Clinical trial results:
A multicentre, randomised, double-blind (sponsor-unblinded), placebo-controlled study with open label extension to investigate the safety and tolerability, pharmacokinetics, pharmacodynamics, and efficacy of GSK2982772 in subjects with active ulcerative colitis

Summary

EudraCT number	2016-001833-29
Trial protocol	SE GB PL NL
Global end of trial date	17 June 2019

Results information

Result version number	v1 (current)
This version publication date	03 June 2020
First version publication date	03 June 2020

Trial information

Trial identification

Sponsor protocol code	202152

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 September 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the safety and tolerability of 60 mg three daily doses of GSK2982772 in subjects with moderate to severe ulcerative colitis

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 November 2016
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	Germany: 1
Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Russian Federation: 14
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	36
EEA total number of subjects	18

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)	34

From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study evaluated the safety and tolerability of repeat oral doses of GSK2982772 60 milligram (mg) or placebo three times daily (TID) in Part A (double blind [DB]) followed by GSK2982772 60 mg TID in Part B open label extension (OL) in active ulcerative colitis (UC) participants.

Pre-assignment

Screening details:

A total of 77 participants were screened, of which 36 eligible participants were enrolled (41 were screening failure). All 36 participants were randomized to receive GSK2982772 60 mg or Placebo in Part A of the study.

Period 1

Period 1 title	Part A (Day 1 to 43)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo TID DB /GSK2982772 60 mg TID OL

Arm description:

Eligible participants with UC, received two tablets of placebo TID orally for 42 days (from Day 1 to 43) in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 44 to 85) in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112.

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

Dosage and administration details:

Participants received two tablets of placebo TID orally for 42 days in Part A (double blind phase).

Arm title	GSK2982772 60 mg TID DB/ GSK2982772 60 mg TID OL

Arm description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 1 to 43) in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 44 to 85) in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112. 1 participant was randomized to receive BID regimen instead of TID regimen prior to protocol amendment; however, BID and TID are presented in the same arm because the pharmacokinetic (PK) profile is comparable for BID & TID regimen.

Arm type	Experimental
Investigational medicinal product name	GSK2982772
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days in Part A (double blind phase) and in Part B (open label phase).

Number of subjects in period 1	Placebo TID DB /GSK2982772 60 mg TID OL	GSK2982772 60 mg TID DB/ GSK2982772 60 mg TID OL
Started	12	24
Completed	11	24
Not completed	1	0
Adverse event, non-fatal	1	-

Period 2

Period 2 title	Part B (Day 44 to 112)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo TID DB /GSK2982772 60 mg TID OL

Arm description:

Eligible participants with UC, received two tablets of placebo TID orally for 42 days (from Day 1 to 43) in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 44 to 85) in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112.

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

Dosage and administration details:

Participants received two tablets of placebo TID orally for 42 days in Part A (double blind phase).

Arm title	GSK2982772 60 mg TID DB/ GSK2982772 60 mg TID OL

Arm description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 1 to 43) in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 44 to 85) in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112. 1 participant was randomized to receive BID regimen instead of TID regimen prior to protocol amendment; however, BID and TID are presented in the same arm because the pharmacokinetic (PK) profile is comparable for BID & TID regimen.

Arm type	Experimental
Investigational medicinal product name	GSK2982772
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days in Part A (double blind phase) and in Part B (open label phase).

Number of subjects in period 2	Placebo TID DB /GSK2982772 60 mg TID OL	GSK2982772 60 mg TID DB/ GSK2982772 60 mg TID OL
Started	11	24
Completed	11	22
Not completed	0	2
Consent withdrawn by subject	-	1
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo TID DB /GSK2982772 60 mg TID OL
Reporting group description:	
Eligible participants with UC, received two tablets of placebo TID orally for 42 days (from Day 1 to 43) in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 44 to 85) in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112.	
Reporting group title	GSK2982772 60 mg TID DB/ GSK2982772 60 mg TID OL
Reporting group description:	
Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 1 to 43) in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 44 to 85) in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112. 1 participant was randomized to receive BID regimen instead of TID regimen prior to protocol amendment; however, BID and TID are presented in the same arm because the pharmacokinetic (PK) profile is comparable for BID & TID regimen.	

Reporting group values	Placebo TID DB /GSK2982772 60 mg TID OL	GSK2982772 60 mg TID DB/ GSK2982772 60 mg TID OL	Total
Number of subjects	12	24	36
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	11	23	34
From 65-84 years	1	1	2
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	50.4	39.0	
standard deviation	± 11.17	± 13.69	-
Sex: Female, Male Units: Participants			
Female	6	8	14
Male	6	16	22
Race/Ethnicity, Customized Units: Subjects			
White - Arabic/North African Heritage	0	1	1
White - White/Caucasian/European Heritage	12	23	35

End points reporting groups

Reporting group title	Placebo TID DB /GSK2982772 60 mg TID OL

Reporting group description:

Eligible participants with UC, received two tablets of placebo TID orally for 42 days (from Day 1 to 43) in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 44 to 85) in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112.

Reporting group title	GSK2982772 60 mg TID DB/ GSK2982772 60 mg TID OL

Reporting group description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 1 to 43) in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 44 to 85) in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112. 1 participant was randomized to receive BID regimen instead of TID regimen prior to protocol amendment; however, BID and TID are presented in the same arm because the pharmacokinetic (PK) profile is comparable for BID & TID regimen.

Reporting group title	Placebo TID DB /GSK2982772 60 mg TID OL

Reporting group description:

Eligible participants with UC, received two tablets of placebo TID orally for 42 days (from Day 1 to 43) in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 44 to 85) in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112.

Reporting group title	GSK2982772 60 mg TID DB/ GSK2982772 60 mg TID OL

Reporting group description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 1 to 43) in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 44 to 85) in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112. 1 participant was randomized to receive BID regimen instead of TID regimen prior to protocol amendment; however, BID and TID are presented in the same arm because the pharmacokinetic (PK) profile is comparable for BID & TID regimen.

Subject analysis set title	Part A: Placebo TID DB
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants with UC, received two tablets of placebo TID orally for 42 days in Part A (double blind phase).

Subject analysis set title	Part A: GSK2982772 60 mg TID DB
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days in Part A (double blind phase).

Subject analysis set title	Part B: GSK2982772 60 mg TID OL
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days in Part B (open label phase).

Subject analysis set title	Part A: Placebo TID DB
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants with UC, received two tablets of placebo TID orally for 42 days in Part A (double blind phase).

Subject analysis set title	Part B: GSK2982772 60 mg TID OL
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for

42 days in Part B (open label phase).

Subject analysis set title	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 1 to 43) in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 44 to 85) in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112. 1 participant was randomized to receive BID regimen instead of TID regimen prior to protocol amendment; however, BID and TID are presented in the same arm because the PK profile is comparable for BID & TID regimen

Subject analysis set title	Part A: Placebo TID DB
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days in Part A (double blind phase).

Subject analysis set title	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 1 to 43) in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 44 to 85) in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112. 1 participant was randomized to receive BID regimen instead of TID regimen prior to protocol amendment; however, BID and TID are presented in the same arm because the PK profile is comparable for BID & TID regimen

Subject analysis set title	Part A: GSK2982772 60 mg TID DB
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days in Part A (double blind phase).

Subject analysis set title	Part A: Placebo TID DB
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants with UC, received two tablets of placebo TID orally for 42 days in Part A (double blind phase).

Subject analysis set title	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 1 to 43) in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days (from Day 44 to 85) in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112. 1 participant was randomized to receive BID regimen instead of TID regimen prior to protocol amendment; however, BID and TID are presented in the same arm because the PK profile is comparable for BID & TID regimen

Subject analysis set title	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days in Part A (double blind phase), followed by GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days in Part B (open label phase). There was no wash out period in between Part A and B. All participants were followed up until Day 112. 1 participant was randomized to receive BID regimen instead of TID regimen prior to protocol amendment; however, BID and TID are presented in the same arm because the PK profile is comparable for BID & TID regimen

Primary: Part A: Number of participants with common (>=5%) non-serious adverse events (non-SAEs) and any serious adverse events (SAEs)

End point title	Part A: Number of participants with common (>=5%) non-serious adverse events (non-SAEs) and any serious adverse events (SAEs)[1]

End point description:

An AE is 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. 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; is a congenital anomaly/birth defect; other important medical events; is associated with liver injury and impaired liver function. Safety population comprised of all participants who received at least one dose of study treatment.

