# Clinical trial results:
# A repeat-dose, open-label, parallel-group study to assess the pharmacokinetics of GSK1278863 and metabolites in subjects with End Stage Renal Disease undergoing peritoneal dialysis

## Summary

| | |
|---|---|
| EudraCT number | 2014-001197-34 |
| Trial protocol | GB |
| Global end of trial date | 10 May 2017 |

**Results information**

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 20 May 2018 |
| First version publication date | 20 May 2018 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 200942 |

**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, 1 866-435-7343, |
| Scientific contact | GSK Response Center, GlaxoSmithKline, 1 866-435-7343, |

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 21 March 2018 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 10 May 2017 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Characterize the steady-state pharmacokinetics (PK) of GSK1278863 and metabolites (GSK2391220 (M2), GSK2506104 (M3), GSK2487818 (M4), GSK2506102 (M5), GSK2531398 (M6), GSK2531401 (M13) in end-stage renal disease (ESRD) participants undergoing peritoneal dialysis

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 24 October 2014 |
| 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 | United States: 8 |
| Worldwide total number of subjects | 8 |
| EEA total number of subjects | 0 |

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) | 6 |
| From 65 to 84 years | 2 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

This repeat-dose, pharmacokinetic (PK) study of GSK1278863 was conducted at two centers in the United States (US). Participants with End Stage Renal Disease (ESRD) undergoing continuous ambulatory peritoneal dialysis (CAPD) or automated peritoneal dialysis (APD) were included in this study.

### Pre-assignment

Screening details:

A total of 20 participants with ESRD were screened; of which 12 were screen failures and 8 entered the study to receive 5 milligrams (mg) of GSK1278863 once daily for 14 days.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Participants undergoing CAPD |

Arm description:

Participants on CAPD received 1 tablet (5 mg) of GSK1278863 by oral route once daily with half glass of water for 14 days. On Day 1 and Day 14, the dose was administered within 30 minutes after completion of night CAPD treatment or morning last fill of peritoneal dialysis fluid; on any other study days, the dose was administered within 2 hours after completion of night CAPD treatment or morning last fill of peritoneal dialysis fluid.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | GSK1278863 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received 1 tablet (5 milligrams [mg]) of GSK1278863 by oral route once daily with half glass of water for 14 days.

| | |
|---|---|
| **Arm title** | Participants undergoing APD |

Arm description:

Participants on APD received 1 tablet (5 mg) of GSK1278863 by oral route once daily with half glass of water for 14 days. On Day 1 and Day 14, the dose was administered within 30 minutes after completion of night APD treatment or morning last fill of peritoneal dialysis fluid; on any other study days, the dose was administered within 2 hours after completion of night APD treatment or morning last fill of peritoneal dialysis fluid.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | GSK1278863 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received 1 tablet (5 milligrams [mg]) of GSK1278863 by oral route once daily with half glass of water for 14 days.

| **Number of subjects in period 1** | Participants undergoing CAPD | Participants undergoing APD |
|---|---|---|
| Started | 1 | 7 |
| Completed | 1 | 4 |
| Not completed | 0 | 3 |
| Other: Reached stopping criteria | - | 1 |
| Physician decision | - | 1 |
| Adverse event, non-fatal | - | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Participants undergoing CAPD |
| Reporting group description: | |
| Participants on CAPD received 1 tablet (5 mg) of GSK1278863 by oral route once daily with half glass of water for 14 days. On Day 1 and Day 14, the dose was administered within 30 minutes after completion of night CAPD treatment or morning last fill of peritoneal dialysis fluid; on any other study days, the dose was administered within 2 hours after completion of night CAPD treatment or morning last fill of peritoneal dialysis fluid. | |
| Reporting group title | Participants undergoing APD |
| Reporting group description: | |
| Participants on APD received 1 tablet (5 mg) of GSK1278863 by oral route once daily with half glass of water for 14 days. On Day 1 and Day 14, the dose was administered within 30 minutes after completion of night APD treatment or morning last fill of peritoneal dialysis fluid; on any other study days, the dose was administered within 2 hours after completion of night APD treatment or morning last fill of peritoneal dialysis fluid. | |

| Reporting group values | Participants undergoing CAPD | Participants undergoing APD | Total |
|---|---|---|---|
| Number of subjects | 1 | 7 | 8 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous | | | |
| Standard deviation could not be calculated for CAPD arm due to low number of participants | | | |
| Units: years | | | |
| arithmetic mean | 44.0 | 57.4 | |
| standard deviation | ± 99999 | ± 12.01 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 0 | 2 | 2 |
| Male | 1 | 5 | 6 |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| American Indian or Alaska Native Heritage | 0 | 1 | 1 |
| Black or African American Heritage | 0 | 3 | 3 |
| White- White/Caucasian/European Heritage | 1 | 3 | 4 |

## End points

### End points reporting groups

| Reporting group title | Participants undergoing CAPD |
|---|---|

Reporting group description:

Participants on CAPD received 1 tablet (5 mg) of GSK1278863 by oral route once daily with half glass of water for 14 days. On Day 1 and Day 14, the dose was administered within 30 minutes after completion of night CAPD treatment or morning last fill of peritoneal dialysis fluid; on any other study days, the dose was administered within 2 hours after completion of night CAPD treatment or morning last fill of peritoneal dialysis fluid.

| Reporting group title | Participants undergoing APD |
|---|---|

Reporting group description:

Participants on APD received 1 tablet (5 mg) of GSK1278863 by oral route once daily with half glass of water for 14 days. On Day 1 and Day 14, the dose was administered within 30 minutes after completion of night APD treatment or morning last fill of peritoneal dialysis fluid; on any other study days, the dose was administered within 2 hours after completion of night APD treatment or morning last fill of peritoneal dialysis fluid.

| Subject analysis set title | all participants |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants received 1 tablet (5 mg) of GSK1278863 by oral route once daily with half glass of water for 14 days.

### Primary: Area under the concentration-time curve (AUC) over the dosing interval (AUC[0-tau]) of GSK1278863 and its metabolites

| End point title | Area under the concentration-time curve (AUC) over the dosing interval (AUC[0-tau]) of GSK1278863 and its metabolites[1] |
|---|---|

End point description:

Serial blood samples were collected from participants at indicated time points for Pharmacokinetic (PK) analysis of GSK1278863 and its metabolites (GSK2391220, GSK2487818, GSK2506102, GSK2531398, GSK2531403 and GSK2531401). Geometric mean and geometric coefficient of variation has been presented for all metabolites. 99999 indicates data is not available. Geometric coefficient of variation could not be calculated for CAPD cohort due to small number of participants. PK Population comprised of participants in the 'All Subjects' Population for whom a PK sample was obtained and analyzed.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose and 0.5, 1, 2, 3, 4, 6, 8, 12, 16, 24 hours post-dose on Day 1; Pre-dose and 0.5, 1, 2, 3, 4, 6, 8, 12, 16, 24, 48, 72 hours post-dose on Day 14

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[2] | 7[3] | | |
| Units: Hour into nanograms per milliliter | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| GSK1278863; Day 1; n=1, 7 | 184.9863 (± 99999) | 138.6511 (± 93.5) | | |
| GSK1278863; Day 14; n=1, 4 | 162.9366 (± 99999) | 131.2826 (± 78.8) | | |
| GSK2391220; Day 1; n=1, 7 | 245.8999 (± 99999) | 147.8039 (± 47.7) | | |

| | | | | |
|---|---|---|---|---|
| GSK2391220; Day 14; n=1, 4 | 258.1199 (± 99999) | 162.0324 (± 50.7) | | |
| GSK2487818; Day 1; n=1, 7 | 116.2608 (± 99999) | 67.4130 (± 39.1) | | |
| GSK2487818; Day 14; n=1, 4 | 114.1857 (± 99999) | 59.6501 (± 51.5) | | |
| GSK2506102; Day 1; n=1,6 | 59.0619 (± 99999) | 44.8180 (± 37.8) | | |
| GSK2506102; Day 14; n=1, 4 | 82.9794 (± 99999) | 65.2188 (± 63.0) | | |
| GSK2531398; Day 1; n=1, 7 | 97.0339 (± 99999) | 63.0979 (± 45.5) | | |
| GSK2531398; Day 14; n=1, 4 | 97.6587 (± 99999) | 65.9664 (± 53.5) | | |
| GSK2531403; Day 1; n=1, 7 | 291.3067 (± 99999) | 170.4958 (± 45.5) | | |
| GSK2531403; Day 14; n=1, 4 | 360.2268 (± 99999) | 228.6081 (± 69.4) | | |
| GSK2531401; Day 1; n=1, 6 | 173.5919 (± 99999) | 104.2971 (± 48.6) | | |
| GSK2531401; Day 14; n=1, 4 | 242.0514 (± 99999) | 205.7281 (± 20.1) | | |

Notes:

[2] - PK Population

[3] - PK Population

## Statistical analyses

No statistical analyses for this end point

## Primary: AUC from time zero (pre-dose) extrapolated to infinite time (AUC [0-inf]) of GSK1278863 and its metabolites

| | |
|---|---|
| End point title | AUC from time zero (pre-dose) extrapolated to infinite time (AUC [0-inf]) of GSK1278863 and its metabolites[4] |

End point description:

Serial blood samples were collected from participants at indicated time points for PK analysis of GSK1278863 and its metabolites (GSK2487818 and GSK2531398). Geometric mean and geometric coefficient of variation has been presented for all metabolites. 99999 indicates data is not available. Geometric coefficient of variation could not be calculated for CAPD cohort due to small number of participants.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Pre-dose and 0.5, 1, 2, 3, 4, 6, 8, 12, 16, 24 hours post-dose on Day 1

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 are no statistical data to report.

| **End point values** | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[5] | 7[6] | | |
| Units: Hour into nanograms per milliliter | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| GSK1278863 | 184.9888 (± 99999) | 138.6860 (± 93.6) | | |

| | | | | |
|---|---|---|---|---|
| GSK2487818 | 117.2111 (± 99999) | 68.5089 (± 39.9) | | |
| GSK2531398 | 104.5268 (± 99999) | 73.9865 (± 51.3) | | |

Notes:

[5] - PK Population

[6] - PK Population

### Statistical analyses

No statistical analyses for this end point

## Primary: Maximum observed concentration (Cmax) of GSK1278863 and its metabolites

| End point title | Maximum observed concentration (Cmax) of GSK1278863 and its metabolites[7] |
|---|---|

End point description:

Serial blood samples were collected from participants at indicated time points for PK analysis of GSK1278863 and its metabolites (GSK2391220, GSK2487818, GSK2506102, GSK2531398, GSK2531403 and GSK2531401). Geometric mean and geometric coefficient of variation has been presented for all metabolites. 99999 indicates data is not available. Geometric coefficient of variation could not be calculated for CAPD cohort due to small number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose and 0.5, 1, 2, 3, 4, 6, 8, 12, 16, 24 hours post-dose on Day 1; Pre-dose and 0.5, 1, 2, 3, 4, 6, 8, 12, 16, 24, 48, 72 hours post-dose on Day 14

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

| **End point values** | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[8] | 7[9] | | |
| Units: Nanograms per milliliter | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| GSK1278863; Day 1; n= 1, 7 | 90.400 (± 99999) | 58.771 (± 96.7) | | |
| GSK1278863; Day 14; n= 1, 4 | 57.800 (± 99999) | 30.303 (± 104.4) | | |
| GSK2391220; Day 1; n= 1, 7 | 19.900 (± 99999) | 11.360 (± 44.3) | | |
| GSK2391220; Day 14; n= 1, 4 | 20.500 (± 99999) | 10.966 (± 33.1) | | |
| GSK2487818; Day 1; n= 1, 7 | 19.400 (± 99999) | 10.117 (± 25.7) | | |
| GSK2487818; Day 14; n= 1, 4 | 18.400 (± 99999) | 7.262 (± 40.4) | | |
| GSK2506102; Day 1; n= 1, 7 | 3.820 (± 99999) | 2.553 (± 42.7) | | |
| GSK2506102; Day 14; n= 1, 4 | 5.050 (± 99999) | 3.590 (± 46.5) | | |
| GSK2531398; Day 1; n= 1, 7 | 9.300 (± 99999) | 5.370 (± 44.2) | | |

| | | | | |
|---|---|---|---|---|
| GSK2531398; Day 14; n= 1, 4 | 9.220 (± 99999) | 4.857 (± 35.6) | | |
| GSK2531403; Day 1; n= 1, 7 | 18.600 (± 99999) | 11.186 (± 36.7) | | |
| GSK2531403; Day 14; n= 1, 4 | 23.400 (± 99999) | 13.267 (± 48.2) | | |
| GSK2531401; Day 1; n= 1, 7 | 9.920 (± 99999) | 4.715 (± 78.4) | | |
| GSK2531401; Day 14; n= 1, 4 | 13.300 (± 99999) | 10.404 (± 17.4) | | |

Notes:

[8] - PK Population

[9] - PK Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with non-serious adverse events (AEs) and serious AEs (SAEs)

| End point title | Number of participants with non-serious adverse events (AEs) and serious AEs (SAEs) |
|---|---|

End point description:

