



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

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 ($\geq 5\%$) non-serious adverse events (non-SAEs) and any serious adverse events (SAEs)

| | |
|-----------------|--|
| End point title | Part A: Number of participants with common ($\geq 5\%$) 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 ($\geq 5\%$) non serious AEs and SAEs

| | |
|-----------------|---|
| End point title | Part B: Number of participants with common ($\geq 5\%$) 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 [μ mol/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 μ mol/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 [$\mu\text{mol/L}$]); 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 $\mu\text{mol/L}$). 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.

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 $\geq 30\%$ 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 $\geq 30\%$ 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 occurrences (all) | 0 / 12 (0.00%) 0 | 2 / 24 (8.33%) 2 | 0 / 35 (0.00%) 0 |
| Abdominal pain subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 2 / 24 (8.33%) 2 | 1 / 35 (2.86%) 1 |
| Diarrhoea subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 24 (0.00%) 0 | 1 / 35 (2.86%) 1 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 24 (0.00%) 0 | 2 / 35 (5.71%) 2 |
| Respiratory, thoracic and mediastinal disorders Nasal ulcer subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 24 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 24 (0.00%) 0 | 2 / 35 (5.71%) 2 |
| Skin and subcutaneous tissue disorders Petechiae subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 24 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Psychiatric disorders Nightmare subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 2 / 24 (8.33%) 2 | 0 / 35 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 1 / 24 (4.17%) 1 | 1 / 35 (2.86%) 1 |
| Spinal pain subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 2 | 0 / 24 (0.00%) 0 | 0 / 35 (0.00%) 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