End point type	Primary

End point timeframe:

Up to Day 43

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 is no statistical analysis to report.

End point values	Part A: Placebo TID DB	Part A: GSK2982772 60 mg TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12[2]	24[3]		
Units: Participants				
Common non-SAEs	7	13		
Any SAEs	1	0		

Notes:

[2] - Safety population

[3] - Safety population

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Number of participants with common (>=5%) non serious AEs and SAEs

End point title	Part B: Number of participants with common (>=5%) non serious AEs and SAEs[4]

End point description:

An AE is 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. 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; is a congenital anomaly/birth defect; other important medical events; is associated with liver injury and impaired liver function. All participants in Part B were presented in a single arm as they all received GSK2982772 60 mg in Part B (OL Phase).

End point type	Primary

End point timeframe:

From Day 44 to Day 112

Notes:

[4] - 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 is no statistical analysis to report.

End point values	Part B: GSK2982772 60 mg TID OL			
Subject group type	Subject analysis set			
Number of subjects analysed	35[5]			
Units: Participants				
Common non-SAEs	7			
Any SAEs	2			

Notes:

[5] - Safety population. Participants with data available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Number of participants with worst case abnormal clinical chemistry parameters by potential clinical importance (PCI) criteria

End point title	Part A: Number of participants with worst case abnormal clinical chemistry parameters by potential clinical importance (PCI) criteria[6]

End point description:

Clinical chemistry parameters with PCI ranges: aspartate amino transferase (AST), alanine amino transferase (ALT), and alkaline phosphatase (ALP) (high: >=2 times upper limit of normal [ULN] units per liter [U/L]); calcium (low: <2 millimoles per liter [mmol/L], high: >2.75 mmol/L); glucose (low: <3, high: >9 mmol/L); potassium (low: <3, high: >5.5 mmol/L); sodium (low: <130, high: >150 mmol/L); total bilirubin (high: >=1.5 times ULN micromoles per liter [µmol/L]); high density lipoproteins (HDL) 0.9 to 99.99 mmol/L; low density lipoprotein (LDL) 0 to 3.35 mmol/L; triglycerides 0 to 2.24 mmol/L and creatinine (high: change from Baseline [BL]>44.2 µmol/L). Participants were counted in the worst case category that their value changed to (low, within range or no change, or high) unless there was no change in their category. Participants whose value category was unchanged (e.g., High to High), or whose value became within range, were recorded in the 'To within Range or No Change'

End point type	Primary

End point timeframe:

Up to Day 43

Notes:

[6] - 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 is no statistical analysis to report.

End point values	Part A: Placebo TID DB	Part A: GSK2982772 60 mg TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12[7]	24[8]		
Units: Participants				
AST, To Low	0	0		
AST, To within range or no change	12	24		
AST, To High	0	0		
ALT, To Low	0	0		
ALT, To within range or no change	12	24		
ALT, To High	0	0		
ALP, To Low	0	0		
ALP, To within range or no change	12	24		
ALP, To High	0	0		
Calcium, To Low	0	0		
Calcium, To within range or no change	12	24		

Calcium, To High	0	0		
Glucose, To Low	0	1		
Glucose, To within range or no change	11	23		
Glucose, To High	1	0		
Potassium, To Low	0	0		
Potassium, To within range or no change	12	24		
Potassium, To High	0	0		
Sodium, To Low	0	0		
Sodium, To within range or no change	12	24		
Sodium, To High	0	0		
Total Bilirubin, To Low	0	0		
Total Bilirubin, To within range or no change	12	24		
Total Bilirubin, To High	0	0		
HDL, To Low	0	0		
HDL, To within range or no change	12	24		
HDL, To High	0	0		
LDL, To Low	0	0		
LDL, To within range or no change	10	22		
LDL To High	2	2		
Triglycerides, To Low	0	0		
Triglycerides, To within range or no change	12	23		
Triglycerides, To High	0	1		
Creatinine, To Low	0	0		
Creatinine, To within range or no change	12	24		
Creatinine, To High	0	0		

Notes:

[7] - Safety population

[8] - Safety population

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Number of participants with worst case abnormal clinical chemistry parameters by potential clinical importance (PCI) criteria

End point title	Part B: Number of participants with worst case abnormal clinical chemistry parameters by potential clinical importance (PCI) criteria[9]

End point description:

Clinical chemistry parameters with their PCI ranges were: AST, ALT, and ALP (high: >=2 ULN [U/L]); calcium (low: <2 mmol/L and high: >2.75 mmol/L); glucose (low: <3 and high: >9 mmol/L); potassium (low: <3 and high: >5.5 mmol/L); sodium (low: <130 and high: >150 mmol/L); total bilirubin (high: >=1.5 times ULN [µmol/L]); HDL 0.9 to 99.99 mmol/L; LDL 0.to 3.35 mmol/L; triglycerides 0 to 2.24 mmol/L, creatinine (high: change from BL >44.2 µmol/L). Participants were counted in the worst case category that their value changed to (low, within range or no change, or high) unless there was no change in their category. Participants whose value category was unchanged (e.g., High to High), or whose value became within range, were recorded in the 'To within Range or No Change' category. All participants in Part B were presented in a single arm as they all received GSK2982772 60 mg in Part B (OL Phase).

End point type	Primary

End point timeframe:

From Day 44 to Day 112

Notes:

[9] - 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 is no statistical analysis to report.

End point values	Part B: GSK2982772 60 mg TID OL			
Subject group type	Subject analysis set			
Number of subjects analysed	35[10]			
Units: Participants				
AST, To Low	0			
AST, To within range or no change	35			
AST, To High	0			
ALT, To Low	0			
ALT, To within range or no change	35			
ALT, To High	0			
ALP, To Low	0			
ALP, To within range or no change	35			
ALP, To High	0			
Calcium, To Low	0			
Calcium, To within range or no change	35			
Calcium, To High	0			
Glucose, To Low	1			
Glucose, To within range or no change	34			
Glucose, To High	0			
Potassium, To Low	0			
Potassium, To within range or no change	33			
Potassium, To High	2			
Sodium, To Low	0			
Sodium, To within range or no change	35			
Sodium, To High	0			
Total Bilirubin, To Low	0			
Total Bilirubin, To within range or no change	34			
Total Bilirubin, To High	1			
HDL, To Low	2			
HDL, To within range or no change	33			
HDL, To High	0			
LDL, To Low	0			
LDL, To within range or no change	33			
LDL, To High	2			
Triglycerides, To Low	0			
Triglycerides, To within range or no change	34			
Triglycerides, To High	1			
Creatinine, To Low	0			
Creatinine, To within range or no change	35			
Creatinine, To High	0			

Notes:

[10] - Safety Population.Participants with data available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Number of participants with worst case abnormal hematology parameters by PCI criteria

End point title	Part A: Number of participants with worst case abnormal hematology parameters by PCI criteria[11]

End point description:

Hematology parameters with their PCI ranges were: hematocrit (high: >0.54 proportion of red blood cells in blood and low: change from BL<0.075); hemoglobin (high: >180 grams per liter [g/L] and low: change from BL<25 g/L); lymphocytes (low: <0.8 Giga cells/L); platelet count (low: <100 Giga cells/L and high: >550 Giga cells/L); neutrophil count (low: <1.5 Giga cells/L); white blood cell (WBC) count (low: <3 Giga cells/L and high: >20 Giga cells/L). Participants were counted in the worst-case category that their value changed to (low, within range or no change, or high) unless there was no change in their category. Participants whose value category was unchanged (e.g., High to High), or whose value became within range, were recorded in the 'To within Range or No Change' category. Participants were counted twice if the participant had both values that changed 'To Low' and 'To High'.

End point type	Primary

End point timeframe:

Up to Day 43

Notes:

[11] - 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 is no statistical analysis to report.

End point values	Part A: Placebo TID DB	Part A: GSK2982772 60 mg TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12[12]	24[13]		
Units: Participants				
Hematocrit, To Low	0	0		
Hematocrit, To within range or no change	12	24		
Hematocrit, To High	0	0		
Hemoglobin, To Low	0	0		
Hemoglobin, To within range or no change	12	24		
Hemoglobin, To High	0	0		
Lymphocytes, To Low	1	0		
Lymphocytes, To within range or no change	11	24		
Lymphocytes, To High	0	0		
Platelet count, To Low	0	0		
Platelet count, To within range or no change	12	22		
Platelet count, To High	0	2		
Neutrophil count, To Low	0	1		

Neutrophil count, To within range or no change	12	23		
Neutrophil count, To High	0	0		
WBC, To Low	0	2		
WBC To within range or no change	12	24		
WBC, To High	0	0		

Notes:

[12] - Safety Population

[13] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Number of participants with worst case abnormal hematology parameters by PCI criteria

End point title	Part B: Number of participants with worst case abnormal hematology parameters by PCI criteria[14]

End point description:

Hematology parameters with their PCI ranges were: hematocrit (high: >0.54 proportion of red blood cells in blood and low: change from BL<0.075); hemoglobin (high: >180 g/L and low: change from BL<25 g/L); lymphocytes (low: <0.8 Giga cells/L); platelet count (low: <100 Giga cells/L and high: >550 Giga cells/L); neutrophil count (low: <1.5 Giga cells/L); WBC count (low: <3 Giga cells/L and high: >20 Giga cells/L). Participants were counted in the worst-case category that their value changed to (low, within range or no change, or high) unless there was no change in their category. Participants whose value category was unchanged (e.g., High to High), or whose value became within range, were recorded in the 'To within Range or No Change' category. Participants were counted twice if the participant had both values that changed 'To Low' and 'To High'. All participants in Part B were presented in a single arm as they all received GSK2982772 60 mg in Part B (OL Phase).

End point type	Primary

End point timeframe:

From Day 44 to Day 112

Notes:

[14] - 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 is no statistical analysis to report.

End point values	Part B: GSK2982772 60 mg TID OL			
Subject group type	Subject analysis set			
Number of subjects analysed	35[15]			
Units: Participants				
Hematocrit, To Low	0			
Hematocrit, To within range or no change	35			
Hematocrit, To High	0			
Hemoglobin, To Low	0			
Hemoglobin, To within range or no change	35			
Hemoglobin, To High	0			
Lymphocytes, To Low	1			
Lymphocytes, To within range or no change	34			
Lymphocytes, To High	0			
Platelet count, To Low	0			

Platelet count, To within range or no change	35			
Platelet count, To High	0			
Neutrophil count, To Low	0			
Neutrophil count, To within range or no change	35			
Neutrophil count, To High	0			
WBC, To Low	1			
WBC To within range or no change	34			
WBC, To High	0			

Notes:

[15] - Safety Population.Participants with data available at the specified time points were analyzed

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Number of participants with worst case abnormal urinalysis results by dipstick method

End point title	Part A: Number of participants with worst case abnormal urinalysis results by dipstick method[16]

End point description:

Urine samples were collected for the assessment of following urine parameters by dipstick method: glucose, protein, blood and ketones. The dipstick test gives results in a semi-quantitative manner, and results for urinalysis parameters of urine glucose, protein, blood and ketones can be read as negative (-), trace, 1+, 2+, 3+, 4+, 5+ indicating proportional concentrations in the urine sample. Number of participants with abnormal results were reported as 'increase to trace' or 'increase to 1+, 2+, 3+, 4+, 5+' relative to BL (Day 1) value. Participants whose value was unchanged (e.g., Trace to Trace), or whose value was decreased, were recorded in the 'No change or Decreased' category. Only those participants with data available at the specified time points were analyzed.

End point type	Primary

End point timeframe:

Up to Day 43

Notes:

[16] - 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 is no statistical analysis to report.

End point values	Part A: GSK2982772 60 mg TID DB	Part A: Placebo TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[17]	11[18]		
Units: Participants				
Glucose, No change or decreased	24	11		
Glucose, Increase to Trace	0	0		
Glucose, Increase to 1+	0	0		
Glucose, Increase to 2+	0	0		
Glucose, Increase to 3+	0	0		
Glucose, Increase to 4+	0	0		
Glucose, Increase to 5+	0	0		
Ketones, No change or decreased	16	10		
Ketones, Increase to Trace	3	0		
Ketones, Increase to 1+	3	0		
Ketones, Increase to 2+	1	1		

Ketones, Increase to 3+	1	0		
Ketones, Increase to 4+	0	0		
Ketones, Increase to 5+	0	0		
Occult Blood, No change or decreased	21	7		
Occult Blood, Increase to Trace,	2	2		
Occult Blood, Increase to 1+	1	0		
Occult Blood, Increase to 2+	0	2		
Occult Blood, Increase to 3+	0	0		
Occult Blood, Increase to 4+	0	0		
Occult Blood, Increase to 5+	0	0		
Protein, No change or Decreased	19	8		
Protein, Increase to Trace	4	2		
Protein, Increase to 1+	1	1		
Protein, Increase to 2+	0	0		
Protein, Increase to 3+	0	0		
Protein, Increase to 4+	0	0		
Protein, Increase to 5+	0	0		

Notes:

[17] - Safety Population

[18] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Number of participants with worst case abnormal urinalysis results by dipstick method

End point title	Part B: Number of participants with worst case abnormal urinalysis results by dipstick method[19]

End point description:

Urine samples were collected for the assessment of following urine parameters by dipstick method: glucose, protein, blood and ketones. The dipstick test gives results in a semi-quantitative manner, and results for urinalysis parameters of urine glucose, protein, blood and ketones can be read as negative (-), trace, 1+, 2+, 3+, 4+, 5+ indicating proportional concentrations in the urine sample. Number of participants with abnormal results were reported as 'increase to trace' or 'increase to 1+, 2+, 3+, 4+, 5+' relative to BL (Day 1) value. Participants whose value was unchanged (e.g., Trace to Trace), or whose value was decreased, were recorded in the 'No change or Decreased' category. All participants in Part B were presented in a single arm as they all received GSK2982772 60 mg in Part B (OL Phase).

End point type	Primary

End point timeframe:

From Day 44 to Day 112

Notes:

[19] - 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 is no statistical analysis to report.

End point values	Part B: GSK2982772 60 mg TID OL			
Subject group type	Subject analysis set			
Number of subjects analysed	34[20]			
Units: Participants				
Glucose, No change or Decreased	34			
Glucose, Increase to Trace	0			
Glucose, Increase to 1+	0			

Glucose, Increase to 2+	0			
Glucose, Increase to 3+	0			
Glucose, Increase to 4+	0			
Glucose, Increase to 5+	0			
Ketones, No change or Decrease	21			
Ketones, Increase to Trace	9			
Ketones, Increase to 1+	2			
Ketones, Increase to 2+	2			
Ketones, Increase to 3+	0			
Ketones, Increase to 4+	0			
Ketones, Increase to 5+	0			
Occult Blood, No change or Decreased	30			
Occult Blood, Increase to Trace	2			
Occult Blood, Increase to 1+	1			
Occult Blood, Increase to 2+	1			
Occult Blood, Increase to 3+	0			
Occult Blood, Increase to 4+	0			
Occult Blood, Increase to 5+	0			
Protein, No change or Decreased	30			
Protein, Increase to Trace	3			
Protein, Increase to 1+	1			
Protein, Increase to 2+	0			
Protein, Increase to 3+	0			
Protein, Increase to 4+	0			
Protein, Increase to 5+	0			

Notes:

[20] - Safety Population.Participants with data available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Number of participants with worst case abnormal blood pressure results by PCI criteria

End point title	Part A: Number of participants with worst case abnormal blood pressure results by PCI criteria[21]

End point description:

Vital signs were measured in a semi-supine position after 5 minutes rest and included body temperature, systolic and diastolic blood pressure. The clinical concern range for vital signs were: systolic blood pressure (SBP) (low: <85 and high: >160 millimeters of mercury [mmHg]); diastolic blood pressure (DBP) (low: <45 and high: >100 mmHg). Participants were counted in the worst case category that their value changed to (low, within range or no change, or high) unless there was no change in their category. Participants whose value category was unchanged (e.g., High to High), or whose value became within range, were recorded in the 'To within Range or No Change' category.

End point type	Primary

End point timeframe:

Up to Day 43

Notes:

[21] - 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 is no statistical analysis to report.

End point values	Part A: Placebo TID DB	Part A: GSK2982772 60 mg TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12[22]	24[23]		
Units: Participants				
DBP, To Low	0	0		
DBP, To within range or no change	12	24		
DBP, To High	0	0		
SBP, To Low	0	0		
SBP, To within range or no change	12	24		
SBP, To High	0	0		

Notes:

[22] - Safety Population

[23] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Number of participants with worst case abnormal blood pressure results by PCI criteria

End point title	Part B: Number of participants with worst case abnormal blood pressure results by PCI criteria[24]

End point description:

Vital signs were measured in a semi-supine position after 5 minutes rest and included body temperature, systolic and diastolic blood pressure. The clinical concern range for vital signs were: SBP (low: <85 and high: >160 mmHg); DBP (low: <45 and high: >100 mmHg). Participants were counted in the worst case category that their value changed to (low, within range or no change, or high) unless there was no change in their category. Participants whose value category was unchanged (e.g., High to High), or whose value became within range, were recorded in the 'To within Range or No Change' category. All participants in Part B were presented in a single arm as they all received GSK2982772 60 mg in Part B (OL Phase).

End point type	Primary

End point timeframe:

From Day 44 to Day 112

Notes:

[24] - 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 is no statistical analysis to report.

End point values	Part B: GSK2982772 60 mg TID OL			
Subject group type	Subject analysis set			
Number of subjects analysed	35[25]			
Units: Participants				
DBP, To Low	0			
DBP, To within range or no change	34			
DBP, To High	1			
SBP, To Low	0			
SBP, To within range or no change	33			
SBP, To High	2			

Notes:

[25] - Safety Population.Participants with data available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Number of participants with worst case abnormal heart rate (HR) results by PCI criteria

End point title	Part A: Number of participants with worst case abnormal heart rate (HR) results by PCI criteria[26]

End point description:

Vital signs were measured in a semi-supine position after 5 minutes rest which included HR. The clinical concern range for HR (low <40 beats per min [bpm] and high >100 bpm). Participants were counted in the worst case category that their value changed to (low, within range or no change, or high) unless there was no change in their category. Participants whose value category was unchanged (e.g., High to High), or whose value became within range, were recorded in the 'To within Range or No Change' category.

End point type	Primary

End point timeframe:

Up to Day 43

Notes:

[26] - 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 is no statistical analysis to report.

End point values	Part A: Placebo TID DB	Part A: GSK2982772 60 mg TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12[27]	24[28]		
Units: Participants				
HR, To Low	0	0		
HR, To within range or no change	11	24		
HR, To High	1	0		

Notes:

[27] - Safety Population

[28] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Number of participants with worst case abnormal HR results by PCI criteria

End point title	Part B: Number of participants with worst case abnormal HR results by PCI criteria[29]

End point description:

Vital signs were measured in a semi-supine position after 5 minutes rest which included HR. The clinical concern range for HR (low <40 bpm and high >100 bpm). Participants were counted in the worst case category that their value changed to (low, within range or no change, or high) unless there was no change in their category. Participants whose value category was unchanged (e.g., High to High), or whose value became within range, were recorded in the 'To within Range or No Change' category.

End point type	Primary

End point timeframe:

From Day 44 to Day 112

Notes:

[29] - 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 is no statistical analysis to report.

End point values	Part B: GSK2982772 60 mg TID OL			
Subject group type	Subject analysis set			
Number of subjects analysed	35[30]			
Units: Participants				
HR, To Low	0			
HR, To within range or no change	35			
HR, To High	0			

Notes:

[30] - Safety Population.Participants with data available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Number of participants with worst-case abnormal Electrocardiogram (ECG) findings

End point title	Part A: Number of participants with worst-case abnormal Electrocardiogram (ECG) findings[31]

End point description:

12-lead ECGs were recorded with the participants in a supine position using an ECG machine. Number of participants with worst-case clinically significant and not clinically significant abnormal ECG findings have been presented. Clinically significant abnormal findings are those which are not associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition.

End point type	Primary

End point timeframe:

Up to Day 43

Notes:

[31] - 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 is no statistical analysis to report.

End point values	Part A: Placebo TID DB	Part A: GSK2982772 60 mg TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12[32]	24[33]		
Units: Participants				
Abnormal-not clinically significant	5	11		
Abnormal-clinically significant	0	0		

Notes:

[32] - Safety Population

[33] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Number of participants with worst-case abnormal ECG findings

End point title	Part B: Number of participants with worst-case abnormal ECG findings[34]

End point description:

12-lead ECGs were recorded with the participants in a supine position using an ECG machine. Number of participants with worst-case clinically significant and not clinically significant abnormal ECG findings have been presented. Clinically significant abnormal findings are those which are not associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition. All participants in Part B were presented in a single arm as they all received GSK2982772 60 mg in Part B (OL Phase).

End point type	Primary

End point timeframe:

From Day 44 to Day 112

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 is no statistical analysis to report.

End point values	Part B: GSK2982772 60 mg TID OL			
Subject group type	Subject analysis set			
Number of subjects analysed	35[35]			
Units: Participants				
Abnormal-not clinically significant	18			
Abnormal-clinically significant	1			

Notes:

[35] - Safety Population.Participants with data available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of participants who achieved an absolute mayo endoscopy subscore of 0 or 1 at Day 43

End point title	Part A: Percentage of participants who achieved an absolute mayo endoscopy subscore of 0 or 1 at Day 43

End point description:

The Mayo scoring system was used to assess UC disease activity, scoring ranges from 0 to 12, calculated as sum of 4 sub-scores, higher scores indicating more severe disease. The 4 sub-scores are stool frequency (0=normal number of stools; 1=1 to 2 stools/day more than normal;2=3 to 4 stools/day more than normal;3= >4 stools/day more than normal);rectal bleeding (0=no blood seen;1=visible blood with stools less than half the time;2= visible blood with stool half the time or more;3=passing blood alone);findings at endoscopy (0=normal or inactive disease;1=mild disease [erythema, decreased vascular pattern, mild friability];2=moderate disease [marked erythema, lack of vascular pattern, friability, erosions];3=severe disease [spontaneous bleeding, ulceration]); and physician's global assessment (PGA) (0=normal;1=mild;2=moderate;3=severe). Number of participants with Mayo endoscopic sub-score of 0 or 1 are presented. (range=0 to 3, higher scores indicating more severe disease).

End point type	Secondary

End point timeframe:

Day 43

End point values	Part A: GSK2982772 60 mg TID DB	Part A: Placebo TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[36]	11[37]		
Units: Percentage of participants				
Mayo endoscopy sub-score =0	4	0		
Mayo endoscopy sub-score=1	8	0		

Notes:

[36] - Safety population

[37] - Safety population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of participants who achieved an absolute Mayo endoscopy subscore of 0 or 1 at Day 85

End point title	Part B: Percentage of participants who achieved an absolute Mayo endoscopy subscore of 0 or 1 at Day 85[38]

End point description:

The Mayo scoring system was used to assess UC disease activity, scoring ranges from 0 to 12, calculated as sum of 4 sub-scores, higher scores indicating more severe disease. The 4 sub-scores (0=normal number of stools;1=1 to 2 stools/day more than normal;2=3 to 4 stools/day more than normal;3= >4 stools/day more than normal);rectal bleeding (0=no blood seen;1=visible blood with stools less than half the time; 2= visible blood with stool half the time or more;3=passing blood alone); findings at endoscopy (0=normal or inactive disease;1=mild disease [erythema, decreased vascular pattern, mild friability]; 2=moderate disease [marked erythema, lack of vascular pattern, friability, erosions];3=severe disease [spontaneous bleeding, ulceration]); and PGA (0=normal;3=severe). Number of participants with Mayo endoscopic sub-score of 0 or 1 are presented. (range=0 to 3). Participants were split into 2 arms as randomized in Part A to allow statistical comparison of efficacy outcomes.

End point type	Secondary

End point timeframe:

Day 85

Notes:

[38] - 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 is no statistical analysis to report.

End point values	Placebo TID DB /GSK2982772 60 mg TID OL	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9[39]	22[40]		
Units: Percentage of participants				
Mayo endoscopy sub-score =0	0	5		
Mayo endoscopy sub-score=1	11	9		

Notes:

[39] - Safety Population.Participants with data available at the specified time points were analyzed.

[40] - Safety population.Participants with data available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Change from Baseline in Ulcerative Colitis Endoscopic Index of Severity (UCEIS) total score

End point title	Part A: Change from Baseline in Ulcerative Colitis Endoscopic Index of Severity (UCEIS) total score

End point description:

UCEIS was used as an additional tool to assess disease activity based on 3 sub-scales: 'endoscopic vascular pattern, bleeding, erosions and ulcerations'. UCEIS total score was calculated by sum of all 3 sub-scale scores. Total score ranges from 0 to 8, with higher scores indicating more severe disease. Individual sub-scales were vascular pattern (0=Normal, 1=Patchy loss, 2=Obliterated); bleeding (0=None, 1=Mucosal, 2=Luminal mild, 3=Luminal severe); erosions and ulcerations (0=None, 1=Erosions, 2=Superficial ulcer, 3=Deep ulcer). BL is defined as the latest pre-dose assessment at Screening (within 30 days prior to Day 1). Change from BL was calculated as post-BL visit value minus BL value. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Baseline (screening - within 30 days prior to Day 1) and Day 43

End point values	Part A: Placebo TID DB	Part A: GSK2982772 60 mg TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11[41]	24[42]		
Units: Scores on scale				
least squares mean (standard error)	-0.24 (± 0.428)	-0.42 (± 0.289)		

Notes:

[41] - Safety Population

[42] - Safety Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using a Mixed Models Repeated Measures (MMRM) model, adjusting for the following covariates: treatment, visit, Baseline value, and the treatment by visit and baseline value by visit interactions.

Comparison groups	Part A: Placebo TID DB v Part A: GSK2982772 60 mg TID DB

Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.23
upper limit	0.87

Secondary: Part B: Change from Baseline in Ulcerative Colitis Endoscopic Index of Severity (UCEIS) total score

End point title	Part B: Change from Baseline in Ulcerative Colitis Endoscopic Index of Severity (UCEIS) total score[43]

End point description:

UCEIS was used as an additional tool to assess disease activity based on 3 sub-scales: 'endoscopic vascular pattern, bleeding, erosions and ulcerations'. UCEIS total score was calculated by sum of all 3 sub-scale scores. Total score ranges from 0 to 8, with higher scores indicating more severe disease. Individual sub-scales were vascular pattern (0=Normal, 1=Patchy loss, 2=Obliterated); bleeding (0=None, 1=Mucosal, 2=Luminal mild, 3=Luminal severe); erosions and ulcerations (0=None, 1=Erosions, 2=Superficial ulcer, 3=Deep ulcer). BL is defined as the latest pre-dose assessment at Screening (within 30 days prior to Day 1). Change from BL was calculated as post-BL visit value minus BL value. Participants were split into 2 arms as randomized in Part A to allow statistical comparison of efficacy outcomes.

End point type	Secondary

End point timeframe:

Baseline (screening - within 30 days prior to Day 1) and Day 85

Notes:

[43] - 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 is no statistical analysis to report.

End point values	Placebo TID DB /GSK2982772 60 mg TID OL	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9[44]	22[45]		
Units: Scores on scale				
least squares mean (standard error)	-0.84 (± 0.495)	-0.82 (± 0.318)		

Notes:

[44] - Safety Population.Participants with data available at the specified time points were analyzed.

[45] - Safety Population.Participants with data available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline value, and the treatment by visit and baseline value by visit interactions.

Comparison groups	Placebo TID DB /GSK2982772 60 mg TID OL v GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL

Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.18
upper limit	1.22

Secondary: Part A: Change from Baseline in mean C reactive protein (CRP)

End point title	Part A: Change from Baseline in mean C reactive protein (CRP)

End point description:

Blood samples were collected to measure CRP. BL is defined as the latest pre-dose assessment on Day 1. Change from BL is the value at indicated time point minus BL value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, pre-dose) and Days 15, 29, 43

End point values	Part A: GSK2982772 60 mg TID DB	Part A: Placebo TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[46]	11[47]		
Units: Milligrams per liter				
least squares mean (standard error)				
Day 15, n=11,24	0.20 (± 1.112)	0.25 (± 1.648)		
Day 29, n=11, 23	-1.84 (± 0.782)	1.34 (± 1.119)		
Day 43, n=11, 24	-0.64 (± 1.251)	1.06 (± 1.854)		

Notes:

[46] - Safety population

[47] - Safety population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Day 15. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline value, and the treatment by visit and Baseline value by visit interactions.

Comparison groups	Part A: Placebo TID DB v Part A: GSK2982772 60 mg TID DB

Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.11
upper limit	4.02

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Day 29. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline value, and the treatment by visit and Baseline value by visit interactions.	
Comparison groups	Part A: Placebo TID DB v Part A: GSK2982772 60 mg TID DB
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	-3.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.99
upper limit	-0.35

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Day 43. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline value, and the treatment by visit and Baseline value by visit interactions.	
Comparison groups	Part A: Placebo TID DB v Part A: GSK2982772 60 mg TID DB
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	-1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.26
upper limit	2.88

Secondary: Part B:Change from Baseline in mean CRP

End point title	Part B:Change from Baseline in mean CRP[48]

End point description:

Blood samples were collected to measure CRP. BL is defined as the latest pre-dose assessment on Day 1. Change from BL is the value at indicated time point minus BL value. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles). All participants in Part B received GSK2982772 60 mg in Part B (OL Phase), however they were split into 2 arms as randomized in Part A to allow statistical comparison of efficacy outcomes.

End point type	Secondary

End point timeframe:

Baseline (Day 1, pre-dose) and Days 57, 71, 85

Notes:

[48] - 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 is no statistical analysis to report.

End point values	Placebo TID DB /GSK2982772 60 mg TID OL	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	11[49]	23[50]		
Units: Milligrams per liter				
least squares mean (standard error)				
Day 57, n=11,23	-2.61 (± 1.740)	-2.32 (± 1.186)		
Day 71, n=11, 22	-2.82 (± 1.510)	-2.71 (± 1.040)		
Day 85, n=10, 22	-2.77 (± 1.616)	-1.66 (± 1.092)		

Notes:

[49] - Safety population

[50] - Safety population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Day 57. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline value, and the treatment by visit and Baseline value by visit interactions.

Comparison groups	Placebo TID DB /GSK2982772 60 mg TID OL v GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.01
upper limit	4.59

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Day 71. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline value, and the treatment by visit and Baseline value by visit interactions.

Comparison groups	Placebo TID DB /GSK2982772 60 mg TID OL v GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.64
upper limit	3.85

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Day 85. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline value, and the treatment by visit and Baseline value by visit interactions

Comparison groups	Placebo TID DB /GSK2982772 60 mg TID OL v GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.87
upper limit	5.1

Secondary: Part A: Change from Baseline in fecal calprotectin (FCP)

End point title	Part A: Change from Baseline in fecal calprotectin (FCP)

End point description:

Fecal sample were collected to measure FCP. BL is defined as the latest pre-dose assessment on Day 1. Change from BL is the value at indicated time point minus BL value. Geometric Mean and Geometric Coefficient of Variation has been presented. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1, pre-dose) and Days 15, 29, 43

End point values	Part A: Placebo TID DB	Part A: GSK2982772 60 mg TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11[51]	23[52]		
Units: Microgram per gram				
geometric mean (geometric coefficient of variation)				
Day 15, n=10, 23	0.78 (± 39.2)	0.55 (± 25.1)		
Day 29, n=11, 23	1.23 (± 33.5)	0.54 (± 22.3)		
Day 43, n=11, 22	1.90 (± 40.7)	0.44 (± 27.1)		

Notes:

[51] - Safety Population

[52] - Safety Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Day 15. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, log-transformed Baseline value, and the treatment by visit and log-transformed baseline value by visit interactions.

Comparison groups	Part A: Placebo TID DB v Part A: GSK2982772 60 mg TID DB
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Ratio
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	1.8

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Day 29. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, log-transformed Baseline value, and the treatment by visit and log-transformed baseline value by visit interactions.

Comparison groups	Part A: Placebo TID DB v Part A: GSK2982772 60 mg TID DB
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Ratio
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	1

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Day 43. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, log-transformed Baseline value, and the treatment by visit and log-transformed baseline value by visit interactions.

Comparison groups	Part A: Placebo TID DB v Part A: GSK2982772 60 mg TID DB
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Ratio
Point estimate	0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	0.62

Secondary: Part B:Change from Baseline in fecal calprotectin (FCP)

End point title	Part B:Change from Baseline in fecal calprotectin (FCP)[53]

End point description:

Fecal sample were collected to measure FCP. BL is defined as the latest pre-dose assessment on Day 1. Change from BL is the value at indicated time point minus BL value. Geometric Mean and Geometric Coefficient of Variation has been presented. Only those participants with data available at the specified time points were analyzed (indicated by n=X in category titles). All participants in Part B received GSK2982772 60 mg in Part B (OL Phase), however they were split into 2 arms as randomized in Part A to allow statistical comparison of efficacy outcomes.

End point type	Secondary

End point timeframe:

Baseline (Day 1, pre-dose) and Days 57, 71, 85

Notes:

[53] - 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 is no statistical analysis to report.

End point values	Placebo TID DB /GSK2982772 60 mg TID OL	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	11[54]	23[55]		
Units: Microgram per gram				
geometric mean (geometric coefficient of variation)				
Day 57, n=11, 23	1.13 (± 27.7)	0.56 (± 18.7)		
Day 71, n=11, 22	0.69 (± 42.1)	0.39 (± 28.9)		
Day 85, n=11, 22	0.48 (± 39.9)	0.40 (± 27.2)		

Notes:
[54] - Safety Population
[55] - Safety Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Day 57. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, log-transformed Baseline value, and the treatment by visit and log-transformed baseline value by visit interactions.

Comparison groups	Placebo TID DB /GSK2982772 60 mg TID OL v GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Ratio
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.97

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Day 71. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, log-transformed Baseline value, and the treatment by visit and log-transformed baseline value by visit interactions.

Comparison groups	Placebo TID DB /GSK2982772 60 mg TID OL v GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Ratio
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	1.57

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Day 85. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, log-transformed Baseline value, and the treatment by visit and log-transformed baseline value by

visit interactions.

Comparison groups	Placebo TID DB /GSK2982772 60 mg TID OL v GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	2.18

Secondary: Part A: Change from Baseline in Modified Riley Scale score (MRS)

End point title	Part A: Change from Baseline in Modified Riley Scale score (MRS)

End point description:

MRS is 4-point scale (none, mild, moderate and severe) which scores histologic activity based on localization and quantification of neutrophils in the mucosa, score ranges from 0 to 7, with higher scores indicates more severity. 0= Normal biopsy, 1= Lamina propria neutrophils only (Scattered individual neutrophils), 2= Lamina propria neutrophils only (Patchy collections of neutrophils), 3= Lamina propria neutrophils only (Diffuse neutrophils infiltrate), 4= Cryptitis/crypt abscesses (<25% crypts involved), 5= Cryptitis/crypt abscesses (25% to 74% crypts involved), 6= Cryptitis/crypt abscesses (>=75% crypts involved), 7= Erosion or ulceration present. Score 0 indicates normal condition; 1 to 3 mild condition; 4 to 6 moderate condition and score 7 severe condition. BL is defined as the latest pre-dose assessment. Change from BL is the value at indicated time point minus BL value. Only those participants with data available at the specified time points were analyzed

End point type	Secondary

End point timeframe:

Baseline (Day 1, pre-dose) and Day 43

End point values	Part A: GSK2982772 60 mg TID DB	Part A: Placebo TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23[56]	10[57]		
Units: Scores on scale				
least squares mean (standard error)	0.04 (± 0.558)	0.04 (± 0.842)		

Notes:

[56] - Safety Population.

[57] - Safety Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline score, and the treatment by visit and Baseline score by visit interactions.

Comparison groups	Part A: Placebo TID DB v Part A: GSK2982772 60 mg TID DB

Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.05
upper limit	2.07

Secondary: Part B: Change from Baseline in MRS score

End point title	Part B: Change from Baseline in MRS score[58]

End point description:

MRS is 4-point scale (none, mild, moderate and severe) which scores histologic activity based on localization and quantification of neutrophils in the mucosa, score ranges from 0 to 7, with higher scores indicates more severity. 0=Normal biopsy, 1=Lamina propria neutrophils only (Scattered individual neutrophils), 2=Lamina propria neutrophils only (Patchy collections of neutrophils), 3=Lamina propria neutrophils only (Diffuse neutrophils infiltrate), 4=Cryptitis/crypt abscesses (<25% crypts involved), 5=Cryptitis/crypt abscesses (25% to 74% crypts involved), 6=Cryptitis/crypt abscesses (>=75% crypts involved), 7=Erosion or ulceration present. Score 0 indicates normal condition; 1 to 3 mild condition; 4 to 6 moderate condition and score 7 severe condition. BL is defined as the latest pre-dose assessment. Change from BL is the value at indicated time point minus BL value. Participants were split into 2 arms as randomized in Part A to allow statistical comparison of efficacy outcomes.

End point type	Secondary

End point timeframe:

Baseline (Day 1, pre-dose) and Day 85

Notes:

[58] - 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 is no statistical analysis to report.

End point values	Placebo TID DB /GSK2982772 60 mg TID OL	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9[59]	21[60]		
Units: Scores on scale				
least squares mean (standard error)	-0.72 (± 0.894)	-0.65 (± 0.576)		

Notes:

[59] - Safety Population. Participants with data available at the specified time points were analyzed.

[60] - Safety Population. Participants with data available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline score, and the treatment by visit and Baseline score by visit interactions.

Comparison groups	Placebo TID DB /GSK2982772 60 mg TID OL v GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.11
upper limit	2.27

Secondary: Part A: Change from Baseline in Geboes Index Total Score

End point title	Part A: Change from Baseline in Geboes Index Total Score

End point description:

Geboes score is a 7-items instrument which classifies histologic changes and generates a score from 0 to 5.4. The 7 items are: grade 0=structural-architectural changes (scored from 0.0 to 0.3); grade 1=chronic inflammatory infiltrate (scored from 1.0 to 1.3); grade 2A=lamina propria neutrophils (scored from 2.0 to 2.3), grade 2B= lamina propria eosinophils (scored from 2.0 to 2.3); 3=neutrophils in the epithelium (scored from 3.0 to 3.3); 4=crypt destruction (scored from 4.0 to 4.3); 5=erosions or ulceration (scored from 5.0 to 5.4). The most severe observation that the histopathologist sees on the slide is considered as the Geboes index total score, ranges from 0 to 5.4, with higher scores indicates severe disease. BL is defined as the latest pre-dose assessment before Day 1. Change from BL is the value at indicated time point minus BL value. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Day 43

End point values	Part A: GSK2982772 60 mg TID DB	Part A: Placebo TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23[61]	10[62]		
Units: Scores on scale				
least squares mean (standard error)	0.28 (± 1.223)	1.04 (± 1.847)		

Notes:

[61] - Safety Population

[62] - Safety Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline score, and the treatment by visit and Baseline score by visit interactions.

Comparison groups	Part A: Placebo TID DB v Part A: GSK2982772 60 mg TID DB

Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	-0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.29
upper limit	3.77

Secondary: Part B: Change from Baseline in Geboes Index Total Score

End point title	Part B: Change from Baseline in Geboes Index Total Score[63]

End point description:

Geboes score is a 7-items instrument which classifies histologic changes and generates a score from 0 to 5.4. The 7 items are: grade 0=structural-architectural changes (scored from 0.0 to 0.3); grade 1=chronic inflammatory infiltrate (scored from 1.0 to 1.3); grade 2A=lamina propria neutrophils (scored from 2.0 to 2.3), grade 2B= lamina propria eosinophils (scored from 2.0 to 2.3); 3=neutrophils in the epithelium (scored from 3.0 to 3.3); 4=crypt destruction (scored from 4.0 to 4.3); 5=erosions or ulceration (scored from 5.0 to 5.4). The most severe observation that the histopathologist sees on the slide is considered as the Geboes index total score, ranges from 0 to 5.4, with higher scores indicates severe disease. BL is defined as the latest pre-dose assessment before Day 1. Change from BL is the value at indicated time point minus BL value. Participants were split into 2 arms as randomized in Part A to allow statistical comparison of efficacy outcomes.

End point type	Secondary

End point timeframe:

Baseline and Day 85

Notes:

[63] - 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 is no statistical analysis to report.

End point values	Placebo TID DB /GSK2982772 60 mg TID OL	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9[64]	21[65]		
Units: Scores on scale				
least squares mean (standard error)	-0.67 (± 1.981)	-1.47 (± 1.286)		

Notes:

[64] - Safety Population. Participants with data available at the specified time points were analyzed.

[65] - Safety Population. Participants with data available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline score, and the treatment by visit and Baseline score by visit interactions.

Comparison groups	Placebo TID DB /GSK2982772 60 mg TID OL v GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.68
upper limit	4.08

Secondary: Part A: Number of participants who achieved Mayo clinical response

End point title	Part A: Number of participants who achieved Mayo clinical response

End point description:

Mayo Clinical Response defined as >=3 points or >=30% improvement from BL in Total Mayo Score, along with a decrease in the rectal bleeding sub-score of >= 1 point. Scoring ranges 0 to 12, calculated as sum of 4 sub-scores, higher scores indicating more severe disease. The 4 sub-scores are stool frequency (0=normal number of stools; 1=1 to 2 stools/day more than normal; 2=3 to 4 stools/day more than normal; 3= >4 stools/day more than normal); rectal bleeding (0=no blood seen; 1=visible blood with stools less than half the time; 2= visible blood with stool half the time or more; 3=passing blood alone); findings at endoscopy (0=normal or inactive disease; 1=mild disease [erythema, decreased vascular pattern, mild friability]; 2=moderate disease [marked erythema, lack of vascular pattern, friability, erosions]; 3=severe disease [spontaneous bleeding, ulceration]); and PGA (0=normal, 3=severe). Only those participants with data available at the specified time points were analyzed

End point type	Secondary

End point timeframe:

Day 43

End point values	Part A: GSK2982772 60 mg TID DB	Part A: Placebo TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[66]	11[67]		
Units: Participants	9	4		

Notes:

[66] - Safety Population

[67] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of participants who achieved Mayo clinical response

End point title	Part B: Number of participants who achieved Mayo clinical response[68]

End point description:

Mayo Clinical Response defined as >=3 points or >=30% improvement from BL in Total Mayo Score, along with a decrease in the rectal bleeding sub-score of >= 1 point. Scoring ranges 0 to 12, calculated as sum of 4 sub-scores, higher scores indicating more severe disease. The 4 sub-scores are stool

frequency (0=normal number of stools;1=1 to 2 stools/day more than normal;2=3 to 4 stools/day more than normal;3= >4 stools/day more than normal);rectal bleeding (0=no blood seen; 1=visible blood with stools less than half the time;2= visible blood with stool half the time or more;3=passing blood alone); findings at endoscopy (0=normal; 1=mild disease [erythema, decreased vascular pattern, mild friability];2=moderate disease [marked erythema, lack of vascular pattern, friability, erosions];3=severe disease [spontaneous bleeding, ulceration]);and PGA (0=normal, 3=severe). Participants were split into 2 arms as randomized in Part A to allow statistical comparison of efficacy

End point type	Secondary

End point timeframe:

Day 85

Notes:

[68] - 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 is no statistical analysis to report.

End point values	Placebo TID DB /GSK2982772 60 mg TID OL	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9[69]	22[70]		
Units: Participants	5	11		

Notes:

[69] - Safety Population. Participants with data available at the specified time points were analyzed.

[70] - Safety Population. Participants with data available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Number of participants who achieved Mayo clinical remission

End point title	Part A: Number of participants who achieved Mayo clinical remission

End point description:

Mayo clinical remission is defined as total mayo score of 2 points or lower, with no individual subscore exceeding 1 point. Scoring ranges 0 to 12, calculated as sum of 4 sub-scores, higher scores indicating more severe disease. The 4 sub-scores are stool frequency (0=normal number of stools; 1=1 to 2 stools/day more than normal; 2=3 to 4 stools/day more than normal; 3= >4 stools/day more than normal); rectal bleeding (0=no blood seen; 1=visible blood with stools less than half the time; 2= visible blood with stool half the time or more; 3=passing blood alone); findings at endoscopy (0=normal or inactive disease; 1=mild disease [erythema, decreased vascular pattern, mild friability]; 2=moderate disease [marked erythema, lack of vascular pattern, friability, erosions]; 3=severe disease [spontaneous bleeding, ulceration]); and PGA (0=normal, 3=severe). Only those participants with data available at the specified time points were analyzed

End point type	Secondary

End point timeframe:

Day 43

End point values	Part A: GSK2982772 60 mg TID DB	Part A: Placebo TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[71]	11[72]		
Units: Participants	0	0		

Notes:

[71] - Safety Population

[72] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of participants who achieved Mayo clinical remission

End point title	Part B: Number of participants who achieved Mayo clinical remission[73]

End point description:

Mayo clinical remission is defined as total mayo score of 2 points or lower, with no individual subscore exceeding 1 point. Score ranges from 0 to 12, calculated as sum of 4 sub-scores, higher scores indicating more severe disease. The 4 sub-scores are stool frequency (0=normal number of stools; 1=1 to 2 stools/day more than normal; 2=3 to 4 stools/day more than normal; 3= >4 stools/day more than normal); rectal bleeding (0=no blood seen; 1=visible blood with stools less than half the time; 2= visible blood with stool half the time or more; 3=passing blood alone); findings at endoscopy (0=normal or inactive disease; 1=mild disease [erythema, decreased vascular pattern, mild friability]; 2=moderate disease [marked erythema, lack of vascular pattern, friability, erosions]; 3=severe disease [spontaneous bleeding, ulceration]); and PGA(0=normal;1=mild;2=moderate;3=severe). Participants were split into 2 arms as randomized in Part A to allow statistical comparison of efficacy outcomes.

End point type	Secondary

End point timeframe:

Day 85

Notes:

[73] - 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 is no statistical analysis to report.

End point values	Placebo TID DB /GSK2982772 60 mg TID OL	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	9[74]	22[75]		
Units: Participants	1	2		

Notes:

[74] - Safety Population. Participants with data available at the specified time points were analyzed.

[75] - Safety Population. Participants with data available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Change from Baseline in partial mayo score

End point title	Part A: Change from Baseline in partial mayo score

End point description:

Partial Mayo Score defined as total score of 3 domain subscores-stool frequency, rectal bleeding and PGA, ranges from 0 to 9, higher score indicate more severe disease. It has 4 sub-scores: Stool

frequency (0=normal number of stools; 1=1 to 2 stools/day more than normal; 2=3 to 4 stools/day more than normal; 3= >4 stools/day more than normal); rectal bleeding (0=no blood seen; 1=visible blood with stools less than half the time; 2= visible blood with stool half the time or more;3=passing blood alone); findings at endoscopy (0=normal or inactive disease;1=mild disease[erythema,decreased vascular pattern,mild friability];2=moderate disease[marked erythema,lack of vascular pattern,friability,erosions];3=severe disease [spontaneous bleeding,ulceration]);and PGA (0=normal, 3=severe). Change from BL=post-BL value minus BL value (screening-within 30 days prior to Day 1). Only those participants with data available at the specified time points were analyzed

End point type	Secondary

End point timeframe:

Baseline (Screening - within 30 days prior to Day 1) and at Days 15, 29, 43

End point values	Part A: GSK2982772 60 mg TID DB	Part A: Placebo TID DB		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24[76]	11[77]		
Units: Scores on scale				
least squares mean (standard error)				
Day 15	-1.04 (± 0.333)	-0.68 (± 0.493)		
Day 29	-1.16 (± 0.324)	-1.05 (± 0.480)		
Day 43	-1.64 (± 0.376)	-1.30 (± 0.557)		

Notes:

[76] - Safety Population

[77] - Safety Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Day 15. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline score, and the treatment by visit and Baseline score by visit interactions.

Comparison groups	Part A: Placebo TID DB v Part A: GSK2982772 60 mg TID DB
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.58
upper limit	0.86

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Day 29. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline score, and the treatment by visit and Baseline score by visit interactions.

Comparison groups	Part A: Placebo TID DB v Part A: GSK2982772 60 mg TID DB
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.29
upper limit	1.08

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Day 43. Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline score, and the treatment by visit and Baseline score by visit interactions.

Comparison groups	Part A: Placebo TID DB v Part A: GSK2982772 60 mg TID DB
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.72
upper limit	1.04

Secondary: Part B: Change from Baseline in partial mayo score

End point title	Part B: Change from Baseline in partial mayo score[78]

End point description:

Partial Mayo Score defined as total score of 3 domain subscores-stool frequency, rectal bleeding and PGA, ranges from 0 to 9, higher score indicate more severe disease. It has 4 sub-scores: Stool frequency (0=normal number of stools; 1=1 to 2 stools/day more than normal; 2=3 to 4 stools/day more than normal; 3= >4 stools/day more than normal); rectal bleeding (0=no blood seen; 1=visible blood with stools less than half the time; 2= visible blood with stool half the time or more;3=passing blood alone); findings at endoscopy (0=normal or inactive disease;1=mild disease[erythema,decreased vascular pattern,mild friability];2=moderate disease[marked erythema,lack of vascular pattern, friability, erosions];3=severe disease [spontaneous bleeding,ulceration]);and PGA (0=normal, 3=severe). Change from BL=post-BL value minus BL value (screening-within 30 days prior to Day 1). Participants were split into 2 arms as randomized in Part A to allow statistical comparison of efficacy outcomes.

End point type	Secondary

End point timeframe:

Baseline and Day 85

Notes:

[78] - 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 is no statistical analysis to report.

End point values	Placebo TID DB /GSK2982772 60 mg TID OL	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	11[79]	22[80]		
Units: Scores on scale				
least squares mean (standard error)	-2.87 (± 0.728)	-2.93 (± 0.502)		

Notes:

[79] - Safety Population. Participants with data available at the specified time points were analyzed

[80] - Safety Population. Participants with data available at the specified time points were analyzed

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using a MMRM model, adjusting for the following covariates: treatment, visit, Baseline score, and the treatment by visit and Baseline score by visit interactions.

Comparison groups	Placebo TID DB /GSK2982772 60 mg TID OL v GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Least Square Mean Difference
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.87
upper limit	1.75

Secondary: Part A: Pre-dose plasma concentration of GSK2982772

End point title	Part A: Pre-dose plasma concentration of GSK2982772

End point description:

Pre-dose blood sample was collected on Day 43 for the measurement of plasma concentration of GSK2982772. PK Population is defined as the participants in the safety population who received an active dose and for whom a GSK2982772 pharmacokinetic sample was obtained and analyzed. All participants in Part B received GSK2982772 60 mg in Part B (OL Phase), however they were split into 2 arms as randomized in Part A to allow statistical comparison of efficacy outcomes.

End point type	Secondary

End point timeframe:

Day 43

End point values	Part A: GSK2982772 60 mg TID DB			
Subject group type	Subject analysis set			
Number of subjects analysed	23[81]			
Units: Nanogram/milliliter				
arithmetic mean (standard deviation)	131.749 (± 214.9127)			

Notes:

[81] - PK Population. Participants with data available at the specified time points were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Post-dose plasma concentrations of GSK2982772

End point title	Part A: Post-dose plasma concentrations of GSK2982772

End point description:

Post-dose blood sample were collected on Days 1 and 43 at 1, 2, 4 and 6 hours for the measurement of plasma concentration of GSK2982772. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Days 1 and 43: 1, 2, 4 and 6 hours post dose

End point values	Part A: GSK2982772 60 mg TID DB			
Subject group type	Subject analysis set			
Number of subjects analysed	23[82]			
Units: Nanogram/milliliter				
arithmetic mean (standard deviation)				
Day 1, 1 hour	674.588 (± 412.8928)			
Day 1, 2 hours	772.043 (± 378.5145)			
Day 1, 4 hours	474.248 (± 309.5524)			
Day 1, 6 hours	481.304 (± 679.5678)			
Day 43, 1 hour	918.926 (± 508.8658)			
Day 43, 2 hours	851.391 (± 340.6479)			
Day 43, 4 hours	472.132 (± 246.0718)			
Day 43, 6 hours	278.039 (± 187.2142)			

Notes:

[82] - PK Population. Participants with data available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Trough concentrations of GSK2982772 on Day 85

End point title	Part B: Trough concentrations of GSK2982772 on Day 85[83]

End point description:

Blood samples were collected for the measurement of trough plasma concentration of GSK2982772 on Day 85. Only those participants with data available at the specified time points were analyzed. All participants in Part B received GSK2982772 60 mg in Part B (OL Phase), however they were split into 2 arms as randomized in Part A to compare trough concentrations.

End point type	Secondary

End point timeframe:

Day 85

Notes:

[83] - 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 is no statistical analysis to report.

End point values	Placebo TID DB /GSK2982772 60 mg TID OL	GSK2982772 60 mg TID DB /GSK2982772 60 mg TID OL		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10[84]	24[85]		
Units: Nanogram/milliliter				
arithmetic mean (standard deviation)	47.970 (± 78.9909)	150.642 (± 305.3144)		

Notes:

[84] - PK Population. Participants with data available at the specified time points were analyzed.

[85] - PK Population. Participants with data available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs and non-serious AEs were collected from the start of study treatment (Day 1) up to Day 43 in Part A and from Day 44 till follow up visit (Day 112) in Part B.

Adverse event reporting additional description:

SAEs and Non-SAEs were reported for the Safety Population which comprised of all participants who received at least one dose of study treatment. Adverse events are presented treatment wise.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Part A: Placebo TID DB

Reporting group description:

Eligible participants with UC, received two tablets of placebo TID orally for 42 days in Part A (double blind phase).

Reporting group title	Part A: GSK2982772 60 mg TID DB

Reporting group description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days in Part A (double blind phase).

Reporting group title	Part B: GSK2982772 60 mg TID OL

Reporting group description:

Eligible participants with UC, received GSK2982772 60 mg (given as 2 tablets of 30 mg) TID orally for 42 days in Part B (open label phase).

Serious adverse events	Part A: Placebo TID DB	Part A: GSK2982772 60 mg TID DB	Part B: GSK2982772 60 mg TID OL
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)	0 / 24 (0.00%)	2 / 35 (5.71%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 24 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Comminuted fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 24 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	1 / 12 (8.33%)	0 / 24 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Part A: Placebo TID DB	Part A: GSK2982772 60 mg TID DB	Part B: GSK2982772 60 mg TID OL
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	13 / 24 (54.17%)	7 / 35 (20.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 12 (8.33%)	6 / 24 (25.00%)	6 / 35 (17.14%)
occurrences (all)	1	10	7
Dizziness			
subjects affected / exposed	1 / 12 (8.33%)	1 / 24 (4.17%)	1 / 35 (2.86%)
occurrences (all)	1	1	1
Dysgeusia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 24 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	0 / 12 (0.00%)	0 / 24 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 24 (4.17%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 12 (16.67%)	3 / 24 (12.50%)	1 / 35 (2.86%)
occurrences (all)	2	3	1
Abdominal pain upper			
subjects affected / exposed	0 / 12 (0.00%)	3 / 24 (12.50%)	1 / 35 (2.86%)
occurrences (all)	0	4	2
Abdominal distension			

subjects affected / exposed	0 / 12 (0.00%)	2 / 24 (8.33%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	2 / 24 (8.33%)	1 / 35 (2.86%)
occurrences (all)	0	2	1
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 24 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Constipation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 24 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Nasal ulcer			
subjects affected / exposed	1 / 12 (8.33%)	0 / 24 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 24 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Petechiae			
subjects affected / exposed	1 / 12 (8.33%)	0 / 24 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Nightmare			
subjects affected / exposed	0 / 12 (0.00%)	2 / 24 (8.33%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 24 (4.17%)	1 / 35 (2.86%)
occurrences (all)	1	1	1
Spinal pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 24 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	1 / 12 (8.33%)	3 / 24 (12.50%)	2 / 35 (5.71%)
occurrences (all)	1	4	2
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	1 / 24 (4.17%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Borrelia infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 24 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 April 2017	Protocol Amendment 1: Change in dosing regimen from 60 mg twice daily (BID) to 60 mg thrice daily (TID), updates to Inclusion criteria 3 and 6 and Exclusion criteria 3, 9, 21 and 22, allowance for rescreening, and addition of suicidality stopping criteria plus some minor protocol clarifications and administrative changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported