, Week 108, n=6	-7.7 (± 12.83)			
HR, 4 week post treatment, n=298	-0.8 (± 12.89)			

Notes:

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

Statistical analyses

No statistical analyses for this end point

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

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

Hematology parameters measured included platelets, neutrophils (NL), lymphocytes, monocytes, eosinophils, basophils, hematocrit, band cells, red blood cell (RBC) count, hemoglobin, white blood cell (WBC) count, and segmented (seg) NL. The Baseline value is defined as the value obtained at Week 0. The number of participants with the indicated hematology parameters data reference range shifts from Baseline (defined as shift to low, shift to normal or no change, shift to high) until 4 weeks post treatment are presented. A value of 99999 is used where no participants were analyzed for the indicated category therefore there is no data to present.

End point type	Secondary
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End point timeframe:

From Baseline until Week 112

End point values	GSK1605786A 500 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	398 ^[5]			
Units: Participants				
number (not applicable)				
Platelets, shift to low, n=393	2			
Platelets, shift to normal or no change, n=394	325			
Platelets, shift to high, n=295	67			
NL, shift to low, n=393	5			
NL, shift to normal or no change, n=395	284			
NL, shift to high, n=214	106			
Lymphocytes, shift to low, n=239	99			
Lymphocytes, shift to normal or no change, n=395	292			
Lymphocytes, shift to high, n=392	4			
Monocytes, shift to low, n=395	0			
Monocytes, shift to normal or no change, n=395	372			
Monocytes, shift to high, n=383	23			
Eosinophils, shift to low, n=0	99999			
Eosinophils, shift to normal or no change, n=395	366			
Eosinophils, shift to high, n=382	29			
Basophils, shift to low, n=0	99999			
Basophils, shift to normal or no change, n=395	395			
Basophils, shift to high, n=394	0			
Hematocrit, shift to low, n=249	75			
Hematocrit, shift to normal or no change, n=395	312			
Hematocrit, shift to high, n=392	8			
Band cells, shift to low, n=0	99999			
Band cells, shift to normal or no change, n=6	5			
Band cells, shift to high, n=2	1			
RBC Count, shift to low, n=293	62			
RBC Count, shift to normal or no change, n=395	322			
RBC Count, shift to high, n=393	11			
Hemoglobin, shift to low, n=191	74			
Hemoglobin, shift to normal or no change, n=395	320			
Hemoglobin, shift to high, n=395	1			
WBC Count, shift to low, n=388	23			
WBC Count, shift to normal or no change, n=395	289			
WBC Count, shift to high, n=313	83			
Segmented (Seg) NL, shift to low, n=393	5			
Seg NL, shift to normal or no change, n=395	283			
Seg NL, shift to high, n=215	107			

Notes:

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

Statistical analyses

No statistical analyses for this end point

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

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

Clinical chemistry parameters included platelets, total protein, phosphorous, albumin, sodium, potassium, chloride, calcium, glucose, gamma-glutamyl transferase, total bilirubin (TB), direct bilirubin (DB), alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN)/urea, creatinine, uric acid, bicarbonate, lactate dehydrogenase, cholesterol, and creatine kinase. The Baseline value is defined as the value obtained at Week 0. The number of participants with the indicated clinical chemistry parameters' data reference range shifts from Baseline (defined as shift to low, shift to normal or no change, or shift to high) until 4 weeks post-treatment are presented. A value of 99999 is used where no participants were analyzed for the indicated category therefore there is no data to present.

End point type	Secondary
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End point timeframe:

From Baseline until Week 112

End point values	GSK1605786A 500 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	398 ^[6]			
Units: Participants				
number (not applicable)				
Total Protein, shift to low, n=370	27			
Total Protein, shift to normal or no change, n=395	367			
Total Protein, shift to high, n=395	1			
Phosphorous, shift to low, n=369	85			
Phosphorous, shift to normal or no change, n=395	283			
Phosphorous, shift to high, n=385	30			
Albumin, shift to low, n=372	19			
Albumin, shift to normal or no change, n=395	373			
Albumin, shift to high, n=395	3			
Sodium, shift to low, n=392	18			
Sodium, shift to normal or no change, n=395	376			
Sodium, shift to high, n=395	1			
Potassium, shift to low, n=379	25			
Potassium, shift to normal or no change, n=395	360			

Potassium, shift to high, n=393	10			
Chloride, shift to low, n=395	3			
Chloride, shift to normal or no change, n=395	361			
Chloride, shift to high, n=381	31			
Calcium, shift to low, n=363	43			
Calcium, shift to normal or no change, n=395	340			
Calcium, shift to high, n=394	12			
Glucose, shift to low, n=370	54			
Glucose, shift to normal or no change, n=395	279			
Glucose, shift to high, n=361	66			
GGT, shift to low, n=0	99999			
GGT, shift to normal or no change, n=397	330			
GGT, shift to high, n=355	67			
TB, shift to low, n=0	99999			
TB, shift to normal or no change, n=397	391			
TB, shift to high, n=393	6			
DB, shift to low, n=0	99999			
DB, shift to normal or no change, n=397	397			
DB, shift to high, n=397	0			
ALP, shift to low, n=395	0			
ALP, shift to normal or no change, n=397	357			
ALP, shift to high, n=370	40			
ALT, shift to low, n=0	99999			
ALT, shift to normal or no change, n=397	349			
ALT, shift to high, n=390	48			
AST, shift to low, n=0	99999			
AST, shift to normal or no change, n=397	362			
AST, shift to high, n=390	35			
BUN/Urea, shift to low, n=367	44			
BUN/Urea, shift to normal or no change, n=395	345			
BUN/Urea, shift to high, n=393	6			
Creatinine, shift to low, n=326	50			
Creatinine, shift to normal or no change, n=395	335			
Creatinine, shift to high, n=392	10			
Uric Acid, shift to low, n=382	21			
Uric Acid, shift to normal or no change, n=395	350			
Uric Acid, shift to high, n=390	24			
Bicarbonate, shift to low, n=355	92			
Bicarbonate, shift to normal or no change, n=395	303			
Bicarbonate, shift to high, n=394	0			
LDH, shift to low, n=0	99999			
LDH, shift to normal or no change, n=395	386			
LDH, shift to high, n=392	9			

Cholesterol, shift to low, n=0	99999			
Cholesterol, shift to normal or no change, n=395	330			
Cholesterol, shift to high, n=335	65			
CK, shift to low, n=0	99999			
CK, shift to normal or no change, n=395	357			
CK, shift to high, n=335	38			

Notes:

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

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in ALT, AST, ALP, and gamma-glutamyl transferase (GGT)

End point title	Change from Baseline in ALT, AST, ALP, and gamma-glutamyl transferase (GGT)
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End point description:

Changes in Baseline in Alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT) were assessed to monitor liver function. Blood samples were taken at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 60, 72, 84, 96, 108, and 4 Weeks post-treatment. The last value on or prior to the treatment start date was considered the Baseline value. Change from Baseline was calculated as the post-Baseline value at the timepoint indicated minus the value at Baseline.

End point type	Secondary
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End point timeframe:

Baseline and Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 60, 72, 84, 96, 108, and 112

End point values	GSK1605786A 500 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	398 ^[7]			
Units: International Unit per Liter (IU/L)				
arithmetic mean (standard deviation)				
ALT, Week 2, n=374	-0.4 (± 9.18)			
ALT, Week 4, n=365	4.1 (± 42.63)			
ALT, Week 6, n=348	2 (± 16.12)			
ALT, Week 8, n=322	2.3 (± 22.27)			
ALT, Week 10, n=297	1.1 (± 13.96)			
ALT, Week 12, n=281	1.6 (± 16.03)			
ALT, Week 16, n=229	0.7 (± 12.99)			
ALT, Week 20, n=203	2.5 (± 33.03)			
ALT, Week 24, n=182	-0.4 (± 10.36)			
ALT, Week 28, n=158	1.9 (± 19.93)			
ALT, Week 32, n=141	0.4 (± 12.19)			
ALT, Week 36, n=121	0.9 (± 9.95)			
ALT, Week 40, n=102	1.9 (± 9.29)			
ALT, Week 44, n=95	2.9 (± 12.13)			
ALT, Week 48, n=89	0.1 (± 7.99)			

ALT, Week 52, n=77	0.7 (± 8.75)			
ALT, Week 60, n=55	1.1 (± 9.49)			
ALT, Week 72, n=36	0.9 (± 4.73)			
ALT, Week 84, n=18	1.5 (± 5.81)			
ALT, Week 96, n=13	1.5 (± 9.63)			
ALT, Week 108, n=6	2.2 (± 6.74)			
ALT, 4 week post treatment, n=299	3 (± 24.12)			
AST, Week 2, n=373	-0.1 (± 4.7)			
AST, Week 4, n=365	1.8 (± 18.11)			
AST, Week 6, n=348	0.9 (± 8.29)			
AST, Week 8, n=322	1.1 (± 13.49)			
AST, Week 10, n=296	0.5 (± 8.12)			
AST, Week 12, n=280	2.2 (± 25.34)			
AST, Week 16, n=228	0.5 (± 8.59)			
AST, Week 20, n=202	1.9 (± 21.69)			
AST, Week 24, n=182	0.3 (± 6.82)			
AST, Week 28, n=158	1.1 (± 13.05)			
AST, Week 32, n=141	0.6 (± 7.96)			
AST, Week 36, n=120	1.5 (± 7.84)			
AST, Week 40, n=102	1.4 (± 6.94)			
AST, Week 44, n=95	2 (± 8.63)			
AST, Week 48, n=89	0.2 (± 6.2)			
AST, Week 52, n=77	-0.1 (± 6.4)			
AST, Week 60, n=55	0.6 (± 6.83)			
AST, Week 72, n=36	0.6 (± 4.2)			
AST, Week 84, n=18	0.8 (± 4.37)			
AST, Week 96, n=13	2 (± 9.17)			
AST, Week 108, n=6	1 (± 5.93)			
AST, 4 week post treatment, n=298	2.5 (± 12.91)			
ALP, Week 2, n=374	-0.5 (± 11.23)			
ALP, Week 4, n=365	0.7 (± 14.35)			
ALP, Week 6, n=348	0.3 (± 15.25)			
ALP, Week 8, n=322	0.2 (± 14.66)			
ALP, Week 10, n=297	0.7 (± 14.72)			
ALP, Week 12, n=281	0.6 (± 16.16)			
ALP, Week 16, n=229	1 (± 14.35)			
ALP, Week 20, n=203	0.8 (± 15.57)			
ALP, Week 24, n=182	3.1 (± 16.41)			
ALP, Week 28, n=158	3.6 (± 19.19)			
ALP, Week 32, n=141	3.7 (± 17.16)			
ALP, Week 36, n=121	5 (± 19.31)			
ALP, Week 40, n=102	5.5 (± 17.36)			
ALP, Week 44, n=95	3.5 (± 15.21)			
ALP, Week 48, n=89	3.8 (± 19.78)			
ALP, Week 52, n=77	1.8 (± 16.41)			
ALP, Week 60, n=55	2.1 (± 16.62)			
ALP, Week 72, n=36	3.5 (± 14.34)			
ALP, Week 84, n=18	4.6 (± 15.53)			
ALP, Week 96, n=13	2.9 (± 10.51)			
ALP, Week 108, n=6	0.8 (± 11.94)			
ALP, 4 week post treatment, n=299	1.3 (± 23.34)			
GGT, Week 2, n=374	1.8 (± 12.47)			

GGT, Week 4, n=365	4.6 (± 18.39)			
GGT, Week 6, n=347	3.2 (± 17.48)			
GGT, Week 8, n=322	3 (± 14.4)			
GGT, Week 10, n=297	2.6 (± 15.39)			
GGT, Week 12, n=281	3.2 (± 18.24)			
GGT, Week 16, n=229	2.1 (± 16.99)			
GGT, Week 20, n=203	2.4 (± 17.5)			
GGT, Week 24, n=182	3 (± 23.22)			
GGT, Week 28, n=158	4.7 (± 27.54)			
GGT, Week 32, n=141	4.2 (± 23.18)			
GGT, Week 36, n=121	4.1 (± 22.19)			
GGT, Week 40, n=102	6.1 (± 23.2)			
GGT, Week 44, n=95	3 (± 19.38)			
GGT, Week 48, n=89	3.6 (± 28.93)			
GGT, Week 52, n=77	2 (± 13.83)			
GGT, Week 60, n=55	4.3 (± 11.66)			
GGT, Week 72, n=36	2.4 (± 9.84)			
GGT, Week 84, n=18	1.7 (± 12.16)			
GGT, Week 96, n=13	-3.6 (± 14.18)			
GGT, Week 108, n=6	-8.5 (± 15.25)			
GGT, 4 week post treatment, n=297	1.3 (± 24.77)			

Notes:

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

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total bilirubin

End point title	Change from Baseline in total bilirubin
End point description:	
Changes from Baseline in total bilirubin (TB) was assessed to monitor liver function. Blood samples were taken at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 60, 72, 84, 96, 108, and 4 Weeks post-treatment. The last value on or prior to the treatment start date was considered the Baseline value. Change from Baseline was calculated as the post-Baseline value at the timepoint indicated minus the value at Baseline.	
End point type	Secondary
End point timeframe:	
Baseline and Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 60, 72, 84, 96, 108, and 112	

End point values	GSK1605786A 500 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	398 ^[8]			
Units: micromole/Liter (umol/L)				
arithmetic mean (standard deviation)				
TB, Week 2, n=374	-0.2 (± 2.44)			
TB, Week 4, n=365	0.1 (± 2.75)			
TB, Week 6, n=348	-0.2 (± 2.44)			

TB, Week 8, n=322	-0.2 (± 2.51)			
TB, Week 10, n=297	0.1 (± 2.7)			
TB, Week 12, n=281	-0.2 (± 2.31)			
TB, Week 16, n=229	-0.1 (± 2.37)			
TB, Week 20, n=203	-0.2 (± 2.31)			
TB, Week 24, n=182	0.3 (± 2.15)			
TB, Week 28, n=158	0.2 (± 2.48)			
TB, Week 32, n=141	0 (± 2.48)			
TB, Week 36, n=121	0.1 (± 2.4)			
TB, Week 40, n=102	0.5 (± 2.84)			
TB, Week 44, n=95	0.4 (± 2.56)			
TB, Week 48, n=89	0.2 (± 2.16)			
TB, Week 52, n=77	0.3 (± 2.58)			
TB, Week 60, n=55	0.3 (± 2.44)			
TB, Week 72, n=36	0.2 (± 3.05)			
TB, Week 84, n=18	0.4 (± 2.15)			
TB, Week 96, n=13	1.2 (± 2.28)			
TB, Week 108, n=6	0.7 (± 1.51)			
TB, 4 week post treatment, n=299	1 (± 3.25)			

Notes:

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

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in albumin

End point title	Change from Baseline in albumin
End point description:	
Change from Baseline in albumin was assessed to monitor liver function. Blood samples were taken at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 60, 72, 84, 96, 108, and 4 Weeks post-treatment. The last value on or prior to the treatment start date was considered the Baseline value. Change from Baseline was calculated as the post-Baseline value at the timepoint indicated minus the value at Baseline. A value of 99999 is used to indicate too few participants were analyzed to determine a standard deviation therefore there is no data to present.	
End point type	Secondary
End point timeframe:	
Baseline and Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 60, 72, 84, 96, 108, and 112	

End point values	GSK1605786A 500 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	398 ^[9]			
Units: Gram/Liter (G/L)				
arithmetic mean (standard deviation)				
Albumin, Week 2, n=20	-0.5 (± 3.97)			
Albumin, Week 4, n=356	0.2 (± 2.52)			
Albumin, Week 6, n=31	0.1 (± 2.36)			
Albumin, Week 8, n=317	0.3 (± 2.72)			

Albumin, Week 10, n=19	-0.2 (± 2.79)			
Albumin, Week 12, n=277	0.4 (± 2.7)			
Albumin, Week 16, n=22	-1 (± 3.88)			
Albumin, Week 20, n=19	0.2 (± 2.52)			
Albumin, Week 24, n=181	0.9 (± 3.36)			
Albumin, Week 28, n=8	-0.4 (± 6.21)			
Albumin, Week 32, n=8	-1 (± 3.51)			
Albumin, Week 36, n=121	1.2 (± 3.42)			
Albumin, Week 40, n=6	0.5 (± 4.23)			
Albumin, Week 44, n=1	-2 (± 99999)			
Albumin, Week 48, n=88	1.1 (± 3.09)			
Albumin, Week 52, n=6	1 (± 3.58)			
Albumin, Week 60, n=55	0.8 (± 3.54)			
Albumin, Week 72, n=36	1.4 (± 3.54)			
Albumin, Week 84, n=18	1.6 (± 3.29)			
Albumin, Week 96, n=13	1.5 (± 3.95)			
Albumin, Week 108, n=6	0.8 (± 1.17)			
Albumin, 4 week post treatment, n=295	0.5 (± 3.3)			

Notes:

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

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated change from Baseline in corrected QT interval (QTc) value

End point title	Number of participants with the indicated change from Baseline in corrected QT interval (QTc) value
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End point description:

QTc is the corrected QT interval as measured by the electrocardiogram (ECG). ECG parameters including the change from Baseline in the QTc interval values QTcF and QTcB were summarised. The QTcF is Fridericia's formula and defined as the QT interval/cubed root of the R-R interval. The QTcB is the Bazett's formula defined as the QT/squared root of the R-R interval. The number of participants with change from Baseline in the QTcF and QTcB intervals of >30, 30-<60 and ≥60 milliseconds were assessed at Week 24, 48, 72 and Week 108. The last value on or prior to the treatment start date was considered the Baseline value. Change from Baseline was calculated as the post-Baseline value minus the value at Baseline.

End point type	Secondary
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End point timeframe:

Baseline and Week 24, 48, 72 and Week 108

End point values	GSK1605786A 500 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	398 ^[10]			
Units: Participants				
number (not applicable)				
QTcB, Week 24, <30, n=70	66			
QTcB, Week 24, 30-<60, n=70	3			
QTcB, Week 24, ≥60, n=70	1			

QTcB, Week 48, <30, n=35	34			
QTcB, Week 48, 30-<60, n=35	0			
QTcB, Week 48, ≥60, n=35	1			
QTcB, Week 72, <30, n=17	15			
QTcB, Week 72, 30-<60, n=17	1			
QTcB, Week 72, ≥60, n=17	1			
QTcB, Week 108, <30, n=3	3			
QTcB, Week 108, 30-<60, n=3	0			
QTcB, Week 108, ≥60, n=3	0			
QTcB, 4 Weeks Post Treatment, <30, n=96	89			
QTcB, 4 Weeks Post Treatment, 30-<60, n=96	6			
QTcB, 4 Weeks Post Treatment, ≥60, n=96	1			
QTcF, Week 24, <30, n=23	22			
QTcF, Week 24, 30-<60, n=23	1			
QTcF, Week 24, ≥60, n=23	0			
QTcF, Week 48, <30, n=13	13			
QTcF, Week 48, 30-<60, n=13	0			
QTcB, Week 48, ≥60, n=13	0			
QTcF, Week 72, <30, n=7	7			
QTcF, Week 72, 30-<60, n=7	0			
QTcF, Week 72, ≥60, n=7	0			
QTcF, Week 108, <30, n=2	1			
QTcF, Week 108, 30-<60, n=2	1			
QTcF, Week 108, ≥60, n=2	0			
QTcF, 4 Weeks Post Treatment, <30, n=32	32			
QTcF, 4 Weeks Post Treatment, 30-<60, n=32	0			
QTcF, 4 Weeks Post Treatment, ≥60, n=32	0			

Notes:

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the start of study medication until the follow-up visit (up to 112 weeks).

Adverse event reporting additional description:

On-treatment SAEs and non-serious AEs are reported for members of the safety Population, comprised of all participants who enrolled in the study except those who did not take at least one dose of investigational product.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	GSK1605786A 500 mg BID
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Reporting group description:

Participants received two GSK1605786A 250 milligram (mg), oral capsules twice daily (BID), once in the morning and once in the evening, for 216 weeks.

Serious adverse events	GSK1605786A 500 mg BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	41 / 398 (10.30%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon Neoplasm			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Intermittent Claudication			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Drug Ineffective			

subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Bartholinitis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Liver Function Test Abnormal			
subjects affected / exposed	2 / 398 (0.50%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Incisional Hernia			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative Ileus			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple Sclerosis			

subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myoclonus			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Iron Deficiency Anemia			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Crohn's Disease			
subjects affected / exposed	8 / 398 (2.01%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Anal Fistula			
subjects affected / exposed	2 / 398 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Small Intestine Obstruction			
subjects affected / exposed	2 / 398 (0.50%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Abdominal Pain			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal Pain Upper			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal Stenosis			

subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal Obstruction			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal Perforation			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large Intestinal Stenosis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis Acute			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Subilieus			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal Insufficiency			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Fistula			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Anal Abscess			
subjects affected / exposed	2 / 398 (0.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	2 / 398 (0.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abdominal Abscess			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Campylobacter Gastroenteritis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis Viral			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lobar Pneumonia			

subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shigella Infection			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalemia			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypomagnesemia			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	1 / 398 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	GSK1605786A 500 mg BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	295 / 398 (74.12%)		
Nervous system disorders			
Headache			
subjects affected / exposed	42 / 398 (10.55%)		
occurrences (all)	78		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	49 / 398 (12.31%)		
occurrences (all)	64		
Crohn's Disease			
subjects affected / exposed	49 / 398 (12.31%)		
occurrences (all)	56		
Nausea			
subjects affected / exposed	26 / 398 (6.53%)		
occurrences (all)	36		
Diarrhea			
subjects affected / exposed	24 / 398 (6.03%)		
occurrences (all)	29		
Dyspepsia			
subjects affected / exposed	20 / 398 (5.03%)		
occurrences (all)	28		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	20 / 398 (5.03%)		
occurrences (all)	26		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	66 / 398 (16.58%)		
occurrences (all)	95		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 February 2011	<p>To clarify in study description that subjects who withdraw early from the placebo-controlled maintenance study, CCX114157, due to worsening of Crohn's disease requiring a treatment change, may also be eligible for the open-label extension study. Addition of a new author, Jatin Patel, To add contact details for David J Chang as Medical Monitor,</p> <p>To delete abbreviations not referenced in the protocol, to clarify that subjects can enter Study CCX114644 if they complete Study CCX114151 and do not achieve clinical response (CDAI \geq 100 point decrease) or remission (CDAI $<$ 150) or they complete any other GSK-sponsored induction study of GSK1605786A as designated by the sponsor.</p> <p>To specify that study will be conducted for 108 weeks with amendment of study duration to be considered following results of Study CCX114151, to amend wording for CDAI assessments every 3 months to every 12 weeks for consistency within the protocol</p> <p>To amend other endpoints for assessment of effectiveness to include the key outcome measures of proportion of subjects in remission (CDAI $<$ 150), proportion of subjects in remission for subjects in remission at baseline, proportion of subjects in remission for subjects not in remission at baseline, and to remove endpoints of remission and response by previous study and include as subgroup analyses; to clarify that response will be measured relative to baseline of previous study, to correct typographical errors to specify 108 weeks rather than 104 weeks or Week 108 rather than Week 104, to amend wording of exclusion criterion #2 to clarify testing requirement for anti-tTG antibodies. To amend wording of exclusion criterion #3 to clarify fixed symptomatic stenoses or strictures of small bowel or colon, to include new exclusion criterion #7 to exclude subjects who have demonstrated safety or tolerability issues which were possibly related to study treatment (in the investigator's opinion) during participation in a previous clinical study with GSK1605786A.</p>
10 February 2011	<p>To clarify that subjects may be enrolled in the study prior to receiving baseline results for LFTs and anti-tTG antibodies (if applicable). Subjects who fulfill these exclusion criteria should be withdrawn due to inability to meet continuation criteria and recorded as screen failures, To include a withdrawal criterion at Week 12 based on investigator assessment that subject is not receiving clinical benefit , to remove reference to randomised subjects, randomisation code or treatment groups made as typographical errors, to clarify text on procedures for an Early Withdrawal visit, to include wording to direct investigators to the Study Procedures Manual for details on Investigational Product, to include immunisation with live vaccines as prohibited therapy</p> <p>To clarify requirements for permitted medications, including allowance for steroid taper and additional use of corticosteroids, 5-ASAs, opioid analgesics and paracetamol/acetaminophen (including correction of daily allowed dose to 2 g/day) and inclusion of treatment for fistulae under permitted medications section, to make the following corrections or amendments to the Time and Events schedule: Correction of visit numbers, as Visit 12 had been replicated in error, Expansion of footnote to clarify only LFTs are assessed at certain visits, Addition of 12 lead ECG at Week 72 and deletion at Weeks 12, 60 and 84, Addition of haematology assessment at Week 96, Deletion of pregnancy testing at Weeks 16, 24, 32, 40 and 48, consistent with initial testing every 4 weeks, and then every 8 weeks after Week 20 and every 12 weeks after Week 60; Amendment of footnote to specify home pregnancy testing every 4 weeks after Week 60</p>

10 February 2011	<p>Addition of CRP assessment at Weeks 8, 72 and 96 and at Early Withdrawal and Follow-up visits to align with CDAI assessments</p> <p>Deletion of assessment of fistula closure at Weeks 12, 60 and 84 and addition of assessment of fistula closure at Week 0 (this is not a repeated assessment but carry over from Study CCX114151 Week 12 assessment or end of study visit from any other preceding study of GSK1605786A), Weeks 72 and 108, Addition of * to pregnancy test at Week 0, indicating that the test is not repeated but the result is carried over from the preceding study of GSK1605786A, Inclusion of test for coeliac disease at baseline if indicated and corresponding footnote to specify that testing should be performed upon suspicion of coeliac disease</p> <p>Inclusion of Week 12 investigator assessment of clinical benefit, Amendment of timepoints for assessment of IBDQ, SF-36, EQ5D, WPAI-CD, disability and resource utilisation from Weeks 60 and 84 to Weeks 48 and 72 in Time and Events schedule; Inclusion in footnote that Week 0 disability assessment will not be available for subjects entering from a prior induction study and is not required, To amend timepoints for efficacy, safety and health outcomes assessments in protocol text to correspond with timepoints and changes in timepoints in the Time and Events schedule detailed above, To clarify that the treatment allocation from the previous study will not be available prior to enrolment, To remove the requirement for locally determined haematocrit values for CDAI calculation, To clarify timings for adverse event reporting and wording regarding serious adverse events as reported, To clarify wording for frequency of assessment of LFTs, To include assessment of concomitant medications and CRP in Follow Up visit, To include response and remission status at end of previous induction study as a subgroup analysis with clarification that response will be measured relative to baseline of previous study</p>
10 February 2011	<p>To incorporate revisions into description of efficacy analyses to correspond with changes to endpoints</p> <p>To amend CDAI in Appendix 4 to reflect that investigator assessments should be performed based on findings on day of examination</p> <p>To include correct version of IBDQ in Appendix 5</p> <p>To correct other minor typographical errors in the protocol</p>
02 August 2011	<p>To update information on sponsor departmental information</p> <p>To update abbreviations to include revised information</p> <p>To clarify that subjects who completed Study CCX114643 are not eligible to participate in this study</p> <p>To include additional secondary objectives of assessment of activity impairment, unemployment and disability rates and biomarkers of inflammation to clarify that these evaluations are secondary objectives of this study</p> <p>To include exploratory objective of assessment of fistula closure to clarify that this will be an exploratory objective of this study.</p> <p>To clarify for secondary endpoints that changes in body weight and temperature will be performed only in relation to CDAI scoring and not as separate assessments</p> <p>To clarify that changes in CRP concentrations as a biomarker of inflammation will be assessed as an endpoint</p> <p>To amend Inclusion Criteria to include updated criteria for acceptable contraceptive methods of birth control according to sponsor standards</p> <p>To amend Exclusion Criteria</p> <ul style="list-style-type: none"> • To clarify criteria for fixed symptomatic stenoses and stricture • To include use of prohibited medications at baseline and throughout the study to ensure subject safety. <p>To update withdrawal and stopping criteria and testing procedures for liver chemistry abnormalities and ECG findings to be consistent with revisions to GSK standard withdrawal criteria</p> <p>To clarify that the Investigator should conduct a Follow-up visit in addition to an Early Withdrawal visit for safety follow up</p> <p>To clarify that prohibited medications should not be taken throughout the study and that use of stable doses of Crohn's disease medications ongoing from a previous study are permissible</p> <p>To include use of digoxin or related cardiac glycosides (e.g digitoxin, deslanoside, lanatoside C, metildigoxin) as a prohibited medication</p> <p>To correct typographical errors in Time and Events table and to amend assessments to be consistent with protocol content.</p>

02 August 2011	<p>To extend visit windows with longer intervals between visits to allow flexibility in scheduling</p> <p>To clarify that subjects should initiate study drug administration the evening of the day of the baseline (Week 0) visit</p> <p>To provide additional clarification regarding reporting of worsening of Crohn's disease as an AE</p> <p>To include information on reporting and analyses of Disease-related events common in Crohn's disease for consistency with new FDA safety reporting guidance. Protocol-specified events related to worsening of Crohn's disease will not be reported as SAEs</p> <p>To delete concomitant medications as a safety outcome</p> <p>To provide additional clarification on data handling</p> <p>To include additional information on analyses of components of SF-36v2 and disability benefit data</p> <p>To provide additional clarification on IDMC purpose and safety review</p> <p>To amend CDAI to clarify that Investigator should assess symptoms/findings for subject based on current conditions and fever should be documented if present over the past week</p>
19 March 2013	<p>To amend the study duration to 216 weeks, to revise the list of authors, to revise sponsor address and medical monitor contact information, to correct typographical errors, to consistently define draining fistulae as "open."</p> <p>To indicate that in 2012, GSK1605786A received approval for the generic name vercirnon, to remove information concerning the method of confirming male partner sterilization from the protocol to the Study Procedure Manual, to remove the exclusion prohibiting subjects with fistulae likely to require surgery from entering the study, to clarify that subjects who have been withdrawn early from study CCX114157 due to disease worsening and have received, or are receiving, certain rescue treatments shall be excluded from entry into study CCX114644, to clarify that enteral or parenteral nutritional supplementation to treat malnutrition is permitted, to clarify that any biologic or investigational agent, including – but not limited to – janus kinase inhibitors, vedolizumab and ustekinumab are prohibited medications, to revise the Time & Events table to provide for ongoing assessments from week 108 to week 216, to extend the visit window for visits from week 16 onward, to clarify the definition of the safety population, to clarify the analysis of data by subgroups, to clarify the purpose of the interim analyses that will be performed, to clarify the definition of baseline for statistical analysis purposes, to clarify how the extent of treatment exposure will be defined and summarized. To clarify that the incidence rate of adverse events will be summarized by overall duration of exposure as well as by 6-month intervals of exposure.</p> <p>To clarify that ECG data will be summarized separately for data calculated manually and by machine.</p> <p>To clarify the efficacy analyses that will be performed based on CDAI score and fistulae closure.</p> <p>To clarify how the CRP concentration data will be summarized and analyzed for statistical purposes.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 August 2013	Discontinued investigational product and discontinued enrollment of new subjects. Study termination occurred on 04Sep2013	-

Notes:

Limitations and caveats

None reported