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	v2
This version publication date	20 October 2018
First version publication date	20 May 2018
Version creation reason	

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 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 Units: Subjects			
Female	0	2	2
Male	1	5	6
Race/Ethnicity, Customized 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 of AUC				
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 of AUC				
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 subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	2 / 7 (28.57%) 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. Section 4.2.2. Exclusion Criteria, the numbering of exclusion criteria was inadvertently incremented from previous section. The numbering now starts from "1". 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). 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. 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. 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. 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. The EudraCT number is now updated as "2014-001197-34" with this amendment which is the correct number for this specific protocol. Section 4.2.1 Inclusion criteria number 5, the urine output and Kt/V values were revised for participant's eligibility. 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. 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. 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. 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. 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. 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