An AE is any untoward medical occurrence in a 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, is a congenital anomaly/birth defect, other situations, and is associated with liver injury and impaired liver function. Analysis was performed on All Subjects Population which comprised of all enrolled participants who received at least one dose of study treatment.

| End point type | Secondary |
|---|---|

End point timeframe:

Up to Day 24

| **End point values** | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[10] | 7[11] | | |
| Units: Participants | | | | |
| Non-serious AEs | 1 | 5 | | |
| SAEs | 0 | 0 | | |

Notes:

[10] - All subjects Population

[11] - All subjects Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in glucose, calcium, chloride, carbon-dioxide (CO2), potassium, sodium and urea levels

| End point title | Change from Baseline in glucose, calcium, chloride, carbon-dioxide (CO2), potassium, sodium and urea levels |
|---|---|

End point description:

Blood samples were collected from participants to evaluate clinical chemistry parameters including glucose, calcium, chloride, CO2, potassium, sodium and urea. Change from Baseline in clinical chemistry parameters at Day 17 are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. Mean and standard deviation are presented. 99999 indicates data is not available. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only participants with data available at the specified time point were analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and Day 17

| **End point values** | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[12] | 4[13] | | |
| Units: Millimoles per liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Glucose | -0.10 (± 99999) | 0.27 (± 7.191) | | |
| Calcium | 0.360 (± 99999) | 0.040 (± 0.2026) | | |
| Chloride | -2.0 (± 99999) | -1.3 (± 2.99) | | |
| CO2 | 0.0 (± 99999) | 0.3 (± 5.19) | | |
| Potassium | 0.20 (± 99999) | -0.45 (± 0.580) | | |
| Sodium | 2.0 (± 99999) | -1.5 (± 3.70) | | |
| Urea | 12.50 (± 99999) | -0.38 (± 3.568) | | |

Notes:

[12] - All subjects Population

[13] - All subjects Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in albumin and protein levels

| End point title | Change from Baseline in albumin and protein levels |
|---|---|

End point description:

Blood samples were collected from participants to evaluate clinical chemistry parameters including albumin and protein. Change from Baseline in clinical chemistry parameters at Day 17 are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. Mean and standard deviation are presented. 99999 indicates data is not available. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only participants with data available at the specified time point were analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and Day 17

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[14] | 4[15] | | |
| Units: Gram per liter (g/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Albumin | 3.0 (± 99999) | -1.3 (± 3.20) | | |
| Protein | 5.0 (± 99999) | -2.0 (± 5.48) | | |

Notes:

[14] - All subjects Population

[15] - All subjects Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in direct bilirubin, bilirubin, creatinine and urate levels

| End point title | Change from Baseline in direct bilirubin, bilirubin, creatinine and urate levels |
|---|---|

End point description:

Blood samples were collected from participants to evaluate clinical chemistry parameters including direct bilirubin, bilirubin, creatinine and urate. Change from Baseline in clinical chemistry parameters at Day 17 are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. Mean and standard deviation are presented. 99999 indicates data is not available. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only participants with data available at the specified time point were analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and Day 17

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[16] | 4[17] | | |
| Units: Micromoles per liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Direct bilirubin | 0.0 (± 99999) | -0.5 (± 1.91) | | |
| Bilirubin | -2.0 (± 99999) | 0.5 (± 1.00) | | |
| Creatinine | 13.30 (± 99999) | -119.12 (± 312.679) | | |
| Urate | -30.0 (± 99999) | -25.0 (± 87.37) | | |

Notes:

[16] - All Subjects Population

[17] - All Subjects Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in alkaline phosphatase (ALP), aspartate aminotransferase (AST) and gamma glutamyl aminotransferase (GGT) levels

| End point title | Change from Baseline in alkaline phosphatase (ALP), aspartate aminotransferase (AST) and gamma glutamyl aminotransferase (GGT) levels |
|---|---|

End point description:

Blood samples were collected from participants to evaluate clinical chemistry parameters including ALP, AST and GGT. Change from Baseline in clinical chemistry parameters at Day 17 are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. Mean and standard deviation are presented. 99999 indicates data is not available. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only participants with data available at the specified time point were analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and Day 17

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[18] | 4[19] | | |
| Units: International unit per liter (IU/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| ALP | 5.0 (± 99999) | -0.5 (± 16.52) | | |
| AST | -1.0 (± 99999) | -3.3 (± 3.77) | | |
| GGT | 0.0 (± 99999) | -6.3 (± 8.77) | | |

Notes:

[18] - All Subjects Population

[19] - All Subjects Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in alanine aminotransferase (ALT) and creatinine kinase levels

| End point title | Change from Baseline in alanine aminotransferase (ALT) and creatinine kinase levels |
|---|---|

End point description:

Blood samples were collected from participants to evaluate clinical chemistry parameters including ALT and creatinine kinase. Change from Baseline in clinical chemistry parameters at Day 3, Day 7, Day 11, Day 14 and Day 17 are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. Mean and standard deviation are presented. 99999 indicates data is not available. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and Day 3, 7, 11, 14, 17

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[20] | 7[21] | | |
| Units: IU/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| ALT; Day 3; n= 1, 6 | -3.0 (± 99999) | -0.7 (± 3.98) | | |
| ALT; Day 7; n= 1, 4 | -7.0 (± 99999) | -2.5 (± 5.32) | | |
| ALT; Day 11; 1, 4 | -9.0 (± 99999) | -3.5 (± 5.80) | | |
| ALT; Day 14; n= 1, 4 | -7.0 (± 99999) | -0.8 (± 3.86) | | |
| ALT; Day 17; n= 1, 4 | -7.0 (± 99999) | -1.0 (± 6.06) | | |
| Creatine kinase; Day 3; n= 1, 6 | -12.0 (± 99999) | -99.7 (± 161.17) | | |
| Creatine kinase; Day 7; n= 1, 4 | -12.0 (± 99999) | -137.8 (± 230.33) | | |
| Creatine kinase; Day 11; n= 1, 4 | 1.0 (± 99999) | -135.8 (± 273.85) | | |
| Creatine kinase; Day 14; n= 1, 4 | 9.0 (± 99999) | -183.5 (± 247.13) | | |
| Creatine kinase; Day 17; n= 1, 4 | -2.0 (± 99999) | -201.5 (± 191.83) | | |

Notes:

[20] - All Subjects Population

[21] - All Subjects Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, neutrophils, platelets and leukocytes levels

| End point title | Change from Baseline in basophils, eosinophils, lymphocytes, monocytes, neutrophils, platelets and leukocytes levels |
|---|---|

End point description:

Blood samples were collected from participants to evaluate clinical hematology parameters including basophils, eosinophils, lymphocytes, monocytes, neutrophils, platelets and leukocytes. Change from Baseline in clinical hematology parameters at Day 17 are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. 99999 indicates data is not available. Mean and standard deviation are presented. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only participants with data available at the specified time point were analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and Day 17

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[22] | 4[23] | | |
| Units: 10^9 cells/liter | | | | |
| arithmetic mean (standard deviation) | | | | |

| | | | | |
|---|---|---|---|---|
| Basophils | -0.020 (± 99999) | 0.010 (± 0.0200) | | |
| Eosinophils | -0.010 (± 99999) | 0.060 (± 0.0804) | | |
| Lymphocytes | 0.260 (± 99999) | -0.138 (± 0.3974) | | |
| Monocytes | 0.230 (± 99999) | 0.060 (± 0.3389) | | |
| Neutrophils | 1.350 (± 99999) | -0.365 (± 1.1957) | | |
| Platelets | 42.0 (± 99999) | -21.0 (± 35.92) | | |
| Leukocytes | 1.80 (± 99999) | -0.35 (± 1.008) | | |

Notes:

[22] - All Subjects Population

[23] - All Subjects Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in erythrocyte and reticulocyte levels

| End point title | Change from Baseline in erythrocyte and reticulocyte levels |
|---|---|

End point description:

Blood samples were collected from participants to evaluate clinical hematology parameters including erythrocyte and reticulocyte. Change from Baseline in clinical hematology parameters at Day 17 are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. 99999 indicates data is not available. Mean and standard deviation are presented. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only participants with data available at the specified time point were analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and Day 17

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[24] | 4[25] | | |
| Units: 10^12 cells/liter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Erythrocytes | 0.00 (± 99999) | -0.05 (± 0.412) | | |
| Reticulocytes | 0.02840 (± 99999) | -0.00165 (± 0.044431) | | |

Notes:

[24] - All Subjects Population

[25] - All Subjects Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in hematocrit levels

| End point title | Change from Baseline in hematocrit levels |
|---|---|

End point description:

Blood samples were collected from participants to evaluate clinical hematology parameters including hematocrit. Change from Baseline in clinical hematology parameters at Day 17 are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. Mean and standard deviation are presented. 99999 indicates data is not available. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only participants with data available at the specified time point were analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and Day 17

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[26] | 4[27] | | |
| Units: Proportion of red blood cells in blood | | | | |
| arithmetic mean (standard deviation) | | | | |
| Proportion of red blood cells in blood | 0.0070 (± 99999) | -0.0100 (± 0.03880) | | |

Notes:

[26] - All Subjects Population

[27] - All Subjects Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in hemoglobin levels

| End point title | Change from Baseline in hemoglobin levels |
|---|---|

End point description:

Blood samples were collected from participants to evaluate clinical hematology parameters including hemoglobin. Change from Baseline in clinical hematology parameters at Day 3, Day 7, Day 11 and Day 17 are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. Mean and standard deviation are presented. 99999 indicates data is not available. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and Day 3, 7, 11, 17

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[28] | 7[29] | | |
| Units: g/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 3; n= 1, 7 | 7.0 (± 99999) | 3.1 (± 11.96) | | |
| Day 7; n= 1, 5 | 4.0 (± 99999) | -2.2 (± 9.78) | | |
| Day 11; n= 1, 5 | 0.0 (± 99999) | -3.2 (± 8.14) | | |
| Day 17; n= 1, 4 | 5.0 (± 99999) | -1.3 (± 13.74) | | |

Notes:

[28] - All Subjects Population

[29] - All Subjects Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in mean corpuscular hemoglobin concentration (MCHC)

| End point title | Change from Baseline in mean corpuscular hemoglobin concentration (MCHC) |
|---|---|

End point description:

Blood samples were collected from participants to evaluate clinical hematology parameters including MCHC. Change from Baseline in clinical hematology parameters at Day 17 are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. Mean and standard deviation are presented. 99999 indicates data is not available. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only participants with data available at the specified time point were analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and Day 17

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[30] | 4[31] | | |
| Units: g/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| g/L | 8.0 (± 99999) | 6.3 (± 3.86) | | |

Notes:

[30] - All Subjects Population.

[31] - All Subjects Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in mean corpuscular volume (MCV)

| End point title | Change from Baseline in mean corpuscular volume (MCV) |
|---|---|

End point description:

Blood samples were collected from participants to evaluate clinical hematology parameters including MCV. Change from Baseline in clinical hematology parameters at Day 17 are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. Mean and standard deviation are presented. 99999 indicates data is not available. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only participants with data available at the specified time point were analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and Day 17

| **End point values** | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[32] | 4[33] | | |
| Units: Femtoliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Femtoliter | 1.0 (± 99999) | -1.5 (± 1.73) | | |

Notes:

[32] - All Subjects Population.

[33] - All Subjects Population.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in mean corpuscular hemoglobin (MCH) levels

| End point title | Change from Baseline in mean corpuscular hemoglobin (MCH) levels |
|---|---|

End point description:

Blood samples were collected from participants to evaluate clinical hematology parameters including MCH. Change from Baseline in clinical hematology parameters at Day 17 are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. Mean and standard deviation are presented. 99999 indicates data is not available. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only participants with data available at the specified time point were analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline and Day 17

| **End point values** | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[34] | 4[35] | | |
| Units: Picograms | | | | |
| arithmetic mean (standard deviation) | | | | |
| Picograms | 1.00 (± 99999) | -0.02 (± 0.866) | | |

Notes:

[34] - All Subjects Population

[35] - All Subjects Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with abnormal electrocardiogram (ECG) findings

| End point title | Number of participants with abnormal electrocardiogram (ECG) findings |
|---|---|

End point description:

Single measurements of 12-lead ECG were obtained in supine position after at least 10 minutes of rest using an ECG machine that automatically calculates the heart rate and measures PR, QRS, QT and corrected QT (QTc) interval. Participants with abnormal ECG findings at worst-case observation Carried Forward for triplicate measurements (WOCF) post-Baseline visit are presented. Only participants with data available at WOCF visit were analyzed.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 17

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[36] | 5[37] | | |
| Units: Participants | | | | |
| Participants | 0 | 3 | | |

Notes:

[36] - All Subjects Population

[37] - All Subjects Population

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Vital sign measurements including SBP and DBP were taken in a supine position after at least 5 minutes of rest. Change from Baseline in SBP and DBP at Day 17 and Day 24 (follow-up) are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. Mean and standard deviation are presented. 99999 indicates data is not available. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Day 17 and Day 24

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[38] | 7[39] | | |
| Units: Millimeters of mercury | | | | |
| arithmetic mean (standard deviation) | | | | |
| SBP; Day 17; n= 1, 5 | 12.0 (± 99999) | -10.4 (± 10.06) | | |
| SBP; follow-up; n= 1, 7 | 24.0 (± 99999) | -10.0 (± 12.46) | | |
| DBP; Day 17; n= 1, 5 | 10.0 (± 99999) | -3.4 (± 13.07) | | |
| DBP; follow-up; n= 1, 7 | -4.0 (± 99999) | 0.1 (± 12.52) | | |

Notes:

[38] - All Subjects Population

[39] - All Subjects Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in pulse rate

| End point title | Change from Baseline in pulse rate |
|---|---|

End point description:

Vital sign measurements including pulse rate were taken in a supine position after at least 5 minutes of rest. Change from Baseline in pulse rate at Day 17 and Day 24 (follow-up) are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. Mean and standard deviation are presented. 99999 indicates data is not available. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Day 17 and Day 24

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[40] | 7[41] | | |
| Units: Beats per minute | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 17; n= 1, 5 | -9.0 (± 99999) | -5.6 (± 9.53) | | |
| Follow-up; n= 1, 7 | -6.0 (± 99999) | -7.0 (± 11.58) | | |

Notes:

[40] - All Subjects Population

[41] - All Subjects Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in body temperature

| End point title | Change from Baseline in body temperature |
|---|---|

End point description:

Vital sign measurements including body temperature were taken in a supine position after at least 5 minutes of rest. Change from Baseline in body temperature at Day 17 and Day 24 (follow-up) are presented. Day-1 was considered as Baseline value. Change from Baseline was calculated as post-randomization values minus Baseline value. Mean and standard deviation are presented. 99999 indicates data is not available. Standard deviation could not be calculated for CAPD cohort due to small number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Day 17 and Day 24

| **End point values** | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[42] | 7[43] | | |
| Units: Degree celsius | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 17; n= 1, 5 | -0.10 (± 99999) | -0.20 (± 0.648) | | |
| Follow-up; n= 1, 7 | -0.90 (± 99999) | -0.30 (± 0.548) | | |

Notes:

[42] - All Subjects Population

[43] - All Subjects Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with abnormal physical examination findings

| End point title | Number of participants with abnormal physical examination findings |
|---|---|

End point description:

A complete physical examination was planned to include assessments of the head, eyes, ears, nose, throat, skin, thyroid, neurological, lungs, cardiovascular, abdomen (liver and spleen), lymph nodes and extremities. This analysis was planned but not performed. Any significant finding was captured as an AE.

| End point type | Secondary |
|---|---|

End point timeframe:

Up to Day 17

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[44] | 0[45] | | |
| Units: Participants | | | | |
| Participants | | | | |

Notes:

[44] - The analysis was planned but not performed.

[45] - The analysis was planned but not performed.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Peritoneal Dialysis Clearance of GSK1278863 and metabolites

| End point title | Peritoneal Dialysis Clearance of GSK1278863 and metabolites |
|---|---|

End point description:

Peritoneal dialysate samples for PK analysis of GSK1278863 and metabolites (GSK2391220, GSK2487818, GSK2506102, GSK2531398, GSK2531403 and GSK2531401) were collected. Peritoneal dialysis clearance of GSK1278863 and metabolites was calculated from Day 14 dialysate excretion data as total amount of analyte excreted over 24 hours divided by plasma AUC(0-tau). Geometric mean and geometric coefficient of variation are presented. 99999 indicates data is not available. Geometric coefficient of variation could not be calculated due to small number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

| End point type | Secondary |
|---|---|

End point timeframe:

Day 14

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[46] | 7[47] | | |
| Units: Milliliter per hour | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| GSK1278863; n= 1, 0 | 12.07 (± 99999) | 99999 (± 99999) | | |
| GSK2391220; n= 1, 4 | 154.68 (± 99999) | 31.68 (± 165.5) | | |
| GSK2487818; n= 1, 3 | 124.40 (± 99999) | 13.08 (± 195.3) | | |
| GSK2506102; n= 1, 4 | 167.89 (± 99999) | 40.05 (± 169.7) | | |
| GSK2531398; n= 1, 4 | 151.29 (± 99999) | 28.39 (± 177.5) | | |
| GSK2531403; n= 1, 4 | 155.75 (± 99999) | 36.18 (± 183.2) | | |
| GSK2531401; n= 1, 4 | 201.80 (± 99999) | 48.89 (± 199.7) | | |

Notes:
[46] - PK Population
[47] - PK Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Terminal phase half-life (t 1/2) of GSK1278863 and Metabolites

| End point title | Terminal phase half-life (t 1/2) of GSK1278863 and Metabolites |
|---|---|

End point description:

Serial blood samples were collected from participants at indicated time points for PK analysis of GSK1278863 and its metabolites (GSK2391220, GSK2487818, GSK2506102, GSK2531398, GSK2531403, GSK2531401). Geometric mean and geometric coefficient of variation have been presented for all metabolites. Geometric coefficient of variation could not be calculated for CAPD cohort due to small number of participants, which is indicated by 99999. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

| End point type | Secondary |
|---|---|

End point timeframe:

Pre-dose and 0.5, 1, 2, 3, 4, 6, 8, 12, 16, 24 hours post-dose on Day 1; Pre-dose and 0.5, 1, 2, 3, 4, 6, 8, 12, 16, 24, 48, 72 hours post-dose on Day 14

| **End point values** | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[48] | 7[49] | | |
| Units: Hours | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| GSK1278863; Day 1; n= 1, 7 | 1.6256 (± 99999) | 1.9870 (± 25.8) | | |
| GSK1278863; Day 14; n= 1, 4 | 1.8088 (± 99999) | 2.5312 (± 35.7) | | |
| GSK2391220; Day 14; n= 1, 4 | 9.2225 (± 99999) | 10.2882 (± 27.2) | | |
| GSK2487818; Day 1; n=1, 7 | 3.6560 (± 99999) | 3.3612 (± 22.7) | | |
| GSK2487818; Day 14; n= 1, 4 | 2.9958 (± 99999) | 3.8955 (± 25.3) | | |
| GSK2506102; Day 14; n= 1,4 | 16.2000 (± 99999) | 17.7692 (± 65.4) | | |
| GSK2531398; Day 1; n=1, 7 | 5.7900 (± 99999) | 7.0659 (± 35.9) | | |
| GSK2531398; Day 14; n= 1, 4 | 5.8275 (± 99999) | 7.3088 (± 40.0) | | |
| GSK2531403; Day 14; n= 1, 4 | 13.0606 (± 99999) | 14.5877 (± 43.5) | | |
| GSK2531401; Day 14; n= 1, 4 | 20.7794 (± 99999) | 26.9981 (± 54.2) | | |

Notes:

[48] - PK Population

[49] - PK Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time of occurrence of Cmax (Tmax) of GSK1278863 and Metabolites

| End point title | Time of occurrence of Cmax (Tmax) of GSK1278863 and Metabolites |
|---|---|

End point description:

Serial blood samples were collected from participants at indicated time points for PK analysis of GSK1278863 and its metabolites (GSK2391220, GSK2487818, GSK2506102, GSK2531398, GSK2531403 and GSK2531401). Median and full range have been presented for all metabolites. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

| End point type | Secondary |
|---|---|

End point timeframe:

Pre-dose and 0.5, 1, 2, 3, 4, 6, 8, 12, 16, 24 hours post-dose on Day 1; Pre-dose and 0.5, 1, 2, 3, 4, 6, 8, 12, 16, 24, 48, 72 hours post-dose on Day 14

| **End point values** | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[50] | 7[51] | | |
| Units: Hour | | | | |
| median (full range (min-max)) | | | | |
| GSK1278863; Day 1; n=1, 7 | 0.50 (0.5 to 0.5) | 1.00 (1.0 to 3.0) | | |
| GSK1278863; Day 14; n= 1, 4 | 2.00 (2.0 to 2.0) | 2.00 (1.0 to 4.0) | | |
| GSK2391220; Day 1; n= 1, 7 | 3.00 (3.0 to 3.0) | 4.00 (3.0 to 8.0) | | |
| GSK2391220; Day 14; n= 1, 4 | 4.00 (4.0 to 4.0) | 5.00 (4.0 to 6.0) | | |
| GSK2487818; Day 1; n= 1, 7 | 3.00 (3.0 to 3.0) | 4.00 (2.0 to 6.0) | | |
| GSK2487818; Day 14; n= 1, 4 | 3.00 (3.0 to 3.0) | 4.00 (3.0 to 4.0) | | |
| GSK2506102; Day 1; n=1, 7 | 4.00 (4.0 to 4.0) | 8.00 (3.0 to 12.0) | | |
| GSK2506102; Day 14; n= 1, 4 | 4.00 (4.0 to 4.0) | 5.00 (4.0 to 6.0) | | |
| GSK2531398; Day 1; n= 1,7 | 4.00 (4.0 to 4.0) | 4.00 (3.0 to 8.0) | | |
| GSK2531398; Day 14; n= 1, 4 | 4.00 (4.0 to 4.0) | 5.00 (4.0 to 6.0) | | |
| GSK2531403; Day 1; n= 1, 7 | 6.00 (6.0 to 6.0) | 6.00 (2.0 to 8.0) | | |
| GSK2531403; Day 14; n= 1, 4 | 4.00 (4.0 to 4.0) | 6.00 (4.0 to 6.0) | | |

| | | | | |
|---|---|---|---|---|
| GSK2531401; Day 1; n= 1, 7 | 8.00 (8.0 to 8.0) | 8.00 (3.0 to 12.0) | | |
| GSK2531401; Day 14; n= 1, 4 | 8.00 (8.0 to 8.0) | 9.00 (6.0 to 12.0) | | |

Notes:

[50] - PK Population

[51] - PK Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Accumulation ratio of GSK1278863 and Metabolites

| End point title | Accumulation ratio of GSK1278863 and Metabolites |
|---|---|

End point description:

The observed accumulation ratio was determined to estimate the extent of accumulation for GSK1278863 and metabolites (GSK2391220, GSK2487818, GSK2506102, GSK2531398, GSK2531403 and GSK2531401) after repeat dosing. Accumulation ratio was calculated by using AUC (0-tau) values at Day 1 and Day 14. Analysis was performed using mixed effect model fitted with day (single and repeat dose) as fixed effect and participant as random effect. Mean ratio and 90% confidence intervals have been presented.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 and Day 14

| **End point values** | all participants | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 8[52] | | | |
| Units: Ratio | | | | |
| arithmetic mean (confidence interval 90%) | | | | |
| GSK1278863 | 0.896 (0.645 to 1.244) | | | |
| GSK2391220 | 1.176 (1.043 to 1.326) | | | |
| GSK2487818 | 1.019 (0.944 to 1.100) | | | |
| GSK2506102 | 1.581 (1.200 to 2.081) | | | |
| GSK2531398 | 1.116 (1.015 to 1.228) | | | |
| GSK2531403 | 1.415 (1.131 to 1.771) | | | |
| GSK2531401 | 1.948 (1.301 to 2.918) | | | |

Notes:

[52] - PK Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time invariance ratio of GSK1278863 and Metabolites

| End point title | Time invariance ratio of GSK1278863 and Metabolites |
|---|---|

End point description:

Time invariance ratio for GSK1278863 and metabolites (GSK2391220, GSK2487818, GSK2506102, GSK2531398, GSK2531403 and GSK2531401) was calculated by analyzing AUC (0-inf) at Day 1 and AUC (0-tau) at Day 14. Analysis was performed using mixed effect model fitted with day (single and repeat dose) as fixed effect and participant as random effect. Mean ratio and 90% confidence intervals have been presented. 99999 indicates data is not available. Data could not be calculated due to insufficient data.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 and Day 14

| **End point values** | all participants | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 8[53] | | | |
| Units: Ratio | | | | |
| arithmetic mean (confidence interval 90%) | | | | |
| GSK1278863; n= 8 | 0.896 (0.645 to 1.244) | | | |
| GSK2391220; n= 0 | 99999 (99999 to 99999) | | | |
| GSK2487818; n= 8 | 1.007 (0.932 to 1.087) | | | |
| GSK2506102; n= 0 | 99999 (99999 to 99999) | | | |
| GSK2531398; n= 8 | 0.986 (0.941 to 1.033) | | | |
| GSK2531403; n= 0 | 99999 (99999 to 99999) | | | |
| GSK2531401; n= 0 | 99999 (99999 to 99999) | | | |

Notes:

[53] - PK Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma concentration of erythropoietin

| End point title | Plasma concentration of erythropoietin |
|---|---|

End point description:

Serial blood samples were collected from participants at indicated time points to analyze plasma concentration of erythropoietin after repeat-dose administration of GSK1278863. Geometric mean and geometric coefficient of variation have been presented. 99999 indicates data is not available. Geometric coefficient of variation could not be calculated for CAPD cohort due to small number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

| End point type | Secondary |
|---|---|

End point timeframe:

Pre-dose and 4, 8 ,12, 24 hours post-dose on Day 1 and Day 14; Pre-dose on Day 3, 7, 11

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[54] | 7[55] | | |
| Units: IU/L | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 1; pre-dose; n= 1, 7 | 13.860 (± 99999) | 11.363 (± 124.9) | | |
| Day 1; 4 hours; n= 1, 7 | 11.590 (± 99999) | 14.494 (± 127.1) | | |
| Day 1; 8 hours; n= 1, 7 | 23.540 (± 99999) | 36.257 (± 96.0) | | |
| Day 1; 12 hours; n= 1, 7 | 32.210 (± 99999) | 32.629 (± 112.4) | | |
| Day 1; 24 hours; n= 1, 7 | 13.570 (± 99999) | 13.005 (± 127.5) | | |
| Day 3; pre-dose; n= 1, 6 | 10.030 (± 99999) | 15.452 (± 152.9) | | |
| Day 7; pre-dose; n= 1, 3 | 5.070 (± 99999) | 8.023 (± 66.4) | | |
| Day 11; pre-dose; n= 1, 3 | 8.690 (± 99999) | 9.466 (± 69.8) | | |
| Day 14; pre-dose; n= 1, 4 | 9.490 (± 99999) | 6.036 (± 71.2) | | |
| Day 14; 4 hours; n= 1, 3 | 12.660 (± 99999) | 7.674 (± 34.9) | | |
| Day 14; 8 hours; n= 1, 4 | 30.220 (± 99999) | 19.313 (± 81.6) | | |
| Day 14; 12 hours; n= 1, 4 | 21.050 (± 99999) | 25.745 (± 74.6) | | |
| Day 14; 24 hours; n= 1, 4 | 6.590 (± 99999) | 6.735 (± 88.1) | | |

Notes:

[54] - All Subjects Population

[55] - All Subjects Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma concentration of hepcidin

| End point title | Plasma concentration of hepcidin |
|---|---|

End point description:

Serial blood samples were collected from participants at indicated time points to analyze plasma concentration of hepcidin after repeat-dose administration of GSK1278863. Geometric mean and geometric coefficient of variation have been presented. 99999 indicates data is not available. Geometric coefficient of variation could not be calculated for CAPD cohort due to small number of participants. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

| End point type | Secondary |
|---|---|

End point timeframe:

Pre-dose and 4, 8 ,12, 24 hours post-dose on Day 1 and Day 14; Pre-dose on Day 3, 7, 11

| End point values | Participants undergoing CAPD | Participants undergoing APD | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1[56] | 7[57] | | |
| Units: Micrograms per liter | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Day 1; pre-dose; n= 1, 7 | 1143.00 (± 99999) | 863.21 (± 100.3) | | |
| Day 1; 4 hours; n= 1, 7 | 1286.00 (± 99999) | 922.86 (± 108.3) | | |
| Day 1; 8 hours; n= 1, 7 | 1427.10 (± 99999) | 760.14 (± 80.1) | | |
| Day 1; 12 hours; n= 1, 7 | 1318.00 (± 99999) | 812.62 (± 86.1) | | |
| Day 1; 24 hours; n= 1, 7 | 867.20 (± 99999) | 802.06 (± 93.5) | | |
| Day 3; pre-dose; n= 1, 6 | 1021.70 (± 99999) | 819.17 (± 90.7) | | |
| Day 7; pre-dose; n= 1, 4 | 825.30 (± 99999) | 839.42 (± 81.5) | | |
| Day 11; pre-dose; n= 1, 4 | 852.90 (± 99999) | 800.77 (± 91.3) | | |
| Day 14; pre-dose; n= 1, 4 | 734.30 (± 99999) | 768.33 (± 86.8) | | |
| Day 14; 4 hours; n= 1, 4 | 847.90 (± 99999) | 782.59 (± 81.9) | | |
| Day 14; 8 hours; n= 1, 4 | 809.90 (± 99999) | 738.96 (± 79.2) | | |
| Day 14; 12 hours; n= 1, 4 | 705.70 (± 99999) | 757.72 (± 87.9) | | |
| Day 14; 24 hours; n= 1, 4 | 801.30 (± 99999) | 733.66 (± 81.9) | | |

Notes:

[56] - All Subjects Population

[57] - All Subjects Population

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| SAEs and non-SAEs are presented from the start of study treatment up to Day 24 | |
| Adverse event reporting additional description: | |
| SAEs and non-serious AEs are reported for members of the All Subjects Population | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 20.1 |

| Reporting groups | |
|---|---|
| Reporting group title | Participants undergoing CAPD |
| Reporting group description: | |
| Participants on CAPD received 1 tablet (5 mg) of GSK1278863 by oral route once daily with half glass of water for 14 days. On Day 1 and Day14, the dose was administered within 30 minutes after completion of night CAPD treatment or morning last fill of peritoneal dialysis fluid; on any other study days, the dose was administered within 2 hours after completion of night CAPD treatment or morning last fill of peritoneal dialysis fluid. | |
| Reporting group title | Participants undergoing APD |
| Reporting group description: | |
| Participants on APD received 1 tablet (5 mg) of GSK1278863 by oral route once daily with half glass of water for 14 days. On Day 1 and Day14, the dose was administered within 30 minutes after completion of night APD treatment or morning last fill of peritoneal dialysis fluid; on any other study days, the dose was administered within 2 hours after completion of night APD treatment or morning last fill of peritoneal dialysis fluid. | |

| Serious adverse events | Participants undergoing CAPD | Participants undergoing APD | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 7 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | Participants undergoing CAPD | Participants undergoing APD | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 1 (100.00%) | 5 / 7 (71.43%) | |
| Injury, poisoning and procedural complications | | | |
| Muscle strain | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 7 (14.29%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|---|---|---|
| General disorders and administration site conditions | | | |
| Face oedema | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 7 (14.29%) | |
| occurrences (all) | 0 | 1 | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 7 (14.29%) | |
| occurrences (all) | 0 | 1 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 7 (14.29%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 1 (100.00%) | 1 / 7 (14.29%) | |
| occurrences (all) | 1 | 1 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 7 (14.29%) | |
| occurrences (all) | 0 | 1 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 7 (14.29%) | |
| occurrences (all) | 0 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 7 (14.29%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 1 (100.00%) | 1 / 7 (14.29%) | |
| occurrences (all) | 1 | 1 | |
| Neck pain | | | |
| subjects affected / exposed | 1 / 1 (100.00%) | 0 / 7 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 7 (14.29%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|---|---|---|
| Hypoglycaemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0 | 2 / 7 (28.57%)<br>2 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 06 June 2014 | Amendment 1: Section 4.2.1. Inclusion Criteria, Inclusion number 8; hemoglobin levels are updated based on the feedback received from food and drug administration (FDA). It was <=11 grams per deciliter (g/dL) for Erythropoiesis stimulating agent (ESA) naïve participants, it is updated as <10.0 g/dL; it was <=12.0 g/dL for participants receiving ongoing ESA treatment, it is updated as <=11.0 g/dL.<br>Section 4.2.2. Exclusion Criteria, the numbering of exclusion criteria was inadvertently incremented from previous section. The numbering now starts from "1".<br>Section 5.3.3. Stopping Criteria, the stopping criteria related to the hemoglobin level is updated per the FDA's feedback received. A previous criterion required participants to have their absolute hemoglobin level >=13.0 g/dL to stop the dosing. The hemoglobin level for stopping the dosing is now updated as >11.0 grams per liter (g/L).<br>Section 6.1. Time and Events Table, Protocol Activity "Urine Drug and Alcohol Screen" is updated as "Drug and Alcohol Screen" with a new footnote "m". Majority of participants with ESRD undergoing peritoneal dialysis will not be able to produce urine samples. For these participants this screening test will be serum-based.<br>Section 6.3.2. Vital Signs; body temperature measurement was not included under vital signs assessment. It is now included as a part of vital signs assessment since it is a measurement performed as a standard practice at the site. Section 6.3.3. Electrocardiogram (ECG), instruction for Day -1 ECG measurement is updated as it indicated that ECG measurement should be done 2 hours prior to dosing. The first dosing day is Day 1, and there will be no ECG measurement on the dosing day. This is now corrected. |
| 24 June 2014 | Amendment 2: Section 6.1. Time and Events Table, Footnote m is revised to make the Drug and Alcohol test type flexible. At screening and on Day -1, this test would have been performed urine based or alternatively serum based. However, it was recognized that each site has their standard tests for this assessment. At the discretion of the investigator, sites will be able to use their standard test in order to ensure that the test results will be ready for an evaluation prior the dosing. Test will also be performed on Day 13.<br>Section 6.1. Time and Events Table, a new footnote, footnote n, is included to clarify how hemoglobin can be assessed on Day 3, Day 7, and Day 11 visits. |
| 01 July 2014 | Amendment 3: Section 4.2.2., Inclusion and Exclusion Criteria, the numbering of each criterion was inadvertently changed starting from subtitles "Efficacy" and "Other". After subtitle "Safety", the numbering was not consecutively increasing for the remaining inclusion and exclusion criteria. The inclusion and exclusion criteria numbers were changed to be consecutive. Inclusion criteria numbers now starts from 1 and goes up to 12, exclusion criteria numbers start from 1 and goes up to 28.<br>Section 4.3.3. Caffeine, Alcohol, and Tobacco, the word "sample" was missing after the word "the final pharmacokinetic" in the last part of the first sentence, this is now included. |

| | |
|---|---|
| 12 December 2014 | Amendment 4: List of Abbreviations, the abbreviation for kilocalorie, kcal, is listed as it is now included in the text.<br>The EudraCT number is now updated as "2014-001197-34" with this amendment which is the correct number for this specific protocol.<br>Section 4.2.1 Inclusion criteria number 5, the urine output and Kt/V values were revised for participant's eligibility.<br>Section 4.2.1. Inclusion number 8; hemoglobin levels are updated to meet with country specific requirements. For united Kingdom (UK) only site(s), hemoglobin value is updated as <=11 g/dL for ESA naïve participants and as <=12.0 g/dL for participants receiving ongoing ESA treatment.<br>Section 5.3.3. the stopping criteria related to the hemoglobin level is updated to meet with country specific requirements. For UK only site(s), stopping criteria for absolute hemoglobin level now is >= 12.0 g/dL to stop the dosing.<br>Section 4.2.2. Exclusion criteria number 15; it was revised to be flexible for those participants who have not received their ophthalmology exam within 12 months prior to Screening.<br>Section 4.3.2 Meals and Dietary Restrictions; it was stated that participants would not consume any food and drinks (except water) during 4 hour fasting period after dosing on Day 1 and Day 14. Based on the initial feedback from one of study sites, some participants on peritoneal dialysis are very hungry after they finish night portion therapy on peritoneal dialysis cycler. Thus this section was revised to allow participants to have a light snack and a beverage which would not exceed 500 kcal during this 4 hours fasting period after dosing.<br>Section 6.4.2. Dialysate Sample Collection, on Day 1 and Day 14, the volume of dialysate solution to be collected for analysis was specified as 10 milliliter (mL) aliquot. This is revised to 1.5 mL.<br>Section 6.1, Time and Events Table, there was a typo error on the Day of Follow-up visit. It was entered as Day 23. This is now corrected as Day 22. |
| 15 December 2014 | Amendment 4 (republishing): The abbreviation "PD" included in Revision Chronology in 2013N179529_04 was required to change to "peritoneal dialysis" as "PD" in this protocol refers to "Pharmacodynamic". The abbreviation "PD" in this section could have been misinterpreted if it was left as is. Thus, Amendment No. 4 was republished with this update in order to prevent any confusions. |
| 10 September 2015 | Amendment 5: This protocol amendment is to clarify several sections of protocol text and to confirm that there will be informal reviews of the available PK data to assist Phase III development of the compound. Additionally, if during the informal review of the available PK data it is determined that there are no clinically-significant differences in PK between the CAPD and APD populations, the planned number of participants may be reduced. All changes are detailed in Appendix 5. In order to ensure transparent reporting of screen failure participants to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements, and respond to queries from Regulatory authorities, a minimal set of screen failure information is required including Demography, Screen Failure details, Eligibility Criteria, and any Serious Adverse Events. Section 4.4 has subsequently been updated to document that screen failure information is being collected. The analysis populations (Section 9.3.1) have also been expanded to clarify the screen failure population. Wording in Section 4.3.2 has been amended to clarify the duration for which participants need to avoid consumption of red wine, grapefruit (juice), blood orange (juice), star fruit, onions, kale, broccoli, green beans, or apples, specifically are all prohibited from 7 days prior to the first dose of GSK1278863 until the Follow-Up visit, unless in the opinion of the investigator and GlaxoSmithKline (GSK) Medical Monitor this will not interfere with the study procedures and compromise participant safety Wording in Section 5.10 has been amended to ensure the text is current regarding use of concomitant medications. The following protocol sections were updated accordingly: Section 4.1, Section 4.3.2, Section 5.10, Section 9.3.1, Section 9.3.2. Section 11, Appendix 5. |
| 20 June 2016 | Amendment 6: This protocol amendment is to reduce the number of participants in the study (either cohort) to a total of 8 completed participants. This study has been active for 2 years and only 6 (1 CAPD and 5 APD) participants have completed the study. Given the recruitment challenges in general, and the CAPD population in particular, the protocol was amended to enroll ESRD participants undergoing peritoneal dialysis from either the CAPD or APD population. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial?  No

## Limitations and caveats

None reported