



Clinical trial results:

A Phase 2B, randomized, blinded, dose-ranging, active-controlled, parallel-group, multi-center study to evaluate the dose response relationship of GSK1278863 over the first 4 weeks of treatment and evaluate the safety and efficacy of GSK1278863 over 24 weeks in hemodialysis-dependent subjects with anemia associated with chronic kidney disease who switch from recombinant human erythropoietin.

Summary

EudraCT number	2013-002682-19
Trial protocol	ES SE CZ GB DK HU FR
Global end of trial date	06 February 2015

Results information

Result version number	v1
This version publication date	03 June 2016
First version publication date	03 June 2016

Trial information

Trial identification

Sponsor protocol code	PHI113633
-----------------------	-----------

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	05 May 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Characterize the dose-response relationship between GSK1278863 and Hgb at Week 4.

Protection of trial subjects:

N/A

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 November 2013
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	Norway: 4
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Czech Republic: 10
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Hungary: 12
Country: Number of subjects enrolled	Russian Federation: 47
Country: Number of subjects enrolled	United States: 46
Country: Number of subjects enrolled	Japan: 24
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Korea, Republic of: 7
Worldwide total number of subjects	216
EEA total number of subjects	70

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)	140
From 65 to 84 years	70
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

Eligible participants (par.) were hemodialysis-dependent with anemia associated with chronic kidney disease who were switched from a stable dose of recombinant human erythropoietin (rhEPO).

Pre-assignment

Screening details:

Study consisted of Screening Phase of at least 4 weeks (wk), 24-wk Treatment Phase and Follow-up visit approximately 4 wk after completion of treatment. A total of 216 par. with a stable hemoglobin (Hgb) between 9.0-11.5 grams (g)/deciliter (dL) (France sites only: 10.0-11.5 g/dL) were randomized and 210 par. entered into the 24-wk Treatment Phase.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Control

Arm description:

Participants received placebo once daily for the first 4 weeks and thereafter received open label rhEPO as required to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Matching film coated tablets were administered orally for 4 weeks.

Arm title	GSK1278863 4 mg
------------------	-----------------

Arm description:

Participants received GSK1278863 4 milligrams (mg) once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.

Arm type	Experimental
Investigational medicinal product name	GSK1278863
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GSK1278863 film coated tablets were administered orally at a dosage of 4 milligrams (mg), 6 mg, 8 mg, 10 mg, or 12 mg per randomization schedule for 4 weeks and then dose adjusted if necessary for every 4 weeks to achieve hemoglobin (Hgb) within the range of 10.0-11.5 grams (g)/deciliter (dL) for the remaining 20 weeks.

Arm title	GSK1278863 6 mg
------------------	-----------------

Arm description:

Participants received GSK1278863 6 mg once daily for the first 4 weeks and thereafter, if necessary the

dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.

Arm type	Experimental
Investigational medicinal product name	GSK1278863
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GSK1278863 film coated tablets were administered orally at a dosage of 4 milligrams (mg), 6 mg, 8 mg, 10 mg, or 12 mg per randomization schedule for 4 weeks and then dose adjusted if necessary for every 4 weeks to achieve hemoglobin (Hgb) within the range of 10.0-11.5 grams (g)/deciliter (dL) for the remaining 20 weeks.

Arm title	GSK1278863 8 mg
------------------	-----------------

Arm description:

Participants received GSK1278863 8 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.

Arm type	Experimental
Investigational medicinal product name	GSK1278863
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GSK1278863 film coated tablets were administered orally at a dosage of 4 milligrams (mg), 6 mg, 8 mg, 10 mg, or 12 mg per randomization schedule for 4 weeks and then dose adjusted if necessary for every 4 weeks to achieve hemoglobin (Hgb) within the range of 10.0-11.5 grams (g)/deciliter (dL) for the remaining 20 weeks.

Arm title	GSK1278863 10 mg
------------------	------------------

Arm description:

Participants received GSK1278863 10 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.

Arm type	Experimental
Investigational medicinal product name	GSK1278863
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GSK1278863 film coated tablets were administered orally at a dosage of 4 milligrams (mg), 6 mg, 8 mg, 10 mg, or 12 mg per randomization schedule for 4 weeks and then dose adjusted if necessary for every 4 weeks to achieve hemoglobin (Hgb) within the range of 10.0-11.5 grams (g)/deciliter (dL) for the remaining 20 weeks.

Arm title	GSK1278863 12 mg
------------------	------------------

Arm description:

Participants received GSK1278863 12 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.

Arm type	Experimental
----------	--------------

Investigational medicinal product name	GSK1278863
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GSK1278863 film coated tablets were administered orally at a dosage of 4 milligrams (mg), 6 mg, 8 mg, 10 mg, or 12 mg per randomization schedule for 4 weeks and then dose adjusted if necessary for every 4 weeks to achieve hemoglobin (Hgb) within the range of 10.0-11.5 grams (g)/deciliter (dL) for the remaining 20 weeks.

Number of subjects in period 1	Control	GSK1278863 4 mg	GSK1278863 6 mg
Started	39	39	40
Completed	36	30	35
Not completed	3	9	5
Adverse event, serious fatal	-	1	1
Consent withdrawn by subject	2	4	1
Physician decision	-	1	-
Protocol-defined Stopping Criteria	-	3	2
Lost to follow-up	1	-	-
Protocol deviation	-	-	1

Number of subjects in period 1	GSK1278863 8 mg	GSK1278863 10 mg	GSK1278863 12 mg
Started	39	40	19
Completed	35	37	14
Not completed	4	3	5
Adverse event, serious fatal	-	2	-
Consent withdrawn by subject	3	1	5
Physician decision	-	-	-
Protocol-defined Stopping Criteria	1	-	-
Lost to follow-up	-	-	-
Protocol deviation	-	-	-

Baseline characteristics

Reporting groups

Reporting group title	Control
Reporting group description: Participants received placebo once daily for the first 4 weeks and thereafter received open label rhEPO as required to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.	
Reporting group title	GSK1278863 4 mg
Reporting group description: Participants received GSK1278863 4 milligrams (mg) once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.	
Reporting group title	GSK1278863 6 mg
Reporting group description: Participants received GSK1278863 6 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.	
Reporting group title	GSK1278863 8 mg
Reporting group description: Participants received GSK1278863 8 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.	
Reporting group title	GSK1278863 10 mg
Reporting group description: Participants received GSK1278863 10 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.	
Reporting group title	GSK1278863 12 mg
Reporting group description: Participants received GSK1278863 12 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.	

Reporting group values	Control	GSK1278863 4 mg	GSK1278863 6 mg
Number of subjects	39	39	40
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	59.7 ± 18.74	58.7 ± 13.33	63.5 ± 14
Gender categorical Units: Subjects			
Female	13	15	12
Male	26	24	28
Race, Customized Units: Subjects			
African American/African Heritage	7	4	5
American Indian Or Alaskan Native	1	0	0
Asian - East Asian Heritage	2	1	3
Asian - Japanese Heritage	5	4	4

Asian - South East Asian Heritage	0	1	0
Native Hawaiian Or Other Pacific Islander	1	0	0
White - Arabic/North African Heritage	0	0	2
White - White/Caucasian/European Heritage	23	28	26
Mixed Race	0	1	0

Reporting group values	GSK1278863 8 mg	GSK1278863 10 mg	GSK1278863 12 mg
Number of subjects	39	40	19
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	60.1	55.4	59.9
standard deviation	± 10.36	± 15.5	± 13.26
Gender categorical			
Units: Subjects			
Female	15	17	8
Male	24	23	11
Race, Customized			
Units: Subjects			
African American/African Heritage	3	4	4
American Indian Or Alaskan Native	0	0	0
Asian - East Asian Heritage	1	1	0
Asian - Japanese Heritage	5	4	2
Asian - South East Asian Heritage	1	0	1
Native Hawaiian Or Other Pacific Islander	1	0	0
White - Arabic/North African Heritage	0	0	0
White - White/Caucasian/European Heritage	28	31	12
Mixed Race	0	0	0

Reporting group values	Total		
Number of subjects	216		
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	80		
Male	136		
Race, Customized			
Units: Subjects			
African American/African Heritage	27		

American Indian Or Alaskan Native	1		
Asian - East Asian Heritage	8		
Asian - Japanese Heritage	24		
Asian - South East Asian Heritage	3		
Native Hawaiian Or Other Pacific Islander	2		
White - Arabic/North African Heritage	2		
White - White/Caucasian/European Heritage	148		
Mixed Race	1		

End points

End points reporting groups

Reporting group title	Control
Reporting group description: Participants received placebo once daily for the first 4 weeks and thereafter received open label rhEPO as required to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.	
Reporting group title	GSK1278863 4 mg
Reporting group description: Participants received GSK1278863 4 milligrams (mg) once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.	
Reporting group title	GSK1278863 6 mg
Reporting group description: Participants received GSK1278863 6 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.	
Reporting group title	GSK1278863 8 mg
Reporting group description: Participants received GSK1278863 8 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.	
Reporting group title	GSK1278863 10 mg
Reporting group description: Participants received GSK1278863 10 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.	
Reporting group title	GSK1278863 12 mg
Reporting group description: Participants received GSK1278863 12 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.	

Primary: Change from Baseline in hemoglobin (Hgb) at Week 4

End point title	Change from Baseline in hemoglobin (Hgb) at Week 4
End point description: Baseline Hgb value was the average of three Hgb values taken during the screening period at Week (W) -4, W-2 and Day 1. Change from Baseline in Hgb was calculated as W4 value minus the Baseline value. To model the dose-response relationship a four-parameter Emax model was used. The dose response dataset was based on all non-missing data collected up to W4. Participants (par.) who had a Week 2 Hgb measurement, but a missing W4 Hgb measurement were included with a change from Baseline at Week 4 value imputed as twice the change from Baseline at Week 2. E0 is the expected Hgb change from Baseline for a par. receiving placebo and experiencing the average Hgb Baseline observed in the study. Emax is the expected Hgb change from Baseline for a par. receiving the highest dose above which no further increase in response can be achieved. ED50 is the dose that attains the intermediate response. Gamma is the slope parameter. Alpha is the coefficient of the model covariate for centred Baseline.	
End point type	Primary
End point timeframe: Baseline (Week -4, Week-2 and Day 1) and Week 4	
Intent-to-Treat (ITT) population consisted of all randomized participants who received one dose of study, have a Baseline and at least one corresponding treatment assessment.	

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39 ^[1]	38 ^[2]	39 ^[3]	38 ^[4]
Units: grams (g)/deciliter (dL)				
arithmetic mean (standard deviation)	-0.64 (± 0.829)	-0.24 (± 0.989)	0.08 (± 1.131)	0.42 (± 0.796)

Notes:

[1] - ITT Population. Only participants with data available at specific time point were analyzed.

[2] - ITT Population. Only participants with data available at specific time point were analyzed.

[3] - ITT Population. Only participants with data available at specific time point were analyzed.

[4] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39 ^[5]	17 ^[6]		
Units: grams (g)/deciliter (dL)				
arithmetic mean (standard deviation)	0.64 (± 1.177)	0.61 (± 1.245)		

Notes:

[5] - ITT Population. Only participants with data available at specific time point were analyzed.

[6] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Posterior median and 95% credibility intervals were estimated using Bayesian methods.	
Comparison groups	Control v GSK1278863 4 mg v GSK1278863 6 mg v GSK1278863 8 mg v GSK1278863 10 mg v GSK1278863 12 mg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	E0 (g/dL)
Point estimate	-0.664
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.96
upper limit	-0.387

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Posterior median and 95% credibility intervals were estimated using Bayesian methods.	
Comparison groups	Control v GSK1278863 4 mg v GSK1278863 6 mg v GSK1278863 8 mg v GSK1278863 10 mg v GSK1278863 12 mg

Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	ED50 (milligrams[mg])
Point estimate	33.531
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.566
upper limit	48.948

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Posterior median and 95% credibility intervals were estimated using Bayesian methods.	
Comparison groups	Control v GSK1278863 4 mg v GSK1278863 6 mg v GSK1278863 8 mg v GSK1278863 10 mg v GSK1278863 12 mg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Emax (g/dL)
Point estimate	5.234
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.691
upper limit	7.94

Statistical analysis title	Statistical analysis 4
Statistical analysis description: Posterior median and 95% credibility intervals were estimated using Bayesian methods.	
Comparison groups	Control v GSK1278863 4 mg v GSK1278863 6 mg v GSK1278863 8 mg v GSK1278863 10 mg v GSK1278863 12 mg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Gamma
Point estimate	1.145
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.748
upper limit	1.738

Statistical analysis title	Statistical analysis 5
Statistical analysis description: Posterior median and 95% credibility intervals were estimated using Bayesian methods.	
Comparison groups	Control v GSK1278863 4 mg v GSK1278863 6 mg v GSK1278863 8 mg v GSK1278863 10 mg v GSK1278863 12 mg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Var
Point estimate	1.012
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.234

Statistical analysis title	Statistical analysis 6
Statistical analysis description: Posterior median and 95% credibility intervals were estimated using Bayesian methods.	
Comparison groups	Control v GSK1278863 4 mg v GSK1278863 6 mg v GSK1278863 8 mg v GSK1278863 10 mg v GSK1278863 12 mg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Alpha
Point estimate	-0.206
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.397
upper limit	-0.014

Statistical analysis title	Statistical analysis 7
Statistical analysis description: Posterior median and 95% credibility intervals were estimated using Bayesian methods.	
Comparison groups	Control v GSK1278863 4 mg v GSK1278863 6 mg v GSK1278863 8 mg v GSK1278863 10 mg v GSK1278863 12 mg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Minimally Effective Dose (MED) (mg)
Point estimate	0.418

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	2.342

Statistical analysis title	Statistical analysis 8
-----------------------------------	------------------------

Statistical analysis description:

Posterior median and 95% credibility intervals were estimated using Bayesian methods.

Comparison groups	Control v GSK1278863 4 mg v GSK1278863 6 mg v GSK1278863 8 mg v GSK1278863 10 mg v GSK1278863 12 mg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Dose that achieves a change of -0.25g/dL
Point estimate	2.423
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	4.15

Statistical analysis title	Statistical analysis 9
-----------------------------------	------------------------

Statistical analysis description:

Posterior median and 95% credibility intervals were estimated using Bayesian methods.

Comparison groups	Control v GSK1278863 4 mg v GSK1278863 6 mg v GSK1278863 8 mg v GSK1278863 10 mg v GSK1278863 12 mg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Target Dose (TD) (mg)
Point estimate	4.406
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.544
upper limit	5.995

Statistical analysis title	Statistical analysis 10
-----------------------------------	-------------------------

Statistical analysis description:

Posterior median and 95% credibility intervals were estimated using Bayesian methods.

Comparison groups	Control v GSK1278863 4 mg v GSK1278863 6 mg v GSK1278863 8 mg v GSK1278863 10 mg v GSK1278863 12
-------------------	--

	mg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Dose that achieves a change of 0.25 g/dL
Point estimate	6.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.698
upper limit	8.01

Statistical analysis title	Statistical analysis 11
Statistical analysis description: Posterior median and 95% credibility intervals were estimated using Bayesian methods.	
Comparison groups	Control v GSK1278863 4 mg v GSK1278863 6 mg v GSK1278863 8 mg v GSK1278863 10 mg v GSK1278863 12 mg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Dose that achieves a change of 0.5 g/dL
Point estimate	8.542
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.931
upper limit	10.523

Statistical analysis title	Statistical analysis 12
Statistical analysis description: Posterior median and 95% credibility intervals were estimated using Bayesian methods.	
Comparison groups	Control v GSK1278863 4 mg v GSK1278863 6 mg v GSK1278863 8 mg v GSK1278863 10 mg v GSK1278863 12 mg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Dose that achieves a change of 0.75 g/dL
Point estimate	10.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.024
upper limit	14.004

Statistical analysis title	Statistical analysis 13
Statistical analysis description: Posterior median and 95% credibility intervals were estimated using Bayesian methods.	
Comparison groups	Control v GSK1278863 4 mg v GSK1278863 6 mg v GSK1278863 8 mg v GSK1278863 10 mg v GSK1278863 12 mg
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Dose that achieves a change of 1 g/dL
Point estimate	13.248
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.891
upper limit	18.916

Secondary: Hgb concentration at Week 24

End point title	Hgb concentration at Week 24
End point description: Hgb values measured at Week 24 are presented.	
End point type	Secondary
End point timeframe: Week 24	

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24 ^[7]	18 ^[8]	27 ^[9]	26 ^[10]
Units: g/dL				
arithmetic mean (standard deviation)	10.56 (± 0.974)	10.29 (± 0.864)	10.54 (± 1.01)	10.63 (± 1.099)

Notes:

[7] - ITT Population. Only participants with data available at specific time point were analyzed.

[8] - ITT Population. Only participants with data available at specific time point were analyzed.

[9] - ITT Population. Only participants with data available at specific time point were analyzed.

[10] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24 ^[11]	11 ^[12]		
Units: g/dL				
arithmetic mean (standard deviation)	10.28 (±	10.7 (± 0.867)		

Notes:

[11] - ITT Population. Only participants with data available at specific time point were analyzed.

[12] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of time within, below, and above Hgb target range between Weeks 20 and 24

End point title	Percentage of time within, below, and above Hgb target range between Weeks 20 and 24
-----------------	--

End point description:

The percentage of time in Hgb target range between Weeks 20 and 24 for a participant was calculated by dividing the total number of days that Hgb was within the target range (10.0 to 11.5 g/dL) while on treatment during Weeks 20 to 24 (using linear interpolation) by the total number of days the participant remained on treatment during the defined period. Similarly, percentage of time above Hgb target range and percentage of time below Hgb target range were calculated.

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

End point timeframe:

Week 20 to Week 24

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31 ^[13]	22 ^[14]	28 ^[15]	27 ^[16]
Units: Percentage of time				
arithmetic mean (standard deviation)				
Percentage of time within target range	54.59 (± 42.044)	74.77 (± 38.797)	57.38 (± 40.505)	37.46 (± 41.775)
Percentage of time above target range	24.65 (± 38.556)	6.89 (± 22.137)	17.18 (± 30.446)	33.15 (± 42.856)
Percentage of time below target range	20.76 (± 36.587)	18.34 (± 35.778)	25.44 (± 40.12)	29.39 (± 42.67)

Notes:

[13] - ITT Population. Only participants with data available at specific time point were analyzed.

[14] - ITT Population. Only participants with data available at specific time point were analyzed.

[15] - ITT Population. Only participants with data available at specific time point were analyzed.

[16] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25 ^[17]	14 ^[18]		
Units: Percentage of time				
arithmetic mean (standard deviation)				
Percentage of time within target range	48.97 (± 42.49)	55.23 (± 40.35)		
Percentage of time above target range	18.27 (± 33.698)	26.88 (± 36.154)		

Percentage of time below target range	32.76 (\pm 43.78)	17.89 (\pm 36.836)		
---------------------------------------	----------------------	-----------------------	--	--

Notes:

[17] - ITT Population. Only participants with data available at specific time point were analyzed.

[18] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Hgb in the target range at Week 24

End point title	Number of participants with Hgb in the target range at Week 24
End point description: The number of participants with Hgb in the target range of 10.0 to 11.5 g/dL at Week 24 was recorded for each arm.	
End point type	Secondary
End point timeframe: Week 24	

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24 ^[19]	18 ^[20]	27 ^[21]	26 ^[22]
Units: Participants	14	13	16	10

Notes:

[19] - ITT Population. Only participants with data available at specific time point were analyzed.

[20] - ITT Population. Only participants with data available at specific time point were analyzed.

[21] - ITT Population. Only participants with data available at specific time point were analyzed.

[22] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24 ^[23]	11 ^[24]		
Units: Participants	15	8		

Notes:

[23] - ITT Population. Only participants with data available at specific time point were analyzed.

[24] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants reaching pre-defined Hgb stopping criteria

End point title	Number of participants reaching pre-defined Hgb stopping criteria
End point description: The number of participants who reached the Hgb stopping criteria of Hgb concentration <7.5 g/dL were presented.	

End point type	Secondary
End point timeframe:	
Up to 24 weeks	

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39 ^[25]	38 ^[26]	39 ^[27]	38 ^[28]
Units: Participants	0	0	0	0

Notes:

[25] - ITT Population

[26] - ITT Population

[27] - ITT Population

[28] - ITT Population

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39 ^[29]	17 ^[30]		
Units: Participants	0	0		

Notes:

[29] - ITT Population

[30] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed change from Baseline in Erythropoietin (EPO)

End point title	Maximum observed change from Baseline in Erythropoietin (EPO)
-----------------	---

End point description:

Blood samples for control arm were collected on Day 1 (pre-dose), Week 4 (5-15 minutes post-dose and 6-12 hours post-dose), Week 8 (pre-dose), Week 12 (pre-dose), Week 16 (pre-dose), Week 20 (pre-dose, 5-15 minutes post-dose), Week 24 (pre-dose), and Week 28 (pre-dose) for EPO measurement. Blood samples for GSK1278863 arms were collected on Day 1 (pre-dose), Week 4 (6-12 hours post-dose), Week 4 (7-13, 8-14, 9-15 hours post-dose), Week 8 (pre-dose), Week 12 (pre-dose), Week 16 (pre-dose), Week 20 (pre-dose, 3 hour post-dose), Week 24 (pre-dose), and Week 28 (pre-dose) for EPO measurement. The maximum observed change from baseline in EPO was recorded for each arm. Baseline value for EPO is the pre-dose value on Day 1. Change from Baseline in EPO was calculated as the individual post-dose values minus the Baseline value.

End point type	Secondary
End point timeframe:	
Baseline (Day 1) to Week 28	

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36 ^[31]	37 ^[32]	37 ^[33]	37 ^[34]
Units: international units(IU)/Liter (L)				
arithmetic mean (standard deviation)	1946.45 (± 8456.313)	48.86 (± 117.05)	36.63 (± 35.485)	84.53 (± 225.768)

Notes:

[31] - ITT Population. Only participants with data available at specific time point were analyzed.

[32] - ITT Population. Only participants with data available at specific time point were analyzed.

[33] - ITT Population. Only participants with data available at specific time point were analyzed.

[34] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36 ^[35]	16 ^[36]		
Units: international units(IU)/Liter (L)				
arithmetic mean (standard deviation)	82 (± 99.66)	24.63 (± 235.82)		

Notes:

[35] - ITT Population. Only participants with data available at specific time point were analyzed.

[36] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed percent change from Baseline in Vascular Endothelial Growth Factor (VEGF)

End point title	Maximum observed percent change from Baseline in Vascular Endothelial Growth Factor (VEGF)
-----------------	--

End point description:

Blood samples for control arm were collected on Day 1 (pre-dose), Week 4 (5-15 minutes post-dose and 6-12 hours post-dose), Week 8 (pre-dose), Week 12 (pre-dose), Week 16 (pre-dose), Week 20 (pre-dose, 5-15 minutes post-dose), Week 24 (pre-dose), and Week 28 (pre-dose) for VEGF measurement. Blood samples for GSK1278863 arms were collected on Day 1 (pre-dose), Week 4 (6-12 hours post-dose), Week 4 (7-13, 8-14, 9-15 hours post-dose), Week 8 (pre-dose), Week 12 (pre-dose), Week 16 (pre-dose), Week 20 (pre-dose, 3 hour post-dose), Week 24 (pre-dose), and Week 28 (pre-dose) for VEGF measurement. The maximum observed percent change from Baseline in VEGF was recorded for each arm. Baseline value for VEGF is the pre-dose value on Day 1. Percent change from Baseline was calculated as 100 multiplied by exponential of mean change in log scale minus 1.

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

End point timeframe:

Baseline (Day 1) to Week 28

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36 ^[37]	37 ^[38]	37 ^[39]	37 ^[40]
Units: Percent change				
geometric mean (confidence interval 95%)	36.02 (16.45 to 58.87)	36.92 (19.33 to 57.11)	41.73 (22.65 to 63.77)	54.91 (37.38 to 74.69)

Notes:

[37] - ITT Population. Only participants with data available at specific time point were analyzed.

[38] - ITT Population. Only participants with data available at specific time point were analyzed.

[39] - ITT Population. Only participants with data available at specific time point were analyzed.

[40] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36 ^[41]	16 ^[42]		
Units: Percent change				
geometric mean (confidence interval 95%)	50.65 (31.88 to 72.1)	50.97 (21.49 to 87.6)		

Notes:

[41] - ITT Population. Only participants with data available at specific time point were analyzed.

[42] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Population plasma Pharmacokinetic (PK) parameters of GSK1278863 and metabolites

End point title	Population plasma Pharmacokinetic (PK) parameters of GSK1278863 and metabolites ^[43]
-----------------	---

End point description:

Blood samples were collected for individual plasma GSK1278863 and metabolite (GSK2391220, GSK2499166, GSK2531403, GSK2531400, GSK2531399, and GSK2531398) concentrations measurement on Day (D) 1 (pre-dose [PrD], at Week (W) 4 (6-12, 7-13, 8-14, and 9-15 hour [hr] post-dose [PoD], and at W20 (PrD, 1, 2, and 3 hour PoD). Pharmacokinetic population: All participants from whom a PK sample has been obtained and analyzed.

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

End point timeframe:

Day 1, Week 4, and Week 20

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical data to report.

End point values	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg	GSK1278863 10 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39 ^[44]	40 ^[45]	39 ^[46]	40 ^[47]
Units: nanograms (ng)/milliliter (mL)				
arithmetic mean (standard deviation)				
GSK1278863, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
GSK1278863, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	6.3 (± 10.04)	9.3 (± 19.06)	7.7 (± 18.46)	25.4 (± 53.37)
GSK1278863, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	10.6 (± 25.15)	16.3 (± 57.24)	8.7 (± 19.85)	19.9 (± 42.65)
GSK1278863, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	7.5 (± 16.8)	8.1 (± 23.76)	5.6 (± 11.75)	12.7 (± 28.6)
GSK1278863, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	6.8 (± 14.53)	4.6 (± 10.49)	4.4 (± 9.19)	11.3 (± 25.36)

GSK1278863, W20, PrD, n=23, 28, 27, 23, 14	2.3 (± 6.44)	0.7 (± 2.55)	0.9 (± 2.82)	7.9 (± 30.99)
GSK1278863, W20, 1 hr PoD, n=23, 27, 27, 24, 13	25.9 (± 35.74)	37.6 (± 53.77)	88.2 (± 153.06)	58.5 (± 85.91)
GSK1278863, W20, 2 hr PoD, n=23, 27, 27, 24, 13	34.2 (± 31.76)	52.4 (± 53.32)	62.8 (± 85.37)	82.7 (± 117.97)
GSK1278863, W20, 3 hr PoD, n=23, 27, 27, 24, 14	43.6 (± 58.36)	39.2 (± 44.59)	44.1 (± 70.53)	71.2 (± 110.91)
GSK2391220, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
GSK2391220, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	9.1 (± 6.68)	12.9 (± 8.32)	18.5 (± 13.72)	20.1 (± 12.32)
GSK2391220, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	5.1 (± 4.22)	6.7 (± 5.51)	10.3 (± 8.55)	10.9 (± 6.37)
GSK2391220, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	3.8 (± 3.66)	4.5 (± 4.16)	7.4 (± 6.44)	7.4 (± 4.51)
GSK2391220, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	3.3 (± 3.76)	3.3 (± 3.15)	5.3 (± 4.86)	5.4 (± 3.63)
GSK2391220, W20, PrD, n=23, 28, 27, 23, 14	5 (± 7.72)	3.2 (± 4.97)	4.1 (± 5.84)	4.6 (± 9.29)
GSK2391220, W20, 1 hr PoD, n=23, 27, 27, 24, 13	3.9 (± 5.59)	2.7 (± 3.6)	4.3 (± 4.9)	5 (± 8.1)
GSK2391220, W20, 2 hr PoD, n=23, 27, 27, 24, 13	5.4 (± 5.58)	4.5 (± 4.96)	6.5 (± 6.93)	8.1 (± 10.33)
GSK2391220, W20, 3 hr PoD, n=23, 27, 27, 24, 14	5.3 (± 4.64)	5 (± 5.26)	7.3 (± 6.69)	8.2 (± 6.52)
GSK2487818, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
GSK2487818, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	3.1 (± 2.82)	4.1 (± 4.47)	5.7 (± 6.31)	7.2 (± 6.57)
GSK2487818, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	1.8 (± 1.75)	2.6 (± 3.81)	3.5 (± 4.55)	4.1 (± 3.73)
GSK2487818, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	1.5 (± 1.67)	1.9 (± 3.21)	2.7 (± 3.58)	2.7 (± 2.44)
GSK2487818, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	1.4 (± 1.88)	1.5 (± 2.46)	1.9 (± 2.85)	1.9 (± 1.92)
GSK2487818, W20, PrD, n=23, 28, 27, 23, 14	1.2 (± 3.38)	0.5 (± 1.05)	0.7 (± 1.28)	1.3 (± 4.09)
GSK2487818, W20, 1 hr PoD, n=23, 27, 27, 24, 13	2 (± 3.82)	1.3 (± 1.73)	2.7 (± 3.97)	3.4 (± 5.88)
GSK2487818, W20, 2 hr PoD, n=23, 27, 27, 24, 13	3.8 (± 4.58)	3.6 (± 4.36)	5 (± 5.82)	6.3 (± 8.04)
GSK2487818, W20, 3 hr PoD, n=23, 27, 27, 24, 14	3.9 (± 3.49)	4.3 (± 4.76)	5.7 (± 5.28)	6.5 (± 5.05)
GSK2506102, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
GSK2506102, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	3.2 (± 1.98)	4.9 (± 2.68)	6.6 (± 4.16)	7.6 (± 4.3)
GSK2506102, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	1.8 (± 1.31)	2.5 (± 1.71)	3.7 (± 2.6)	4.1 (± 2.15)
GSK2506102, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	1.3 (± 1.07)	1.6 (± 1.16)	2.6 (± 1.94)	2.9 (± 1.68)
GSK2506102, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	1.1 (± 1.16)	1.2 (± 0.88)	1.9 (± 1.52)	2.1 (± 1.23)
GSK2506102, W20, PrD, n=23, 28, 27, 23, 14	2.3 (± 1.99)	1.9 (± 2.05)	2.3 (± 2.09)	2.6 (± 2.87)
GSK2506102, W20, 1 hr PoD, n=23, 27, 27, 24, 13	1.4 (± 1.27)	1.1 (± 1.4)	1.4 (± 1.22)	1.8 (± 2.12)
GSK2506102, W20, 2 hr PoD, n=23, 27, 27, 24, 13	1.5 (± 1.25)	1.2 (± 1.24)	1.8 (± 1.72)	2.2 (± 2.53)
GSK2506102, W20, 3 hr PoD, n=23, 27, 27, 24, 14	1.4 (± 1.12)	1.3 (± 1.26)	1.9 (± 1.53)	2.1 (± 1.66)

GSK2531398, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
GSK2531398, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	3.4 (± 2.46)	4.9 (± 3.11)	6.9 (± 4.52)	8 (± 4.87)
GSK2531398, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	2 (± 1.72)	2.7 (± 2.41)	4 (± 2.97)	4.5 (± 2.7)
GSK2531398, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	1.5 (± 1.46)	1.8 (± 1.86)	2.9 (± 2.3)	3.1 (± 1.95)
GSK2531398, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	1.4 (± 1.58)	1.4 (± 1.49)	2.1 (± 1.99)	2.2 (± 1.38)
GSK2531398, W20, PrD, n=23, 28, 27, 23, 14	1.5 (± 2.31)	1.2 (± 2.03)	1.4 (± 1.93)	1.6 (± 3.8)
GSK2531398, W20, 1 hr PoD, n=23, 27, 27, 24, 13	1.3 (± 1.89)	1 (± 1.34)	1.6 (± 1.81)	2 (± 3.58)
GSK2531398, W20, 2 hr PoD, n=23, 27, 27, 24, 13	2.1 (± 2.24)	1.9 (± 2.09)	2.9 (± 3.28)	3.5 (± 4.69)
GSK2531398, W20, 3 hr PoD, n=23, 27, 27, 24, 14	2.3 (± 2.04)	2.2 (± 2.2)	3.3 (± 2.89)	3.8 (± 3.1)
GSK2531401, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
GSK2531401, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	9.9 (± 8)	14.7 (± 10.02)	22.2 (± 14.71)	24.5 (± 18.27)
GSK2531401, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	5.4 (± 4.49)	7.1 (± 5.53)	11.8 (± 8.49)	13.1 (± 9.5)
GSK2531401, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	4 (± 3.63)	4.5 (± 3.5)	8.1 (± 5.74)	9 (± 7.05)
GSK2531401, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	3.3 (± 3.36)	3.2 (± 2.35)	5.9 (± 4.66)	6.3 (± 4.9)
GSK2531401, W20, PrD, n=23, 28, 27, 23, 14	7.7 (± 7.71)	7.3 (± 7.34)	7.9 (± 7.37)	9.3 (± 10.95)
GSK2531401, W20, 1 hr PoD, n=23, 27, 27, 24, 13	4.2 (± 4.52)	4 (± 6.77)	4.7 (± 4.18)	5.6 (± 7.48)
GSK2531401, W20, 2 hr PoD, n=23, 27, 27, 24, 13	4.2 (± 4.44)	3.6 (± 4.5)	4.8 (± 4.08)	6.1 (± 8.21)
GSK2531401, W20, 3 hr PoD, n=23, 27, 27, 24, 14	4.1 (± 4.07)	3.6 (± 4.55)	5 (± 4.64)	5.5 (± 5.38)
GSK2531403, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
GSK2531403, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	11.4 (± 7.47)	17 (± 9.89)	23.1 (± 15.22)	25.4 (± 14.25)
GSK2531403, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	6.3 (± 4.84)	8.6 (± 6.43)	13.1 (± 9.73)	13.9 (± 7.66)
GSK2531403, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	4.7 (± 4.23)	5.7 (± 4.63)	9.3 (± 7.37)	9.6 (± 5.5)
GSK2531403, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	4.1 (± 4.6)	4.1 (± 3.41)	6.7 (± 5.5)	6.9 (± 4.25)
GSK2531403, W20, PrD, n=23, 28, 27, 23, 14	7.8 (± 8.53)	6 (± 8.08)	6.7 (± 6.74)	7.8 (± 11.14)
GSK2531403, W20, 1 hr PoD, n=23, 27, 27, 24, 13	4.9 (± 5.56)	3.8 (± 4.88)	5 (± 4.71)	6.2 (± 8.65)
GSK2531403, W20, 2 hr PoD, n=23, 27, 27, 24, 13	5.7 (± 5.43)	4.7 (± 4.91)	6.8 (± 6.54)	8.5 (± 10.83)
GSK2531403, W20, 3 hr PoD, n=23, 27, 27, 24, 14	5.5 (± 4.52)	5.1 (± 5.18)	7.4 (± 6.43)	8.4 (± 6.86)

Notes:

[44] - PK Population. Only participants with data available at specific time point were analyzed.

[45] - PK Population. Only participants with data available at specific time point were analyzed.

[46] - PK Population. Only participants with data available at specific time point were analyzed.

[47] - PK Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 12 mg			
Subject group type	Reporting group			
Number of subjects analysed	19 ^[48]			
Units: nanograms (ng)/milliliter (mL)				
arithmetic mean (standard deviation)				
GSK1278863, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0)			
GSK1278863, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	9 (± 18.8)			
GSK1278863, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	8 (± 16.92)			
GSK1278863, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	4.6 (± 6.87)			
GSK1278863, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	11.2 (± 33.59)			
GSK1278863, W20, PrD, n=23, 28, 27, 23, 14	6.6 (± 20.22)			
GSK1278863, W20, 1 hr PoD, n=23, 27, 27, 24, 13	65.2 (± 127.21)			
GSK1278863, W20, 2 hr PoD, n=23, 27, 27, 24, 13	63.3 (± 102.15)			
GSK1278863, W20, 3 hr PoD, n=23, 27, 27, 24, 14	65.8 (± 100.8)			
GSK2391220, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0)			
GSK2391220, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	21.3 (± 17.34)			
GSK2391220, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	13.1 (± 12.44)			
GSK2391220, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	7.2 (± 6.97)			
GSK2391220, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	6.6 (± 5.72)			
GSK2391220, W20, PrD, n=23, 28, 27, 23, 14	3.5 (± 6.69)			
GSK2391220, W20, 1 hr PoD, n=23, 27, 27, 24, 13	2.6 (± 3.64)			
GSK2391220, W20, 2 hr PoD, n=23, 27, 27, 24, 13	4.9 (± 4.08)			
GSK2391220, W20, 3 hr PoD, n=23, 27, 27, 24, 14	6.1 (± 4.92)			
GSK2487818, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0)			
GSK2487818, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	5.2 (± 4.66)			
GSK2487818, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	3.7 (± 4.61)			
GSK2487818, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	1.7 (± 1.68)			
GSK2487818, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	1.9 (± 2.21)			
GSK2487818, W20, PrD, n=23, 28, 27, 23, 14	0.7 (± 1.84)			
GSK2487818, W20, 1 hr PoD, n=23, 27, 27, 24, 13	1 (± 1.34)			
GSK2487818, W20, 2 hr PoD, n=23, 27, 27, 24, 13	3.7 (± 3.28)			
GSK2487818, W20, 3 hr PoD, n=23, 27, 27, 24, 14	5 (± 4.43)			

GSK2506102, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0)			
GSK2506102, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	9 (± 6.19)			
GSK2506102, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	5.4 (± 4.1)			
GSK2506102, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	2.9 (± 2.24)			
GSK2506102, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	2.7 (± 2.04)			
GSK2506102, W20, PrD, n=23, 28, 27, 23, 14	2.2 (± 2.87)			
GSK2506102, W20, 1 hr PoD, n=23, 27, 27, 24, 13	1.4 (± 1.57)			
GSK2506102, W20, 2 hr PoD, n=23, 27, 27, 24, 13	1.6 (± 1.37)			
GSK2506102, W20, 3 hr PoD, n=23, 27, 27, 24, 14	1.7 (± 1.42)			
GSK2531398, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0)			
GSK2531398, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	7.9 (± 5.75)			
GSK2531398, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	4.9 (± 4.05)			
GSK2531398, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	2.5 (± 1.78)			
GSK2531398, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	2.3 (± 1.42)			
GSK2531398, W20, PrD, n=23, 28, 27, 23, 14	1.2 (± 2.67)			
GSK2531398, W20, 1 hr PoD, n=23, 27, 27, 24, 13	1 (± 1.45)			
GSK2531398, W20, 2 hr PoD, n=23, 27, 27, 24, 13	2.1 (± 1.79)			
GSK2531398, W20, 3 hr PoD, n=23, 27, 27, 24, 14	2.8 (± 2.34)			
GSK2531401, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0.02)			
GSK2531401, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	29.1 (± 24.55)			
GSK2531401, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	17.3 (± 16.03)			
GSK2531401, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	10.1 (± 10.61)			
GSK2531401, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	8.7 (± 8.72)			
GSK2531401, W20, PrD, n=23, 28, 27, 23, 14	7.2 (± 10.04)			
GSK2531401, W20, 1 hr PoD, n=23, 27, 27, 24, 13	4.5 (± 5.44)			
GSK2531401, W20, 2 hr PoD, n=23, 27, 27, 24, 13	4.4 (± 4.41)			
GSK2531401, W20, 3 hr PoD, n=23, 27, 27, 24, 14	4.5 (± 4.28)			
GSK2531403, D1, PrD, n=39, 40, 39, 40, 18	0 (± 0)			
GSK2531403, W4, 6-12 hr PoD, n=36, 37, 37, 35, 15	28.8 (± 21.46)			
GSK2531403, W4, 7-13 hr PoD, n=36, 37, 35, 35, 15	17.4 (± 14.72)			
GSK2531403, W4, 8-14 hr PoD, n=35, 37, 36, 35, 15	9.9 (± 9.05)			

GSK2531403, W4, 9-15 hr PoD, n=35, 36, 36, 35, 15	8.9 (\pm 7.79)			
GSK2531403, W20, PrD, n=23, 28, 27, 23, 14	6.2 (\pm 8.78)			
GSK2531403, W20, 1 hr PoD, n=23, 27, 27, 24, 13	4 (\pm 4.8)			
GSK2531403, W20, 2 hr PoD, n=23, 27, 27, 24, 13	5.5 (\pm 4.58)			
GSK2531403, W20, 3 hr PoD, n=23, 27, 27, 24, 14	6.5 (\pm 5.14)			

Notes:

[48] - PK Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Baseline in hepcidin at Week 24

End point title	Percent change from Baseline in hepcidin at Week 24
End point description:	
Hepcidin is a regulator of iron metabolism. Baseline value for transferrin saturation is the pre-dose value on Day 1. Percent change from Baseline was calculated as 100 multiplied by exponential of mean change in log scale minus 1.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Week 24	

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32 ^[49]	20 ^[50]	29 ^[51]	26 ^[52]
Units: Percent change				
geometric mean (confidence interval 95%)	3.63 (-20.39 to 34.89)	-17.39 (-42.36 to 18.4)	-11.85 (-26.47 to 5.67)	-30.28 (-48.08 to -6.37)

Notes:

[49] - ITT Population. Only participants with data available at specific time point were analyzed.

[50] - ITT Population. Only participants with data available at specific time point were analyzed.

[51] - ITT Population. Only participants with data available at specific time point were analyzed.

[52] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25 ^[53]	14 ^[54]		
Units: Percent change				
geometric mean (confidence interval 95%)	-6.91 (-28.69 to 21.52)	-42.13 (-62.82 to -9.95)		

Notes:

[53] - ITT Population. Only participants with data available at specific time point were analyzed.

[54] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in ferritin at Week 24

End point title	Change from Baseline in ferritin at Week 24
End point description: Baseline value for ferritin is the pre-dose value on Day 1. Change from Baseline in ferritin was calculated as the Week 24 value minus the Baseline value.	
End point type	Secondary
End point timeframe: Baseline (Day 1) and Week 24	

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33 ^[55]	20 ^[56]	29 ^[57]	27 ^[58]
Units: Micrograms/Liter				
arithmetic mean (standard deviation)	56.8 (± 214.27)	-29.4 (± 357.1)	-50.4 (± 408.99)	-95.6 (± 304.61)

Notes:

[55] - ITT Population. Only participants with data available at specific time point were analyzed.

[56] - ITT Population. Only participants with data available at specific time point were analyzed.

[57] - ITT Population. Only participants with data available at specific time point were analyzed.

[58] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25 ^[59]	14 ^[60]		
Units: Micrograms/Liter				
arithmetic mean (standard deviation)	-20.2 (± 227.34)	-125.2 (± 354.64)		

Notes:

[59] - ITT Population. Only participants with data available at specific time point were analyzed.

[60] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in transferrin at Week 24

End point title	Change from Baseline in transferrin at Week 24
End point description: Baseline value for transferrin is the pre-dose value on Day 1. Change from Baseline in transferrin was calculated as the Week 24 value minus the Baseline value.	
End point type	Secondary
End point timeframe: Baseline (Day 1) and Week 24	

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33 ^[61]	20 ^[62]	29 ^[63]	27 ^[64]
Units: grams (g)/Liter (L)				
arithmetic mean (standard deviation)	-0.133 (± 0.2903)	0.238 (± 0.3709)	0.198 (± 0.2891)	0.226 (± 0.2706)

Notes:

[61] - ITT Population. Only participants with data available at specific time point were analyzed.

[62] - ITT Population. Only participants with data available at specific time point were analyzed.

[63] - ITT Population. Only participants with data available at specific time point were analyzed.

[64] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25 ^[65]	14 ^[66]		
Units: grams (g)/Liter (L)				
arithmetic mean (standard deviation)	0.249 (± 0.3213)	0.393 (± 0.3165)		

Notes:

[65] - ITT Population. Only participants with data available at specific time point were analyzed.

[66] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Baseline in transferrin saturation at Week 24

End point title	Percent change from Baseline in transferrin saturation at Week 24
-----------------	---

End point description:

Transferrin saturation is measured as a percentage, it is the ratio of serum iron and total iron-binding capacity, multiplied by 100. Baseline value for transferrin saturation is the pre-dose value on Day 1. Percent change from Baseline =: 100*(exp[Mean change log scale]-1).

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

End point timeframe:

Baseline (Day 1) and Week 24

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32 ^[67]	20 ^[68]	29 ^[69]	27 ^[70]
Units: Percent change				
geometric mean (confidence interval 95%)	-9 (-27.3 to 13.9)	-3.7 (-22.9 to 20.4)	-12.1 (-23.4 to 0.9)	-8.3 (-22.9 to 9)

Notes:

[67] - ITT Population. Only participants with data available at specific time point were analyzed.

[68] - ITT Population. Only participants with data available at specific time point were analyzed.

[69] - ITT Population. Only participants with data available at specific time point were analyzed.

[70] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25 ^[71]	14 ^[72]		
Units: Percent change				
geometric mean (confidence interval 95%)	8.2 (-7.7 to 26.8)	-2.5 (-16 to 13.2)		

Notes:

[71] - ITT Population. Only participants with data available at specific time point were analyzed.

[72] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total iron at Week 24

End point title	Change from Baseline in total iron at Week 24
End point description:	Baseline value for total iron is the pre-dose value on Day 1. Change from Baseline in total iron was calculated as the Week 24 value minus the Baseline value.
End point type	Secondary
End point timeframe:	Baseline (Day 1) and Week 24

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33 ^[73]	20 ^[74]	29 ^[75]	27 ^[76]
Units: Micromoles/Liter				
arithmetic mean (standard deviation)	-0.8 (± 7.64)	0.9 (± 9.75)	0.3 (± 5.2)	0.2 (± 6.51)

Notes:

[73] - ITT Population. Only participants with data available at specific time point were analyzed.

[74] - ITT Population. Only participants with data available at specific time point were analyzed.

[75] - ITT Population. Only participants with data available at specific time point were analyzed.

[76] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25 ^[77]	14 ^[78]		
Units: Micromoles/Liter				
arithmetic mean (standard deviation)	2 (± 3.96)	1.6 (± 3.18)		

Notes:

[77] - ITT Population. Only participants with data available at specific time point were analyzed.

[78] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total iron binding capacity at Week 24

End point title	Change from Baseline in total iron binding capacity at Week 24
End point description:	
Total iron-binding capacity is a medical laboratory test that measures the blood's capacity to bind iron with transferrin. Baseline value for total iron binding capacity is the pre-dose value on Day 1. Change from Baseline in total iron binding capacity was calculated as the Week 24 value minus the Baseline value.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Week 24	

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32 ^[79]	20 ^[80]	29 ^[81]	27 ^[82]
Units: Micromoles/Liter				
arithmetic mean (standard deviation)	-2 (± 4.48)	6 (± 7.93)	4.2 (± 6.79)	6.6 (± 5.75)

Notes:

[79] - ITT Population. Only participants with data available at specific time point were analyzed.

[80] - ITT Population. Only participants with data available at specific time point were analyzed.

[81] - ITT Population. Only participants with data available at specific time point were analyzed.

[82] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25 ^[83]	14 ^[84]		
Units: Micromoles/Liter				
arithmetic mean (standard deviation)	4.8 (± 6.25)	6.2 (± 6.44)		

Notes:

[83] - ITT Population. Only participants with data available at specific time point were analyzed.

[84] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in reticulocyte hemoglobin at Week 24

End point title	Change from Baseline in reticulocyte hemoglobin at Week 24
End point description:	
Baseline value for reticulocyte hemoglobin is the pre-dose value on Day 1. Change from Baseline in reticulocyte hemoglobin was calculated as the Week 24 value minus the Baseline value.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Week 24	

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30 ^[85]	20 ^[86]	29 ^[87]	26 ^[88]
Units: Picogram				
arithmetic mean (standard deviation)	-0.19 (± 1.61)	-0.28 (± 1.948)	-0.62 (± 2.046)	-0.42 (± 1.458)

Notes:

[85] - ITT Population. Only participants with data available at specific time point were analyzed.

[86] - ITT Population. Only participants with data available at specific time point were analyzed.

[87] - ITT Population. Only participants with data available at specific time point were analyzed.

[88] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24 ^[89]	12 ^[90]		
Units: Picogram				
arithmetic mean (standard deviation)	-0.51 (± 1.377)	-0.63 (± 1.119)		

Notes:

[89] - ITT Population. Only participants with data available at specific time point were analyzed.

[90] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in hematocrit at Week 24

End point title	Change from Baseline in hematocrit at Week 24
-----------------	---

End point description:

Hematocrit is the ratio of the volume of red blood cells to the total volume of blood. Baseline value for hematocrit is the pre-dose value on Day 1. Change from Baseline in hematocrit was calculated as the Week 24 value minus the Baseline value.

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

End point timeframe:

Baseline (Day 1) and Week 24

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30 ^[91]	20 ^[92]	29 ^[93]	28 ^[94]
Units: Fraction of 1				
arithmetic mean (standard deviation)	-0.0028 (± 0.04358)	-0.0096 (± 0.04073)	0.002 (± 0.03579)	0.0043 (± 0.04254)

Notes:

[91] - ITT Population. Only participants with data available at specific time point were analyzed.

[92] - ITT Population. Only participants with data available at specific time point were analyzed.

[93] - ITT Population. Only participants with data available at specific time point were analyzed.

[94] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863	GSK1278863		
------------------	------------	------------	--	--

	10 mg	12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26 ^[95]	13 ^[96]		
Units: Fraction of 1				
arithmetic mean (standard deviation)	-0.0021 (± 0.02678)	0.0108 (± 0.03557)		

Notes:

[95] - ITT Population. Only participants with data available at specific time point were analyzed.

[96] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in red blood cells at Week 24

End point title	Change from Baseline in red blood cells at Week 24
End point description:	
Baseline value for red blood cells is the pre-dose value on Day 1. Change from Baseline in red blood cells was calculated as the Week 24 value minus the Baseline value.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Week 24	

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30 ^[97]	20 ^[98]	29 ^[99]	28 ^[100]
Units: 10 ¹² cells/Liter				
arithmetic mean (standard deviation)	0.01 (± 0.46)	-0.06 (± 0.396)	0.04 (± 0.374)	0.07 (± 0.399)

Notes:

[97] - ITT Population. Only participants with data available at specific time point were analyzed.

[98] - ITT Population. Only participants with data available at specific time point were analyzed.

[99] - ITT Population. Only participants with data available at specific time point were analyzed.

[100] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26 ^[101]	13 ^[102]		
Units: 10 ¹² cells/Liter				
arithmetic mean (standard deviation)	0.03 (± 0.3)	0.17 (± 0.366)		

Notes:

[101] - ITT Population. Only participants with data available at specific time point were analyzed.

[102] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in reticulocyte count at Week 24

End point title	Change from Baseline in reticulocyte count at Week 24
End point description:	
A reticulocyte count is a blood test that measures the percentage of reticulocytes in the blood. Reticulocytes are slightly immature red blood cells. Baseline value for reticulocyte count is the pre-dose value on Day 1. Change from Baseline in reticulocyte count was calculated as the Week 24 value minus the Baseline value.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Week 24	

End point values	Control	GSK1278863 4 mg	GSK1278863 6 mg	GSK1278863 8 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31 ^[103]	20 ^[104]	30 ^[105]	28 ^[106]
Units: Percentage of reticulocytes in blood				
arithmetic mean (standard deviation)	0.4 (± 0.663)	0.16 (± 1.162)	0.18 (± 0.571)	0.03 (± 0.684)

Notes:

[103] - ITT Population. Only participants with data available at specific time point were analyzed.

[104] - ITT Population. Only participants with data available at specific time point were analyzed.

[105] - ITT Population. Only participants with data available at specific time point were analyzed.

[106] - ITT Population. Only participants with data available at specific time point were analyzed.

End point values	GSK1278863 10 mg	GSK1278863 12 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26 ^[107]	12 ^[108]		
Units: Percentage of reticulocytes in blood				
arithmetic mean (standard deviation)	-0.15 (± 0.838)	0.1 (± 0.527)		

Notes:

[107] - ITT Population. Only participants with data available at specific time point were analyzed.

[108] - ITT Population. Only participants with data available at specific time point were analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from the start of study treatment and until the follow up contact (up to 28 weeks).

Adverse event reporting additional description:

On-treatment SAEs and non-serious AEs were reported for the Safety population consisted of all participants who received at least one dose of study drug.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	17.0
--------------------	------

Reporting groups

Reporting group title	Control
-----------------------	---------

Reporting group description:

Participants received placebo once daily for the first 4 weeks and thereafter received open label rhEPO as required to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.

Reporting group title	GSK1278863 4 mg
-----------------------	-----------------

Reporting group description:

Participants received GSK1278863 4 milligrams (mg) once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.

Reporting group title	GSK1278863 6 mg
-----------------------	-----------------

Reporting group description:

Participants received GSK1278863 6 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.

Reporting group title	GSK1278863 8 mg
-----------------------	-----------------

Reporting group description:

Participants received GSK1278863 8 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.

Reporting group title	GSK1278863 10 mg
-----------------------	------------------

Reporting group description:

Participants received GSK1278863 10 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.

Reporting group title	GSK1278863 12 mg
-----------------------	------------------

Reporting group description:

Participants received GSK1278863 12 mg once daily for the first 4 weeks and thereafter, if necessary the dose was adjusted every four weeks to achieve Hgb within the range of 10.0-11.5 g/dL for the remaining 20 weeks.

Serious adverse events	Control	GSK1278863 4 mg	GSK1278863 6 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 39 (28.21%)	10 / 39 (25.64%)	8 / 40 (20.00%)
number of deaths (all causes)	0	2	1
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasma cell myeloma			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural mesothelioma			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Steal syndrome			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Superior vena cava stenosis subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Amyloidosis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Reproductive system and breast disorders			
Oligomenorrhoea			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine inflammation			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			

subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Troponin I increased			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Arteriovenous fistula site haemorrhage			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous fistula thrombosis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complications of transplanted kidney			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dialysis related complication			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft thrombosis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Shunt stenosis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt thrombosis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			

subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sick sinus syndrome			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastric polyps			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal angiodysplasia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal polyp			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			

subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	GSK1278863 8 mg	GSK1278863 10 mg	GSK1278863 12 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 39 (20.51%)	11 / 40 (27.50%)	1 / 19 (5.26%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			

subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasma cell myeloma			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural mesothelioma			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	1 / 39 (2.56%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Steal syndrome			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava stenosis			

subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Amyloidosis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Oligomenorrhoea			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine inflammation			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			

subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Troponin I increased			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Arteriovenous fistula site haemorrhage			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriovenous fistula thrombosis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complications of transplanted kidney			
subjects affected / exposed	1 / 39 (2.56%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dialysis related complication			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft thrombosis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Shunt stenosis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt thrombosis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			

subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 39 (2.56%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sick sinus syndrome			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastric polyps			
subjects affected / exposed	1 / 39 (2.56%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal angiodysplasia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal polyp			
subjects affected / exposed	1 / 39 (2.56%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			

subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Control	GSK1278863 4 mg	GSK1278863 6 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 39 (43.59%)	28 / 39 (71.79%)	17 / 40 (42.50%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Hypertension			

subjects affected / exposed	1 / 39 (2.56%)	6 / 39 (15.38%)	0 / 40 (0.00%)
occurrences (all)	1	6	0
Hypotension			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	3 / 40 (7.50%)
occurrences (all)	0	2	3
Chills			
subjects affected / exposed	1 / 39 (2.56%)	1 / 39 (2.56%)	0 / 40 (0.00%)
occurrences (all)	1	1	0
Face oedema			
subjects affected / exposed	2 / 39 (5.13%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	2 / 40 (5.00%)
occurrences (all)	1	0	2
Pain			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	1 / 40 (2.50%)
occurrences (all)	0	1	1
Dyspnoea			
subjects affected / exposed	1 / 39 (2.56%)	2 / 39 (5.13%)	0 / 40 (0.00%)
occurrences (all)	1	2	0
Epistaxis			

subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 39 (0.00%) 0	2 / 40 (5.00%) 2
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 39 (0.00%) 0	0 / 40 (0.00%) 0
Blood pressure increased subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 39 (2.56%) 1	3 / 40 (7.50%) 3
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 39 (0.00%) 0	0 / 40 (0.00%) 0
Haemoglobin decreased subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	1 / 39 (2.56%) 1	0 / 40 (0.00%) 0
Injury, poisoning and procedural complications			
Arteriovenous fistula thrombosis subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 39 (0.00%) 0	0 / 40 (0.00%) 0
Dialysis related complication subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 39 (2.56%) 1	0 / 40 (0.00%) 0
Procedural site reaction subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 39 (0.00%) 0	0 / 40 (0.00%) 0
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 39 (2.56%) 1	2 / 40 (5.00%) 2
Headache subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	4 / 39 (10.26%) 6	1 / 40 (2.50%) 1
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	2 / 39 (5.13%) 3	2 / 40 (5.00%) 3

Eye disorders			
Cataract			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	1 / 40 (2.50%)
occurrences (all)	0	2	1
Periorbital oedema			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Retinal artery embolism			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 39 (0.00%)	4 / 39 (10.26%)	0 / 40 (0.00%)
occurrences (all)	0	6	0
Diarrhoea			
subjects affected / exposed	2 / 39 (5.13%)	5 / 39 (12.82%)	2 / 40 (5.00%)
occurrences (all)	2	7	2
Dyspepsia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences (all)	2	0	1
Nausea			
subjects affected / exposed	0 / 39 (0.00%)	6 / 39 (15.38%)	3 / 40 (7.50%)
occurrences (all)	0	7	4
Toothache			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
Vomiting			
subjects affected / exposed	1 / 39 (2.56%)	3 / 39 (7.69%)	2 / 40 (5.00%)
occurrences (all)	1	3	2
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Pruritus			

subjects affected / exposed	1 / 39 (2.56%)	3 / 39 (7.69%)	0 / 40 (0.00%)
occurrences (all)	2	3	0
Pruritus generalised			
subjects affected / exposed	2 / 39 (5.13%)	0 / 39 (0.00%)	1 / 40 (2.50%)
occurrences (all)	2	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	2 / 40 (5.00%)
occurrences (all)	0	1	4
Back pain			
subjects affected / exposed	4 / 39 (10.26%)	0 / 39 (0.00%)	2 / 40 (5.00%)
occurrences (all)	4	0	2
Muscle spasms			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	2 / 40 (5.00%)
occurrences (all)	0	2	10
Myalgia			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	2 / 40 (5.00%)
occurrences (all)	0	2	3
Osteoarthritis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	3
Device related infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	5 / 39 (12.82%)	5 / 39 (12.82%)	6 / 40 (15.00%)
occurrences (all)	8	10	9
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 39 (0.00%) 0	0 / 40 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 39 (2.56%) 1	0 / 40 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	2 / 39 (5.13%) 2	1 / 40 (2.50%) 1
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	2 / 39 (5.13%) 2	1 / 40 (2.50%) 1
Hypocalcaemia subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 39 (0.00%) 0	0 / 40 (0.00%) 0

Non-serious adverse events	GSK1278863 8 mg	GSK1278863 10 mg	GSK1278863 12 mg
Total subjects affected by non-serious adverse events subjects affected / exposed	25 / 39 (64.10%)	21 / 40 (52.50%)	6 / 19 (31.58%)
Vascular disorders Haematoma subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	2 / 40 (5.00%) 2	0 / 19 (0.00%) 0
Hypertension subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	4 / 40 (10.00%) 6	0 / 19 (0.00%) 0
Hypotension subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	2 / 40 (5.00%) 2	0 / 19 (0.00%) 0
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 40 (0.00%) 0	0 / 19 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 40 (0.00%) 0	1 / 19 (5.26%) 1
Face oedema			

subjects affected / exposed	1 / 39 (2.56%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	0 / 39 (0.00%)	2 / 40 (5.00%)	0 / 19 (0.00%)
occurrences (all)	0	3	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 39 (0.00%)	2 / 40 (5.00%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Oedema peripheral			
subjects affected / exposed	2 / 39 (5.13%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences (all)	3	1	0
Pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 39 (5.13%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences (all)	2	2	0
Dyspnoea			
subjects affected / exposed	1 / 39 (2.56%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 39 (0.00%)	2 / 40 (5.00%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Blood pressure increased			
subjects affected / exposed	2 / 39 (5.13%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Haemoglobin decreased			

subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	2 / 40 (5.00%) 2	0 / 19 (0.00%) 0
Injury, poisoning and procedural complications			
Arteriovenous fistula thrombosis subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	2 / 40 (5.00%) 2	0 / 19 (0.00%) 0
Dialysis related complication subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	2 / 40 (5.00%) 3	0 / 19 (0.00%) 0
Procedural site reaction subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 40 (0.00%) 0	1 / 19 (5.26%) 1
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 40 (0.00%) 0	0 / 19 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	2 / 40 (5.00%) 8	0 / 19 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 40 (0.00%) 0	0 / 19 (0.00%) 0
Eye disorders			
Cataract subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 40 (0.00%) 0	1 / 19 (5.26%) 1
Periorbital oedema subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 40 (0.00%) 0	0 / 19 (0.00%) 0
Retinal artery embolism subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 40 (0.00%) 0	1 / 19 (5.26%) 1
Vitreous floaters subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 40 (0.00%) 0	1 / 19 (5.26%) 1

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	7 / 39 (17.95%)	2 / 40 (5.00%)	1 / 19 (5.26%)
occurrences (all)	10	2	1
Dyspepsia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 39 (5.13%)	1 / 40 (2.50%)	1 / 19 (5.26%)
occurrences (all)	2	5	1
Toothache			
subjects affected / exposed	2 / 39 (5.13%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Vomiting			
subjects affected / exposed	1 / 39 (2.56%)	2 / 40 (5.00%)	0 / 19 (0.00%)
occurrences (all)	1	2	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	2 / 39 (5.13%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Pruritus			
subjects affected / exposed	1 / 39 (2.56%)	2 / 40 (5.00%)	0 / 19 (0.00%)
occurrences (all)	1	2	0
Pruritus generalised			
subjects affected / exposed	0 / 39 (0.00%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 39 (5.13%)	1 / 40 (2.50%)	0 / 19 (0.00%)
occurrences (all)	2	2	0
Back pain			
subjects affected / exposed	1 / 39 (2.56%)	4 / 40 (10.00%)	0 / 19 (0.00%)
occurrences (all)	1	6	0

Muscle spasms subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	1 / 40 (2.50%) 1	0 / 19 (0.00%) 0
Myalgia subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	1 / 40 (2.50%) 1	0 / 19 (0.00%) 0
Osteoarthritis subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	2 / 40 (5.00%) 3	0 / 19 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 3	1 / 40 (2.50%) 2	0 / 19 (0.00%) 0
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	1 / 40 (2.50%) 1	0 / 19 (0.00%) 0
Device related infection subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	0 / 40 (0.00%) 0	1 / 19 (5.26%) 1
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 4	4 / 40 (10.00%) 5	1 / 19 (5.26%) 1
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 40 (2.50%) 1	1 / 19 (5.26%) 1
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	2 / 40 (5.00%) 3	0 / 19 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 40 (0.00%) 0	0 / 19 (0.00%) 0
Hyperkalaemia subjects affected / exposed occurrences (all)	4 / 39 (10.26%) 4	1 / 40 (2.50%) 1	0 / 19 (0.00%) 0
Hypocalcaemia			

subjects affected / exposed	2 / 39 (5.13%)	0 / 40 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 September 2013	To revise the GSK1278863 Dose Adjustment Algorithm as requested by the United States Food and Drug Administration (FDA) and to clarify and correct language throughout.
04 October 2013	This amendment was for Japan only. To revise the Time and Events Table to add a HemoCue at Week 2 as requested by the Pharmaceuticals and Medical Device Agency (Japan) (PMDA).
06 January 2014	This amendment is for France only. To revise the lower threshold for the hemoglobin inclusion criterion to 10.0 g/dL for sites in France as requested by the National Agency for the Safety of Medicine and Health Products in France.
23 January 2014	To revise lipid and biomarker assessments, to add reconfirmation of the corrected QT (QTc) inclusion criterion at Day 1, to remove requirement for male contraception, to allow an interim cut of data to be taken to facilitate dose modelling, and to make minor clarifications throughout.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported