Clinical trial results:
A 24-week, Phase IIB, Randomized, Controlled, Parallel group, Multi-center Study to Evaluate the Safety and Efficacy of GSK1278863 in Subjects with Anemia Associated with Chronic Kidney Diseases who are not on Dialysis.

Summary

EudraCT number	2013-002681-39
Trial protocol	ES SE GB CZ HU DK
Global end of trial date	14 May 2015

Results information

Result version number	v1
This version publication date	15 May 2016
First version publication date	15 May 2016

Trial information

Trial identification

Sponsor protocol code	113747

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01977573
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Middlesex, Brentford, United Kingdom,
Public contact	GlaxoSmithKline, GlaxoSmithKline, +1 8664357343,
Scientific contact	GlaxoSmithKline, GlaxoSmithKline, +1 8664357343,

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	07 August 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will be conducted in approximately 228 subjects with anemia associated with CKD who are not on dialysis. Two groups of subjects will be enrolled into the study: Group 1: recombinant human erythropoietin (rhEPO) naive subjects; Group 2: rhEPO users, who are currently receiving rhEPO. Subjects who are rhEPO naive will be randomized to receive either GSK1278863 once daily (QD) or rhEPO in a 3:1 fashion; subjects who are receiving an rhEPO before enrolling (rhEPO users) will be randomized in a 1:1 fashion to GSK1278863 QD or to the control arm. For those randomized to the control arm, the decision around whether the subject requires rhEPO, the selection of the type of rhEPO (if needed) and the choice of rhEPO dose to achieve and maintain Hgb concentrations within the target range should be based on Investigator clinical judgment, with the historical rhEPO dose and the current Hgb value being considered.

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Czech Republic: 20
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Hungary: 6
Country: Number of subjects enrolled	Korea, Republic of: 19
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Russian Federation: 38
Country: Number of subjects enrolled	Spain: 24
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	United States: 45
Country: Number of subjects enrolled	Japan: 42

Worldwide total number of subjects	252
EEA total number of subjects	86

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)	93
From 65 to 84 years	149
85 years and over	10

Subject disposition

Recruitment

Recruitment details:

Two groups of participants (par.) were enrolled in this study. Group 1 consisted of recombinant human erythropoietin (rhEPO)-naive par. whereas Group 2 consisted of rhEPO users.

Pre-assignment

Screening details:

Post screening, eligible par. were randomized to receive either GSK1278863 once a day (QD) or to the Control arm in a 3:1 fashion in Group 1 and 1:1 fashion in Group 2.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	rhEPO-Naive GSK1278863

Arm description:

RhEPO-naive participants were randomly assigned to receive GSK1278863 QD for 24 weeks. Participants were blinded to the dose-level they received throughout the study. At Week 24, participants stopped taking GSK1278863, and returned for the follow-up visit at Week 28.

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

Dosage and administration details:

Participants received GSK1278863 once daily for 24 weeks and were blinded to the dose-level they received throughout the study. Blinding was maintained by providing the required dose in an appropriate combination of GSK1278863 and/or placebo tablets.

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

Dosage and administration details:

Participants received GSK1278863 once daily for 24 weeks and were blinded to the dose-level they received throughout the study. Blinding was maintained by providing the required dose in an appropriate combination of GSK1278863 and/or placebo tablets.

Arm title	rhEPO-Naive Control

Arm description:

RhEPO-naive participants were randomly assigned to receive open-label rhEPO (epoetins or their biosimilars, or darbepoetin) as necessary per standard of care, based on the Investigator’s clinical judgment, for 24 weeks. At Week 24, participants stopped taking rhEPO (if applicable) and remained off rhEPO or other Erythropoiesis Stimulating Agents (ESA) until at least the follow-up visit at Week 28.

Arm type	Active comparator

Investigational medicinal product name	Standard of care including RhEPO if needed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Cutaneous use, Intravenous use

Dosage and administration details:

Standard of care provided accordingly.

Arm title	rhEPO-User GSK1278863

Arm description:

RhEPO users were randomly assigned to receive GSK1278863 QD for 24 weeks. Participants were blinded to the dose-level they received throughout the study. At Week 24, participants stopped taking GSK1278863 and did not re-start rhEPO or other ESAs until after the follow-up visit at Week 28 (except in cases where there was a compelling clinical reason [based on Investigator's opinion] to start rhEPO therapy).

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

Dosage and administration details:

Participants received GSK1278863 once daily for 24 weeks and were blinded to the dose-level they received throughout the study. Blinding was maintained by providing the required dose in an appropriate combination of GSK1278863 and/or placebo tablets.

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

Dosage and administration details:

Participants received GSK1278863 once daily for 24 weeks and were blinded to the dose-level they received throughout the study. Blinding was maintained by providing the required dose in an appropriate combination of GSK1278863 and/or placebo tablets.

Arm title	rhEPO-User Control

Arm description:

RhEPO users were randomly assigned to receive rhEPO (epoetins or their biosimilars, or darbepoetin) as necessary per standard of care, based on the Investigator clinical judgment, for 24 weeks. Participants were allowed to continue rhEPO therapy between Week 24 and 28.

Arm type	Active comparator
Investigational medicinal product name	Stardard of care include RhEPO if needed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Cutaneous use, Intravascular use

Dosage and administration details:

Standard of care provided accordingly.

Number of subjects in period 1	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863
Started	136	44	36
Completed	116	41	32
Not completed	20	3	4
Physician decision	1	-	-
Consent withdrawn by subject	6	1	1
Adverse event, non-fatal	7	-	2
Lost to follow-up	1	-	-
Protocol deviation	3	1	-
reached defined stopping criteria	2	1	-
Protocol-Defined Stopping Criteria	-	-	1

Number of subjects in period 1	rhEPO-User Control
Started	36
Completed	33
Not completed	3
Physician decision	-
Consent withdrawn by subject	1
Adverse event, non-fatal	1
Lost to follow-up	1
Protocol deviation	-
reached defined stopping criteria	-
Protocol-Defined Stopping Criteria	-

Baseline characteristics

Reporting groups	
Reporting group title	rhEPO-Naive GSK1278863
Reporting group description:	
RhEPO-naive participants were randomly assigned to receive GSK1278863 QD for 24 weeks. Participants were blinded to the dose-level they received throughout the study. At Week 24, participants stopped taking GSK1278863, and returned for the follow-up visit at Week 28.	
Reporting group title	rhEPO-Naive Control
Reporting group description:	
RhEPO-naive participants were randomly assigned to receive open-label rhEPO (epoetins or their biosimilars, or darbepoetin) as necessary per standard of care, based on the Investigator's clinical judgment, for 24 weeks. At Week 24, participants stopped taking rhEPO (if applicable) and remained off rhEPO or other Erythropoiesis Stimulating Agents (ESA) until at least the follow-up visit at Week 28.	
Reporting group title	rhEPO-User GSK1278863
Reporting group description:	
RhEPO users were randomly assigned to receive GSK1278863 QD for 24 weeks. Participants were blinded to the dose-level they received throughout the study. At Week 24, participants stopped taking GSK1278863 and did not re-start rhEPO or other ESAs until after the follow-up visit at Week 28 (except in cases where there was a compelling clinical reason [based on Investigator's opinion] to start rhEPO therapy).	
Reporting group title	rhEPO-User Control
Reporting group description:	
RhEPO users were randomly assigned to receive rhEPO (epoetins or their biosimilars, or darbepoetin) as necessary per standard of care, based on the Investigator clinical judgment, for 24 weeks. Participants were allowed to continue rhEPO therapy between Week 24 and 28.	

Reporting group values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863
Number of subjects	136	44	36
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	67.7	64.5	61.9
standard deviation	± 12.39	± 14.11	± 14.65
Gender categorical Units: Subjects			
Female	56	20	17
Male	80	24	19
Race, customized Units: Subjects			
White	89	30	25
African American	14	2	2
Asian	33	12	9

Reporting group values	rhEPO-User Control	Total	
Number of subjects	36	252	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	66.7		
standard deviation	± 12.89	-	
Gender categorical Units: Subjects			
Female	13	106	
Male	23	146	
Race, customized Units: Subjects			
White	19	163	
African American	4	22	
Asian	13	67	

End points

End points reporting groups

Reporting group title	rhEPO-Naive GSK1278863

Reporting group description:

RhEPO-naive participants were randomly assigned to receive GSK1278863 QD for 24 weeks. Participants were blinded to the dose-level they received throughout the study. At Week 24, participants stopped taking GSK1278863, and returned for the follow-up visit at Week 28.

Reporting group title	rhEPO-Naive Control

Reporting group description:

RhEPO-naive participants were randomly assigned to receive open-label rhEPO (epoetins or their biosimilars, or darbepoetin) as necessary per standard of care, based on the Investigator's clinical judgment, for 24 weeks. At Week 24, participants stopped taking rhEPO (if applicable) and remained off rhEPO or other Erythropoiesis Stimulating Agents (ESA) until at least the follow-up visit at Week 28.

Reporting group title	rhEPO-User GSK1278863

Reporting group description:

RhEPO users were randomly assigned to receive GSK1278863 QD for 24 weeks. Participants were blinded to the dose-level they received throughout the study. At Week 24, participants stopped taking GSK1278863 and did not re-start rhEPO or other ESAs until after the follow-up visit at Week 28 (except in cases where there was a compelling clinical reason [based on Investigator's opinion] to start rhEPO therapy).

Reporting group title	rhEPO-User Control

Reporting group description:

RhEPO users were randomly assigned to receive rhEPO (epoetins or their biosimilars, or darbepoetin) as necessary per standard of care, based on the Investigator clinical judgment, for 24 weeks. Participants were allowed to continue rhEPO therapy between Week 24 and 28.

Primary: Summary of hemoglobin (Hgb) concentration at Week 24

End point title	Summary of hemoglobin (Hgb) concentration at Week 24[1]

End point description:

The original Hgb target range was 9.0 to 10.5 g/dL for Group 1- rhEPO naive participants with a stable baseline Hgb of 8.0-10.0 g/dL and for Group 2- rhEPO users with a stable baseline Hgb of 9.0-10.5. The amended Hgb target range was 10.0 to 11.5 g/dL for Group 1- rhEPO naive participants with a stable baseline Hgb of 8.0-11.0 g/dL and Group 2- rhEPO users with a stable baseline Hgb of 9.0-11.5 g/dL. Data are presented for those participants following the original criteria ("Original") and those following the amended ("Amended") criteria. Intent-to-Treat (ITT): The ITT population consisted of all randomized participants who received at least one dose of study drug, had a Baseline and at least one corresponding on-treatment assessment. Only participants who were available at the indicated time point were analyzed.

End point type	Primary

End point timeframe:

Week 24

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There was no statistical information to present for this outcome measure.

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	43	33	36
Units: grams per deciliter				
arithmetic mean (standard deviation)				
Original n=45,15,19,13	10.2 (± 0.906)	10.64 (± 0.664)	10.03 (± 0.522)	10.66 (± 0.62)

Amended n=61,21,11,17	10.96 (± 1.044)	11.05 (± 1.144)	10.42 (± 0.827)	10.86 (± 1.182)

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of participants with hemoglobin (Hgb) in the target range at Week 24

End point description:

Target range is defined as: Original Hgb Criteria of 9.0 to 10.5 gram/deciliter (g/dL), and Amended Hgb Criteria of 10.0 to 11.5 g/dL. Sites in the USA used 9.0 to 10.5 g/dL. ITT population. Only participants who were available at the indicated time point were analyzed.

End point type	Secondary

End point timeframe:

Week 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	36	30	30
Units: participants				
number (not applicable)	78	20	22	19

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 Hgb stopping criteria was a value of <7.5 mg/dL obtained on-site via a validated point-of-care Hgb measurement device, which necessitated permanent discontinuation of the study medication. None of the participants met the stopping criteria therefore there is no data to present for this outcome measure. ITT population.

End point type	Secondary

End point timeframe:

Over a period of 24 Weeks

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	136	44	36	36
Units: Participants				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from Baseline in hepcidin concentration at Week 24

End point title	Percent change from Baseline in hepcidin concentration at Week 24

End point description:

Baseline is the last pre-dose hepcidin value. Percent change was calculated as 100 multiplied by (exponential of mean change on log scale minus 1). Change was calculated by subtracting the Baseline value from the Week 24 value. Intent-to-Treat (ITT) population consisted all randomized participants who received at least one dose of study drug, had a Baseline and at least one corresponding on-treatment assessment. Only participants with available hepcidin values at Baseline and Week 24 were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	35	30	29
Units: percent change in Hepcidin				
geometric mean (confidence interval 95%)	-19.27 (-28.1 to -9.36)	6.67 (-13.62 to 31.72)	-9.87 (-28.59 to 13.76)	-17.12 (-33.22 to 2.86)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean maximum observed change from Baseline in serum erythropoietin (EPO)

End point title	Mean maximum observed change from Baseline in serum erythropoietin (EPO)

End point description:

Baseline is the last pre-dose EPO value. Change from Baseline in EPO at each visit was calculated and maximum change from baseline was recorded. Change from Baseline is the post-dose EPO value minus the Baseline EPO value. ITT population. Only participants having a Baseline EPO measurement and at least one post-baseline EPO measurement were analyzed

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	42	33	36
Units: International Units per liter				
arithmetic mean (standard deviation)	7.27 (± 12.744)	27.05 (± 94.999)	3.69 (± 20.554)	25.85 (± 38.89)

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:

Baseline is the last pre-dose VEGF value. Change from Baseline in VEGF was calculated for each visit by subtracting the Baseline value from each post-dose value. Percent change from Baseline was calculated for each visit as 100 multiplied by (exponential of mean change on log scale minus 1). The maximum observed percent change from Baseline was recorded.

End point type	Secondary

End point timeframe:

Baseline and up to Week 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123[2]	42[3]	33[4]	3[5]
Units: percent change in VEGF concentration				
geometric mean (confidence interval 95%)	76.36 (59.46 to 95.06)	26.84 (1.73 to 58.15)	49.99 (28.28 to 75.39)	40.85 (19.14 to 66.52)

Notes:

[2] - ITT population. Only pars with data available at Baseline and a maximum observed change analyzed

[3] - ITT population. Only pars with data available at Baseline and a maximum observed change analyzed

[4] - ITT population. Only pars with data available at Baseline and a maximum observed change analyzed

[5] - ITT population. Only pars with data available at Baseline and a maximum observed change analyzed6

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of time within, below, and above hemoglobin (Hgb) target range, between Weeks 12 and 24

End point title	Percentage of time within, below, and above hemoglobin (Hgb) target range, between Weeks 12 and 24

End point description:

The number of days a participant's Hgb was within target range was calculated by estimating (using linear interpolation) the number of days within target range between two scheduled Hgb visits. Percentage of time within range for a participant was calculated by dividing the total number of days that Hgb was within range during Weeks 12 to 24 by the total number of days the participant remained on treatment during Weeks 12 to 24. Similary, percent of time above and below Hgb target range was calculated. Target range was defined as: Original Hgb Criteria of 9.0 to 10.5 g/dL, and Amended Hgb Criteria of 10.0 to 11.5 g/dL. Sites in the USA used 9.0 to 10.5 g/dL. ITT population. Only participants with data available at specific time points were analyzed.

End point type	Secondary

End point timeframe:

Weeks 12 to 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	38	30	32
Units: percentage of days				
arithmetic mean (standard deviation)				
Percentage of time within target range	68.99 (± 34.612)	51.01 (± 41.403)	75.06 (± 32.485)	61.29 (± 43.352)
Percentage of time above target range	22.84 (± 33.825)	45.1 (± 42.579)	17.96 (± 28.809)	31.1 (± 41.683)
Percentage of time below target range	8.17 (± 20.301)	3.89 (± 16.175)	6.98 (± 21.118)	7.61 (± 25.113)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in ferritin concentration at Week 24

End point title	Change from Baseline in ferritin concentration at Week 24

End point description:

Baseline is the last pre-dose ferritin value. Change was calculated by subtracting the Baseline value from the Week 24 value. ITT population. Only participants with data available at specific time point were analyzed. ITT population. Only participants with data available at specific time point were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	108	36	30	30
Units: micrograms per liter				
arithmetic mean (standard deviation)	-30.8 (± 110.5)	-2.4 (± 77.06)	-63.4 (± 141.93)	-20.4 (± 63.38)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in transferrin concentration at Week 24

End point title	Change from Baseline in transferrin concentration at Week 24

End point description:

Baseline is the last pre-dose transferrin value. Change from Baseline in transferrin was calculated by subtracting the Baseline value from the Week 24 value. ITT population. Only participants with data available at specific time point were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	36	30	30
Units: grams per liter				
arithmetic mean (standard deviation)	0.077 (± 0.3577)	-0.008 (± 0.2694)	0.171 (± 0.4124)	0.018 (± 0.2395)

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 a ratio of serum iron and total iron-binding capacity. Baseline is the last pre-dose transferrin saturation value. Percent change was calculated as 100 multiplied by (exponential of mean change on log scale minus 1). Change was calculated by subtracting the Baseline value from the post-dose value. ITT population. Only participants with data available at specific time point were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	35	30	30
Units: percent change				
geometric mean (confidence interval 95%)	-1.1 (-8 to 6.4)	12.3 (2.2 to 23.3)	-15.7 (-26.8 to -3)	11.4 (-14.7 to 45.6)

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 is the last pre-dose total iron value. Change from Baseline was calculated by subtracting the Baseline value from the Week 24 value. ITT population. Only participants with available total iron values at Baseline and Week 24 were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	36	30	30
Units: micromoles per liter				
arithmetic mean (standard deviation)	1 (± 5.01)	2.5 (± 5.98)	-1.8 (± 5.54)	0.7 (± 8.36)

Statistical analyses

No statistical analyses for this end point

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

End point title	Change from Baseline in total iron binding capacity (TIBC) at Week 24

End point description:

TIBC measures the blood's capacity to bind iron with transferrin. Baseline is the last pre-dose TIBC value. Change from Baseline in TIBC was calculated by subtracting the Baseline value from the Week 24 value. ITT population. Only participants with data available at specific timepoint were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	35	30	30
Units: micromoles per liter				
arithmetic mean (standard deviation)	3.2 (± 6.46)	0.1 (± 5.17)	3 (± 9.44)	-1 (± 6.69)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in reticulocyte hemoglobin (CHr) at Week 24

End point title	Change from Baseline in reticulocyte hemoglobin (CHr) at Week 24

End point description:

Reticulocytes are slightly immature red blood cells. Reticulocyte Hgb content is used to differentiate iron deficiency from other causes of anemia. Baseline is the last pre-dose CHr value. Change from Baseline in reticulocyte Hgb was calculated by subtracting the Baseline value from the post-dose value. ITT population. Only participants with data available at specific timepoint were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	108	35	30	30
Units: picogram				
arithmetic mean (standard deviation)	-0.19 (± 1.109)	-0.33 (± 1.085)	-0.32 (± 0.864)	-0.19 (± 1.546)

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:

Baseline is the last pre-dose hematocrit value. Change from Baseline was calculated by subtracting the Baseline value from the Week 24 value. ITT population. Only participants with data available at specific timepoint were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	111	36	30	30
Units: percentage change in Fraction of 1				
arithmetic mean (standard deviation)	2.64 (± 3.389)	3.13 (± 3.245)	-0.66 (± 3.074)	2.09 (± 3.243)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in red blood cell count at Week 24

End point title	Change from Baseline in red blood cell count at Week 24

End point description:

Baseline is the last pre-dose red blood cell count. Change from Baseline in red blood cell count was calculated by subtracting the Baseline count from the post-dose count.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	111[6]	36[7]	30[8]	30[9]
Units: 10^12 cells per liter				
arithmetic mean (standard deviation)	0.28 (± 0.377)	0.34 (± 0.365)	-0.08 (± 0.312)	0.22 (± 0.318)

Notes:

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

[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.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in reticulocyte cell count at Week 24

End point title	Change from Baseline in reticulocyte cell count at Week 24

End point description:

Reticulocyte count is a blood test that measures the percentage of reticulocytes in the blood. Reticulocytes are slightly immature red blood cells. Baseline is the last pre-dose red reticulocyte count. Change from Baseline in reticulocyte cell count was calculated by subtracting the Baseline count from the Week 24 count. ITT population. Only participants with data available at specific timepoint were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	111	36	30	31
Units: percentage of reticulocytes				
arithmetic mean (standard deviation)	-0.02 (± 0.551)	-0.12 (± 0.648)	0.27 (± 0.892)	-0.09 (± 0.755)

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of GSK1278863 and relevant metabolites as a population pharmacokinetic endpoint

End point title	Concentration of GSK1278863 and relevant metabolites as a population pharmacokinetic endpoint[10]

End point description:

Blood samples were collected for individual plasma GSK1278863 and metabolite (GSK2391220, GSK2487818, GSK2506102, GSK2531398, GSK2531401, and GSK2531403) concentration measurement on Day 1 (pre-dose), Wk 4 (6-12 hour, 7-13 hour, 8-14 hour, 9-15 hour post-dose), and Wk 20 (pre-dose, 1 hour, 2 hour, 3 hour post-dose). Participants available in each arm at the specified time points have been presented. Pharmacokinetics (PK) population: All participants from whom a PK sample was obtained and analyzed. This population did not include participants from the control groups.

End point type	Secondary

End point timeframe:

Day 1 (pre-dose), Week (Wk) 4 (6-12 hour, 7-13 hour, 8-14 hour, 9-15 hour post-dose), and Wk 20 (pre-dose, 1 hour, 2 hour, 3 hour post-dose)

Notes:

[10] - 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: Control groups were not measured for this endpoint, so there are not statistics to present.

End point values	rhEPO-Naive GSK1278863	rhEPO-User GSK1278863		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	35		
Units: nanograms per milliliter				
arithmetic mean (standard deviation)				
GSK1278863, Day 1, Pre-Dose, n=128, 35	0 (± 0)	0 (± 0)		

GSK1278863, Wk 4, 6-12 hour Post-Dose, n=116, 31	2 (± 5.18)	1.1 (± 1.69)		
GSK1278863, Wk 4, 7-13 hour Post-Dose, n=117, 31	2.3 (± 7.06)	0.8 (± 1.22)		
GSK1278863, Wk 4, 8-14 hour Post-Dose, n=116, 31	1.6 (± 4.93)	1.6 (± 5.49)		
GSK1278863, Wk 4, 9-15 hour Post-Dose, n=116, 31	1.4 (± 4.52)	1.6 (± 4.6)		
GSK1278863, Wk 20, Pre-Dose, n=111, 29	0.6 (± 3.07)	0.3 (± 0.92)		
GSK1278863, Wk 20, 1 hour Post-Dose, n=110, 28	22.8 (± 35.93)	19.8 (± 19.66)		
GSK1278863, Wk 20, 2 hour Post-Dose, n=109, 29	17 (± 28.57)	19.4 (± 21.92)		
GSK1278863, Wk 20, 3 hour Post-Dose, n=109, 29	11.6 (± 19.56)	13.9 (± 19.12)		
GSK2391220, Day 1, Pre-Dose, n=128, 35	0 (± 0)	0 (± 0)		
GSK2391220, Wk 4, 6-12 hour Post-Dose, n=116, 31	3.2 (± 5.21)	3.7 (± 2.89)		
GSK2391220, Wk 4, 7-13 hour Post-Dose, n=117, 31	3.1 (± 5.67)	3.2 (± 2.43)		
GSK2391220, Wk 4, 8-14 hour Post-Dose, n=116, 31	2.8 (± 5.01)	2.9 (± 2.54)		
GSK2391220, Wk 4, 9-15 hour Post-Dose, n=116, 31	2.6 (± 4.89)	3.1 (± 2.76)		
GSK2391220, Wk 20, Pre-Dose, n=111, 29	1 (± 2.06)	0.8 (± 0.98)		
GSK2391220, Wk 20, 1 hour Post-Dose, n=110, 28	2.1 (± 3.52)	1.6 (± 1.39)		
GSK2391220, Wk 20, 2 hour Post-Dose, n=109, 29	3.8 (± 5.08)	3.7 (± 2.98)		
GSK2391220, Wk 20, 3 hour Post-Dose, n=109, 29	4.5 (± 5.43)	4.7 (± 3.53)		
GSK2487818, Day 1, Pre-Dose, n=128, 35	0 (± 0)	0 (± 0)		
GSK2487818, Wk 4, 6-12 hour Post-Dose, n=116, 31	1.2 (± 3.87)	1 (± 0.96)		
GSK2487818, Wk 4, 7-13 hour Post-Dose, n=116, 31	1.1 (± 4.11)	0.7 (± 0.7)		
GSK2487818, Wk 4, 8-14 hour Post-Dose, n=116, 31	1 (± 4.48)	0.6 (± 0.66)		
GSK2487818, Wk 4, 9-15 hour Post-Dose, n=116, 31	0.9 (± 4.09)	0.8 (± 1.16)		
GSK2487818, Wk 20, Pre-Dose, n=111, 29	0.2 (± 0.56)	0.1 (± 0.31)		
GSK2487818, Wk 20, 1 hour Post-Dose, n=110, 28	1.4 (± 3.07)	1 (± 1.09)		
GSK2487818, Wk 20, 2 hour Post-Dose, n=109, 29	2.8 (± 4.28)	2.7 (± 2.21)		
GSK2487818, Wk 20, 3 hour Post-Dose, n=109, 29	3.1 (± 4.07)	3.1 (± 2.56)		
GSK2506102, Day 1, Pre-Dose, n=128, 35	0 (± 0)	0 (± 0)		
GSK2506102, Wk 4, 6-12 hour Post-Dose, n=116, 31	1 (± 1.3)	1.2 (± 0.65)		
GSK2506102, Wk 4, 7-13 hour Post-Dose, n=117, 31	1 (± 1.51)	1.1 (± 0.61)		
GSK2506102, Wk 4, 8-14 hour Post-Dose, n=116, 31	0.9 (± 1.19)	1 (± 0.61)		
GSK2506102, Wk 4, 9-15 hour Post-Dose, n=116, 31	0.9 (± 1.29)	1.1 (± 0.69)		

GSK2506102, Wk 20, Pre-Dose, n=111, 29	0.4 (± 0.73)	0.4 (± 0.42)		
GSK2506102, Wk 20, 1 hour Post-Dose, n=110, 28	0.6 (± 0.88)	0.5 (± 0.4)		
GSK2506102, Wk 20, 2 hour Post-Dose, n=109, 29	0.9 (± 1.15)	1 (± 0.71)		
GSK2506102, Wk 20, 3 hour Post-Dose, n=109, 29	1.1 (± 1.25)	1.2 (± 0.88)		
GSK2531398, Day 1, Pre-Dose, n=128, 35	0 (± 0.01)	0 (± 0)		
GSK2531398, Wk 4, 6-12 hour Post-Dose, n=116, 31	1.3 (± 2.06)	1.4 (± 1.08)		
GSK2531398, Wk 4, 7-13 hour Post-Dose, n=117, 31	1.2 (± 2.5)	1.2 (± 0.99)		
GSK2531398, Wk 4, 8-14 hour Post-Dose, n=116, 31	1.1 (± 2.01)	1.1 (± 0.93)		
GSK2531398, Wk 4, 9-15 hour Post-Dose, n=116, 31	1 (± 2.1)	1.2 (± 1.12)		
GSK2531398, Wk 20, Pre-Dose, n=111, 29	0.3 (± 0.87)	0.3 (± 0.38)		
GSK2531398, Wk 20, 1 hour Post-Dose, n=110, 28	0.8 (± 1.53)	0.6 (± 0.54)		
GSK2531398, Wk 20, 2 hour Post-Dose, n=109, 29	1.6 (± 2.31)	1.5 (± 1.22)		
GSK2531398, Wk 20, 3 hour Post-Dose, n=109, 29	2 (± 2.42)	2 (± 1.57)		
GSK2531401, Day 1, Pre-Dose, n=128, 35	0 (± 0)	0 (± 0)		
GSK2531401, Wk 4, 6-12 hour Post-Dose, n=116, 31	2.8 (± 4)	4.3 (± 2.55)		
GSK2531401, Wk 4, 7-13 hour Post-Dose, n=117, 31	2.7 (± 3.58)	4 (± 2.29)		
GSK2531401, Wk 4, 8-14 hour Post-Dose, n=116, 31	2.7 (± 3.74)	3.8 (± 2.31)		
GSK2531401, Wk 4, 9-15 hour Post-Dose, n=116, 31	2.5 (± 3.53)	3.8 (± 2.29)		
GSK2531401, Wk 20, Pre-Dose, n=111, 29	1.3 (± 2.41)	1.4 (± 1.38)		
GSK2531401, Wk 20, 1 hour Post-Dose, n=110, 28	1.6 (± 2.65)	1.6 (± 1.29)		
GSK2531401, Wk 20, 2 hour Post-Dose, n=109, 29	2.3 (± 3.14)	2.5 (± 1.85)		
GSK2531401, Wk 20, 3 hour Post-Dose, n=109, 29	2.8 (± 3.5)	3.2 (± 2.22)		
GSK2531403, Day 1, Pre-Dose, n=128, 35	0 (± 0)	0 (± 0)		
GSK2531403, Wk 4, 6-12 hour Post-Dose, n=116, 31	3.7 (± 5.43)	4.5 (± 3.14)		
GSK2531403, Wk 4, 7-13 hour Post-Dose, n=117, 31	3.5 (± 5.27)	3.9 (± 2.56)		
GSK2531403, Wk 4, 8-14 hour Post-Dose, n=116, 31	3.4 (± 5.68)	3.7 (± 2.72)		
GSK2531403, Wk 4, 9-15 hour Post-Dose, n=116, 31	3.2 (± 5.42)	3.8 (± 3.01)		
GSK2531403, Wk 20, Pre-Dose, n=111, 29	1.4 (± 2.65)	1.2 (± 1.25)		
GSK2531403, Wk 20, 1 hour Post-Dose, n=110, 28	2.3 (± 3.69)	1.9 (± 1.38)		
GSK2531403, Wk 20, 2 hour Post-Dose, n=109, 29	3.9 (± 5.03)	3.8 (± 2.95)		
GSK2531403, Wk 20, 3 hour Post-Dose, n=109, 29	4.7 (± 5.43)	4.9 (± 3.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean number of dose adjustments up to 24 Weeks

End point title	Mean number of dose adjustments up to 24 Weeks[11]

End point description:

After 4 Weeks, the need to adjust the dose of GSK1278863 was evaluated at every scheduled visit, to maintain hemoglobin within the target range. Target range was defined as: Original Hgb Criteria of 9.0 to 10.5 g/dL, and Amended Hgb Criteria of 10.0 to 11.5 g/dL. Sites in the USA used 9.0 to 10.5 g/dL. Dose adjustments were assigned automatically via the interactive voice/web response system. Intent-to-Treat population. Only those participants with at least one dose adjustment of GSK1278863 were analyzed.

End point type	Secondary

End point timeframe:

From Week 4 up to 24 Weeks

Notes:

[11] - 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: Control groups were not measured for this endpoint, so there are not statistics to present.

End point values	rhEPO-Naive GSK1278863	rhEPO-User GSK1278863		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	26		
Units: number of adjustments				
arithmetic mean (standard deviation)	1.8 (± 0.82)	1.7 (± 0.72)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with dose adjustments up to 24 Weeks, as a measure of dose adjustment frequency

End point title	Number of participants with dose adjustments up to 24 Weeks, as a measure of dose adjustment frequency[12]

End point description:

After 4 Weeks, the need to adjust the dose of GSK1278863 was evaluated at every scheduled visit, to maintain hemoglobin within the target range. Target range was defined as: Original Hgb Criteria of 9.0 to 10.5 g/dL, and Amended Hgb Criteria of 10.0 to 11.5 g/dL. Sites in the USA used 9.0 to 10.5 g/dL. Dose adjustments were assigned automatically via the interactive voice/web response system. Frequency is presented as the number of participants with dose adjustment(s) once, twice, thrice, four times, or five times. Intent-to-Treat population. Only those participants with at least one dose adjustment of GSK1278863 were analyzed.

End point type	Secondary

End point timeframe:

From week 4 up to 24 weeks

Notes:

[12] - 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: Control groups were not measured for this endpoint, so there are not statistics to present.

End point values	rhEPO-Naive GSK1278863	rhEPO-User GSK1278863		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	26		
Units: participants				
number (not applicable)				
Once	39	11		
Twice	50	11		
Thrice	8	4		
Four times	4	0		
Five times or more	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Timing of dose adjustments at Weeks 4, 8, 12, 16, and 20

End point title	Timing of dose adjustments at Weeks 4, 8, 12, 16, and 20[13]

End point description:

After 4 Weeks, the need to adjust the dose of GSK1278863 was evaluated at every scheduled visit, to maintain hemoglobin within the target range. Target range was defined as: Original Hgb Criteria of 9.0 to 10.5 g/dL, and Amended Hgb Criteria of 10.0 to 11.5 g/dL. Sites in the USA used 9.0 to 10.5 g/dL. Dose adjustments were assigned automatically via the interactive voice/web response system. The number of participants with an adjustment are presented at the timings at which adjustments were done. ITT population. Only those participants with at least one dose adjustment of GSK1278863 were analyzed.

End point type	Secondary

End point timeframe:

From Week 4 up to Week 20

Notes:

[13] - 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: Control groups were not measured for this endpoint, so there are not statistics to present.

End point values	rhEPO-Naive GSK1278863	rhEPO-User GSK1278863		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	26		
Units: Participants				
number (not applicable)				
Week 4	78	21		
Week 8	24	6		
Week 12	30	7		
Week 16	30	6		

Week 20	22	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean total cumulative dose of GSK1278863 up to 24 Weeks

End point title	Mean total cumulative dose of GSK1278863 up to 24 Weeks[14]

End point description:

The starting dose was kept constant for the first 4 Weeks after randomization. Later, the need to adjust the dose of GSK1288863 was evaluated at every scheduled visit according to a pre-specified algorithm, to achieve and maintain hemoglobin within the specified target range. Target range was defined as: Original Hgb Criteria of 9.0 to 10.5 g/dL, and Amended Hgb Criteria of 10.0 to 11.5 g/dL. Sites in the USA used 9.0 to 10.5 g/dL. ITT population

End point type	Secondary

End point timeframe:

Up to 24 Weeks

Notes:

[14] - 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: Control groups were not measured for this endpoint, so there are not statistics to present.

End point values	rhEPO-Naive GSK1278863	rhEPO-User GSK1278863		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123	33		
Units: milligrams				
arithmetic mean (standard deviation)	249.75 (± 186.921)	320.42 (± 214.865)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean final dose of GSK1278863 up to 24 Weeks

End point title	Mean final dose of GSK1278863 up to 24 Weeks[15]

End point description:

The starting dose was kept constant for the first 4 Weeks after randomization. Later, the need to adjust the dose of GSK1288863 was evaluated at every scheduled visit according to a pre-specified algorithm, to achieve and maintain hemoglobin within the specified target range. Target range was defined as: Original Hgb Criteria of 9.0 to 10.5 g/dL, and Amended Hgb Criteria of 10.0 to 11.5 g/dL. Sites in the USA used 9.0 to 10.5 g/dL. ITT population.

End point type	Secondary

End point timeframe:

Up to 24 Weeks

Notes:

[15] - 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: Control groups were not measured for this endpoint, so there are not statistics to present.

End point values	rhEPO-Naive GSK1278863	rhEPO-User GSK1278863		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123	33		
Units: milligrams per day				
arithmetic mean (standard deviation)	1.75 (± 1.809)	1.86 (± 1.692)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of hemoglobin (Hgb) excursions

End point title	Number of hemoglobin (Hgb) excursions

End point description:

A Hgb excursion is a series of decreasing or increasing Hgb values differing by >=1.5 grams per deciliter. Hgb cycle is calculated as two consecutive Hgb excursions in different directions. Completers Population: ITT participants who fully completed study without prematurely discontinuing study drug. Only participants with Hgb excursions were analyzed.

End point type	Secondary

End point timeframe:

Up to 24 Weeks.

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	10	4	8
Units: number of excursions				
number (not applicable)	26	10	4	9

Statistical analyses

No statistical analyses for this end point

Secondary: Number of hemoglobin (Hgb) cycles up to 24 Weeks

End point title	Number of hemoglobin (Hgb) cycles up to 24 Weeks

End point description:

A Hgb cycle is calculated as two consecutive Hgb excursions in different directions. A Hgb excursion is a series of decreasing or increasing Hgb values differing by >=1.5 grams per deciliter. Completers population. Only participants with Hgb cycles were analyzed.

End point type	Secondary

End point timeframe:

Up to 24 Weeks

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	0[16]	0[17]	0[18]
Units: number of Hgb cycles				
number (not applicable)	3			

Notes:

[16] - There were no subjects for analysis

[17] - There were no subjects for analysis

[18] - There were no subjects for analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Number of dose cycles up to 24 Weeks

End point title	Number of dose cycles up to 24 Weeks[19]

End point description:

A dose cycle is a series of three directional dose changes (that is, increase, decrease, increase; or decrease, increase, decrease). Completers population. Only participants with dose cycles were analyzed. Completers population.

End point type	Secondary

End point timeframe:

Up to 24 weeks

Notes:

[19] - 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: Control groups were not measured for this endpoint, so there are not statistics to present.

End point values	rhEPO-Naive GSK1278863	rhEPO-User GSK1278863		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0[20]		
Units: number				
number (not applicable)	1			

Notes:

[20] - There were no subjects for analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with at least one hemoglobin (Hgb) excursion up to 24 Weeks.

End point title	Number of participants with at least one hemoglobin (Hgb) excursion up to 24 Weeks.

End point description:

A Hgb excursion is a series of decreasing or increasing Hgb values differing by >=1.5 grams per deciliter. Completers population.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	36	30	30
Units: participants				
number (not applicable)	23	10	4	8

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with at least one hemoglobin (Hgb) cycle up to 24 Weeks

End point title	Number of participants with at least one hemoglobin (Hgb) cycle up to 24 Weeks

End point description:

A Hgb excursion is a series of decreasing or increasing Hgb values differing by >=1.5 grams per deciliter. A Hgb cycle is two consecutive Hgb excursions in different directions. Completers population.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	36	30	30
Units: participants				
number (not applicable)	3	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with at least one dose cycle up to 24 Weeks

End point title	Number of participants with at least one dose cycle up to 24 Weeks[21]

End point description:

A dose cycle is a series of three directional dose changes (that is, increase, decrease, increase; or decrease, increase, decrease). Completers population. Only participants in the GSK1278863 arms were analyzed.

End point type	Secondary

End point timeframe:

Up to 24 weeks

Notes:

[21] - 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: Control groups were not measured for this endpoint, so there are not statistics to present.

End point values	rhEPO-Naive GSK1278863	rhEPO-User GSK1278863		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	30		
Units: participants				
number (not applicable)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants receiving additional therapies of blood transfusions, intravenous (IV) iron or rhEPO at any time post-Baseline

End point title	Number of participants receiving additional therapies of blood transfusions, intravenous (IV) iron or rhEPO at any time post-Baseline

End point description:

Participants receiving additional therapies of blood transfusions, intravenous (IV) iron or rhEPO any time Post Baseline were analyzed. RhEPO was not applicable for the control arms since it was a planned therapy in those arms, hence presented as NA. (EudraCT only: A value of 99999 is used where no data is available or NA.) ITT population.

End point type	Secondary

End point timeframe:

From Day 1 up to Week 28

End point values	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863	rhEPO-User Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	123	43	33	36
Units: participants				
number (not applicable)				
Blood Transfusions	3	1	1	0
IV Iron	20	3	3	4
Inadvertent rhEPO use	4	99999	9	99999
Rescue rhEPO	1	99999	0	99999

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Weeks dose withheld because hemoglobin (Hgb) exceeded the upper limit

End point title	Number of Weeks dose withheld because hemoglobin (Hgb) exceeded the upper limit[22]

End point description:

Number of Weeks dose was withheld because hemoglobin exceed the upper limit is presented as the number of participants with withheld dose during the time periods categorized by Weeks. ITT population.

End point type	Secondary

End point timeframe:

From Week 4 up to Week 24

Notes:

[22] - 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: Control groups were not measured for this endpoint, so there are not statistics to present.

End point values	rhEPO-Naive GSK1278863	rhEPO-User GSK1278863		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	123	33		
Units: participants				
number (not applicable)				
0 Weeks	102	30		
>0-4 Weeks	4	2		
>4-8 Weeks	8	0		
>8-12 Weeks	8	0		
>12 Weeks	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

AEs and SAEs were collected from participants of the safety population, comprised of all participants who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	rhEPO-Naive GSK1278863

Reporting group description:

RhEPO-naive participants were randomly assigned to receive GSK1278863 QD for 24 weeks. Participants were blinded to the dose-level they received throughout the study. At Week 24, participants stopped taking GSK1278863, and returned for the follow-up visit at Week 28.

Reporting group title	rhEPO-Naive Control

Reporting group description:

RhEPO-naive participants were randomly assigned to receive open-label rhEPO (epoetins or their biosimilars, or darbepoetin) as necessary per standard of care, based on the Investigator's clinical judgment, for 24 weeks. At Week 24, participants stopped taking rhEPO (if applicable) and remained off rhEPO or other Erythropoiesis Stimulating Agents (ESA) until at least the follow-up visit at Week 28.

Reporting group title	rhEPO-User GSK1278863

Reporting group description:

RhEPO users were randomly assigned to receive GSK1278863 QD for 24 weeks. Participants were blinded to the dose-level they received throughout the study. At Week 24, participants stopped taking GSK1278863 and did not re-start rhEPO or other ESAs until after the follow-up visit at Week 28 (except in cases where there was a compelling clinical reason [based on Investigator's opinion] to start rhEPO therapy).

Reporting group title	rhEPO-User Control

Reporting group description:

RhEPO users were randomly assigned to receive rhEPO (epoetins or their biosimilars, or darbepoetin) as necessary per standard of care, based on the Investigator clinical judgment, for 24 weeks. Participants were allowed to continue rhEPO therapy between Week 24 and 28.

Serious adverse events	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 134 (14.93%)	6 / 45 (13.33%)	6 / 36 (16.67%)
number of deaths (all causes)	2	0	2
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gallbladder adenocarcinoma			

subjects affected / exposed	0 / 134 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
HEPATIC CANCER			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
Vascular disorders			
DIABETIC VASCULAR DISORDER			
subjects affected / exposed	0 / 134 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
HYPERTENSION			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
Hypotension			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 134 (0.00%)	0 / 45 (0.00%)	0 / 36 (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
Fatigue			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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

Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
MENTAL STATUS CHANGES			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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			
FALSE POSITIVE INVESTIGATION RESULT			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Shunt malfunction			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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 disorders			

ANGINA PECTORIS			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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 CONGESTIVE			
subjects affected / exposed	2 / 134 (1.49%)	1 / 45 (2.22%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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			
subjects affected / exposed	0 / 134 (0.00%)	1 / 45 (2.22%)	0 / 36 (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
Acute myocardial infarction			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
Atrial fibrillation			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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			
CARPAL TUNNEL SYNDROME			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
NEURALGIA			
subjects affected / exposed	0 / 134 (0.00%)	0 / 45 (0.00%)	0 / 36 (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
CEREBRAL MICROANGIOPATHY			
subjects affected / exposed	0 / 134 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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 disorders			
GASTRIC ULCER			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 134 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 134 (0.00%)	0 / 45 (0.00%)	0 / 36 (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
Vomiting			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
Renal and urinary disorders			

RENAL FAILURE CHRONIC			
subjects affected / exposed	2 / 134 (1.49%)	2 / 45 (4.44%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GLOMERULONEPHRITIS CHRONIC			
subjects affected / exposed	0 / 134 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC NEPHROPATHY			
subjects affected / exposed	0 / 134 (0.00%)	1 / 45 (2.22%)	0 / 36 (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
RENAL FAILURE			
subjects affected / exposed	0 / 134 (0.00%)	0 / 45 (0.00%)	0 / 36 (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
RENAL IMPAIRMENT			
subjects affected / exposed	0 / 134 (0.00%)	0 / 45 (0.00%)	0 / 36 (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			
CHONDROCALCINOSIS PYROPHOSPHATE			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
Infections and infestations			
PNEUMONIA			
subjects affected / exposed	1 / 134 (0.75%)	1 / 45 (2.22%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary sepsis			

subjects affected / exposed	0 / 134 (0.00%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS CHRONIC			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
APPENDICITIS			
subjects affected / exposed	0 / 134 (0.00%)	1 / 45 (2.22%)	0 / 36 (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
PNEUMONIA PNEUMOCOCCAL			
subjects affected / exposed	0 / 134 (0.00%)	0 / 45 (0.00%)	0 / 36 (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
CELLULITIS			
subjects affected / exposed	0 / 134 (0.00%)	1 / 45 (2.22%)	0 / 36 (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	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
Sepsis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
Subcutaneous abscess			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
Bronchitis			

subjects affected / exposed	0 / 134 (0.00%)	1 / 45 (2.22%)	0 / 36 (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
Metabolism and nutrition disorders			
HYPOKALAEMIA			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
FLUID OVERLOAD			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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
HYPOGLYCAEMIA			
subjects affected / exposed	1 / 134 (0.75%)	1 / 45 (2.22%)	0 / 36 (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
Gout			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	0 / 36 (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

Serious adverse events	rhEPO-User Control		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 35 (20.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gallbladder adenocarcinoma			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HEPATIC CANCER			

subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
DIABETIC VASCULAR DISORDER			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPERTENSION			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			

subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
FALSE POSITIVE INVESTIGATION RESULT			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Shunt malfunction			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
ANGINA PECTORIS			

subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ATRIOVENTRICULAR BLOCK COMPLETE				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CARDIAC FAILURE CONGESTIVE				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
MYOCARDIAL ISCHAEMIA				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CARDIAC FAILURE				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
CARPAL TUNNEL SYNDROME				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

NEURALGIA			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CEREBRAL MICROANGIOPATHY			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolic encephalopathy			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
GASTRIC ULCER			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
RECTAL HAEMORRHAGE			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
RENAL FAILURE CHRONIC			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

GLOMERULONEPHRITIS CHRONIC				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DIABETIC NEPHROPATHY				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RENAL FAILURE				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RENAL IMPAIRMENT				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
CHONDROCALCINOSIS PYROPHOSPHATE				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
PNEUMONIA				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Biliary sepsis				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PYELONEPHRITIS CHRONIC				

subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
APPENDICITIS				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA PNEUMOCOCCAL				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CELLULITIS				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subcutaneous abscess				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 35 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
HYPOKALAEMIA				

subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
FLUID OVERLOAD			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gout			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	rhEPO-Naive GSK1278863	rhEPO-Naive Control	rhEPO-User GSK1278863
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 134 (35.07%)	14 / 45 (31.11%)	20 / 36 (55.56%)
Investigations			
BLOOD PRESSURE INCREASED			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	2
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	2 / 134 (1.49%)	1 / 45 (2.22%)	4 / 36 (11.11%)
occurrences (all)	3	1	6
General disorders and administration site conditions			
OEDEMA PERIPHERAL			
subjects affected / exposed	5 / 134 (3.73%)	0 / 45 (0.00%)	2 / 36 (5.56%)
occurrences (all)	3	0	2
FATIGUE			

subjects affected / exposed	3 / 134 (2.24%)	1 / 45 (2.22%)	1 / 36 (2.78%)
occurrences (all)	3	1	1
ASTHENIA			
subjects affected / exposed	1 / 134 (0.75%)	3 / 45 (6.67%)	1 / 36 (2.78%)
occurrences (all)	1	3	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 45 (2.22%)	3 / 36 (8.33%)
occurrences (all)	0	1	3
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	10 / 134 (7.46%)	0 / 45 (0.00%)	0 / 36 (0.00%)
occurrences (all)	10	0	0
NAUSEA			
subjects affected / exposed	8 / 134 (5.97%)	1 / 45 (2.22%)	1 / 36 (2.78%)
occurrences (all)	10	1	2
CONSTIPATION			
subjects affected / exposed	5 / 134 (3.73%)	1 / 45 (2.22%)	1 / 36 (2.78%)
occurrences (all)	5	1	1
Respiratory, thoracic and mediastinal disorders			
EPISTAXIS			
subjects affected / exposed	3 / 134 (2.24%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences (all)	3	0	1
Skin and subcutaneous tissue disorders			
PRURITUS			
subjects affected / exposed	0 / 134 (0.00%)	4 / 45 (8.89%)	0 / 36 (0.00%)
occurrences (all)	0	4	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	2 / 134 (1.49%)	2 / 45 (4.44%)	1 / 36 (2.78%)
occurrences (all)	2	2	1
BACK PAIN			
subjects affected / exposed	1 / 134 (0.75%)	1 / 45 (2.22%)	1 / 36 (2.78%)
occurrences (all)	1	1	1
Infections and infestations			

NASOPHARYNGITIS			
subjects affected / exposed	15 / 134 (11.19%)	2 / 45 (4.44%)	7 / 36 (19.44%)
occurrences (all)	17	2	8
CONJUNCTIVITIS			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	2
Bronchitis			
subjects affected / exposed	2 / 134 (1.49%)	1 / 45 (2.22%)	0 / 36 (0.00%)
occurrences (all)	2	1	0
Metabolism and nutrition disorders			
HYPERKALAEMIA			
subjects affected / exposed	2 / 134 (1.49%)	0 / 45 (0.00%)	2 / 36 (5.56%)
occurrences (all)	3	0	2
GOUT			
subjects affected / exposed	2 / 134 (1.49%)	0 / 45 (0.00%)	1 / 36 (2.78%)
occurrences (all)	3	0	1
Hypoglycaemia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 45 (0.00%)	2 / 36 (5.56%)
occurrences (all)	3	0	2

Non-serious adverse events	rhEPO-User Control		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 35 (37.14%)		
Investigations			
BLOOD PRESSURE INCREASED			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	3		
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
General disorders and administration site conditions			
OEDEMA PERIPHERAL			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
FATIGUE			

subjects affected / exposed occurrences (all) ASTHENIA subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2 0 / 35 (0.00%) 0		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 0 / 35 (0.00%) 0		
Gastrointestinal disorders DIARRHOEA subjects affected / exposed occurrences (all) NAUSEA subjects affected / exposed occurrences (all) CONSTIPATION subjects affected / exposed occurrences (all)	 6 / 35 (17.14%) 6 0 / 35 (0.00%) 0 2 / 35 (5.71%) 2		
Respiratory, thoracic and mediastinal disorders EPISTAXIS subjects affected / exposed occurrences (all)	 2 / 35 (5.71%) 2		
Skin and subcutaneous tissue disorders PRURITUS subjects affected / exposed occurrences (all)	 0 / 35 (0.00%) 0		
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) BACK PAIN subjects affected / exposed occurrences (all)	 3 / 35 (8.57%) 3 2 / 35 (5.71%) 2		
Infections and infestations			

NASOPHARYNGITIS subjects affected / exposed occurrences (all) CONJUNCTIVITIS subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all)	 2 / 35 (5.71%) 2 0 / 35 (0.00%) 0 3 / 35 (8.57%) 3		
Metabolism and nutrition disorders HYPERKALAEMIA subjects affected / exposed occurrences (all) GOUT subjects affected / exposed occurrences (all) Hypoglycaemia subjects affected / exposed occurrences (all)	 1 / 35 (2.86%) 1 2 / 35 (5.71%) 2 1 / 35 (2.86%) 1		

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 FDA and to clarify and correct language throughout.
03 October 2013	Amendment for Japan only. To revise the Time and Events Table (Table 3) to add a HemoCue and Quest Hgb assessment at Week 2 as requested by PMDA.
23 January 2014	To revise lipid and biomarker assessments, to add reconfirmation of the 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.
04 February 2014	Document version number change only: Change in document number because an error was found after publishing Amendment 03, but before distribution. The error was corrected and the document republished with a new document number.
08 May 2014	To change the Hgb entry criteria and target range for countries outside of the United States, to change the TSAT entry criterion, to clarify that subject who are not able to complete quality of life scales without assistance should not complete the scales, to change to the name of the rhEPO group (now called "the Control arm") as well as to clarify how subjects in the Control arm are to be managed; to make minor clarifications to the analysis section and throughout the document.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported