PLEASE NOTE: *This study has been imported from ClinicalTrials.gov without additional data checks.*

Trial Description

Title

A Phase IIB, 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

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

This study is intended 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 to maintain hemoglobin (Hgb) level in hemodialysis-dependent (HDD) subjects with anemia associated with chronic kidney disease (CKD) who are switched from a stable dose of recombinant human erythropoietin (rhEPO). The data generated will enable selection of the starting dose(s) and optimize dose adjustment regimen(s) for Phase 3 clinical trials.

Brief Summary in Scientific Language

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Organizational Data

- DRKS-ID: **DRKS00006373**
- Date of Registration in DRKS: **2015/04/10**
- Date of Registration in Partner Registry or other Primary Registry: **2013/10/24**
- Investigator Sponsored/Initiated Trial (IST/IIT): **no**

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Investigator Sponsored/Initiated Trial (IST/IIT): **no**

- Ethics Approval/Approval of the Ethics Committee: **[---]***
- (leading) Ethics Committee Nr.: **[---]***

Secondary IDs

- Primary Registry-ID: **NCT01977482 (ClinicalTrials.gov)**
- Sponsor-ID: **113633 (GlaxoSmithKline)**

Health condition or Problem studied

- Free text: **Anaemia**
- ICD10: **D64.8 - Other specified anaemias**

Interventions/Observational Groups

- Arm 1: **Drug: GSK1278863**
- Arm 2: **Drug: Placebo**
- Arm 3: **Drug: rhEPO**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **patient/subject, investigator/therapist, assessor**
- Control: **Placebo**
- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

- Hemoglobin (Hgb) change from baseline at Week 4; time frame: Week 4

Secondary Outcome

- Hgb concentration at Week 24; time frame: Week 24
- Percentage (%) of time within target range between Week 20 and 24; time frame: Week 20- 24; The percentage of time in range between Weeks 20 and 24 for a subject will be calculated by dividing the total number of days that Hgb is within the target range (10.0 to 11.5 grams [g]/deciliter [dL]) while on treatment during Weeks 20 to 24 (using linear interpolation) by the total number of days the subject remained on treatment during the defined period.
- Number of subjects with Hgb in the target range at Week 24; time frame: Week 24; Number of subjects with Hgb in target range (10.0 to11.5 g/dL) at Week 24
- Number of subjects reaching pre-defined Hgb stopping criteria; time frame: Week 24; Number of subjects reaching pre-defined Hgb study medication discontinuation criteria will be summarized by treatment group.
- Maximum observed change from baseline in Erythropoietin (EPO); time frame: Week 4 and Week 20
- Maximum observed change from baseline in Vascular Endothelial Growth Factor (VEGF); time frame: Week 4 and Week 20
- Population Pharmacokinetics; time frame: Week 4 and Week 20; Evaluation of population pharmacokinetic parameters of GSK1278863 and relevant metabolites. These include fixed-effect (clearance, volumes, covariate effects) and random-effect (within and between subject variability, residual variability) parameters
- Percentage of time below target range between Week 20 and 24; time frame: Week 20-24; The percentage of time below range between Weeks 20 and 24 for a subject will be calculated by dividing the total number of days that Hgb is below the target range (10.0 to 11.5 grams [g]/deciliter [dL]) while on treatment during Weeks 20 to 24 (using linear interpolation) by the total number of days the subject remained on treatment during the defined period.
- Percentage of time above target range between Week 20 and 24; time frame: Week 20-24; The percentage of time above range between Weeks 20 and 24 for a subject will be calculated by dividing the total number of days that Hgb is above the target range (10.0 to 11.5 grams [g]/deciliter [dL]) while on treatment during Weeks 20 to 24 (using linear interpolation) by the total number of days the subject remained on treatment during the defined period.
- Hepcidin; time frame: Week 24; Evaluation of change from baseline for hepcidin
- Ferritin; time frame: Week 24; Evaluation of change from baseline for ferritin
- Transferrin; time frame: Week 24; Evaluation of change from baseline for transferrin
- Transferrin Saturation; time frame: Week 24; Evaluation of change from baseline for transferrin saturation
- Total Iron; time frame: Week 24; Evaluation of change from baseline for total iron
- Total Iron Binding Capacity; time frame: Week 24; Evaluation of change from baseline for total iron binding capacity
- Reticulocyte Hemoglobin Content; time frame: Week 24; Evaluation of change from baseline for reticulocyte hemoglobin content
- Hematocrit; time frame: Week 24; Evaluation of change from baseline for Hematocrit
- Red Blood Cells; time frame: Week 24; Evaluation of change from baseline for red blood cells
- Reticulocyte Number; time frame: Week 24; Evaluation of change from baseline for reticulocyte number

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Countries of recruitment

- US **United States**
- AU **Australia**
- CA **Canada**
- CZ **Czech Republic**
- DK **Denmark**
- FR **France**
- DE **Germany**
- HU **Hungary**
- JP **Japan**
- KR **Korea, Republic of**
- NO **Norway**
- PL **Poland**
- RU **Russian Federation**
- ES **Spain**
- SE **Sweden**
- UK **United Kingdom**

Locations of Recruitment

- **GSK Investigational Site, Mannheim**
- **GSK Investigational Site, Muenchen**
- **GSK Investigational Site, Demmin**
- **GSK Investigational Site, Leipzig**
- **GSK Investigational Site, Berlin**
- **GSK Investigational Site, Duesseldorf**
- **GSK Investigational Site, Hamburg**

Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **2013/11/30**
- Target Sample Size: **176**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

- - Subjects are eligible if they meet all of the inclusion criteria below:

- General criteria

- Age: >=18 years of age. (Week -4 verification only)

- Gender: Female and male subjects. (Week -4 verification only) Females: If of childbearing potential, must agree to use one of the approved contraception methods, from Screening until completion of the Follow-up Visit OR of non-childbearing potential defined as pre-menopausal females with a documented tubal ligation, hysterectomy, or oophorectomy; or postmenopausal defined as 12 months of spontaneous amenorrhea [in questionable cases a blood sample with simultaneous follicle stimulating hormone (FSH) 23.0-116.3 International units per liter (IU/L) and estradiol <=10 picomole per liter (pmol/L) is confirmatory]. Females on hormone replacement therapy (HRT) whose menopausal status is in doubt will be required to use one of the approved contraception methods if they wish to continue their HRT during the study. Otherwise they must discontinue HRT to allow confirmation of post-menopausal status prior to study enrolment. For most forms of HRT, at least 2 weeks must elapse between the cessation of therapy and the blood draw; this interval depends on the type and dosage of HRT. Following confirmation of their post-menopausal status, they can resume use of HRT during the study without use of a contraceptive method;

- Q-T Interval Corrected for Heart Rate (QTc): Bazett's Correction of QT Interval (QTcB) <470 millisecond (msec) or QTcB <480 msec in subjects with bundle branch block. There is no QTc inclusion criterion for a subject with a predominantly paced rhythm.

- CKD-related criteria

- Dialysis frequency: On hemodialysis (HD) three to five times weekly for at

least 4 weeks prior to Week -4 Screening through Week 4. NOTE: Combination methods including hemofiltration (HF) or ultrafiltration (UF) with HD are allowed. However, the type of dialysis (HD, hemodiafiltration (HDF) or UF) should not change during the study.

- Dialysis adequacy: A single-pool dialyzer clearance multiplied by dialyzer time divided by volume of distribution of urea (Kt/Vurea) of >=1.2 based on a historical value obtained within the prior month in order to ensure the adequacy of dialysis. If Kt/Vurea is not available, then an average of the last 2 values of urea reduction ratio (URR) of at least 65%. NOTE: Only needs confirming at Week -4.

- Hemoglobin: Baseline Hgb of 9.0-11.5 g/dL (may rescreen in a minimum of 2 weeks).

- Stable rhEPO dose: Using the same rhEPO (epoetins or their biosimilars, or darbepoetin) with total weekly doses varying by no more than 50% during the 4 weeks prior to Week -4. At Day 1 (randomization), confirm that total weekly doses varied by no more than 50% during the screening period.

- Iron replacement therapy: Subjects may be on stable maintenance oral or IV (<=100 mg/week) iron supplementation. If subjects are on oral or IV iron, then doses must be stable for the 4 weeks prior to Week -4, during the screening phase, and through the first 4 weeks after Randomization.

Exclusion criteria

- Subjects are not eligible if they meet any of the exclusion criteria below:

- CKD-related criteria

- Dialysis modality: Planned change from HD to peritoneal dialysis within the study time period.

- Renal transplant: Pre-emptive or scheduled renal transplant.

- High rhEPO dose: An epoetin dose of >=360 IU/Kg/Week IV or >=250 IU/kg/week subcutaneous (SC) or darbepoetin dose of >=1.8 microgram (µg)/Kg/Week IV or SC within the prior 8 weeks through Day 1 (randomization).

- Use of methoxy polyethylene glycol epoetin beta within the prior 8 weeks through Day

1 (randomization).

- Laboratory test-based criteria (Week -4 verification only)

- Vitamin B12: At or below the lower limit of the reference range (may rescreen in a minimum of 8 weeks).

- Folate: <2.0 nanogram (ng)/mL (<4.5 nanomole (nmol)/L) (may rescreen in a minimum of 4 weeks).

- Ferritin: <100 ng/mL (<100 Micrograms per liter).

- Transferrin saturation (TSAT): Outside of the reference range.

- Cardiovascular disease-related criteria

- Myocardial infarction or acute coronary syndrome: Within the 8 weeks prior to Screening through Day 1 (randomization).

- Stroke or transient ischemic attack: Within the 8 weeks prior to Week -4 Screening through Day 1 (randomization).

- Heart failure: Class III/IV heart failure, as defined by the New York Heart Association (NYHA) functional classification system diagnosed prior to Week -4 Screening through Day 1 (randomization); Symptomatic right heart failure diagnosed prior to Week -4 Screening through Day 1 (randomization).

- Hypertension: Defined using pre-dialysis vitals (Week -4, Day 1) of diastolic blood pressure (DBP) >100 millimeters of mercury (mmHg) or systolic blood pressure (SBP) >170 mmHg.

- Thrombotic disease: History of thrombotic disease (e.g., venous thrombosis such as deep vein thrombosis or pulmonary embolism, or arterial thrombosis such as new onset or worsening limb ischemia requiring intervention), except vascular access thrombosis, within the 8 weeks prior to Week -4 Screening through Day 1 (randomization).

- Other disease-related criteria

- Ophthalmology disease: Meeting any ophthalmologic-related exclusion criteria determined at the Screening ophthalmology exam.

- Inflammatory disease: Active chronic inflammatory disease that could impact

erythropoiesis (e.g., scleroderma, systemic lupus erythematosis, rheumatoid arthritis, celiac disease) diagnosed prior to Week -4 Screening through Day 1 (randomization).

- Hematological disease: Any hematological disease including those affecting platelets, white or red blood cells (e.g. sickle cell anemia, myelodysplastic syndromes, hematological malignancy, myeloma, hemolytic anemia and thalassemia), coagulation disorders (e.g., antiphospholipid syndrome, Protein C or S deficiency), or any other cause of anemia other than renal disease diagnosed prior to Week -4 Screening through Day 1 (randomization).

- Liver disease: Current liver disease, known hepatic or biliary abnormalities (with the exception of Gilbert's syndrome or asymptomatic gallstones) or evidence at Screening of abnormal liver function tests [alanine transaminase (ALT) or aspartate transaminase (AST) > 2.0 x upper limit of normal (ULN) or total bilirubin > 1.5 x ULN]; or other hepatic abnormalities that in the opinion of the investigator would preclude the subject from participation in the study. NOTE: Those with Hepatitis B or Hepatitis C are eligible provided these exclusions are not met.

- Major surgery: Major surgery (excluding vascular access surgery) within the prior 8 weeks, during the Week -4 Screening phase or planned during the study.

- Transfusion: Blood transfusion within the prior 8 weeks, during the Week -4 Screening phase or an anticipated need for blood transfusion during the study.

- GI Bleeding: Evidence of actively bleeding peptic, duodenal, or esophageal ulcer disease OR clinically significant GI bleeding within the 8 weeks prior to Week -4 Screening through Day 1 (randomization).

- Acute infection: Clinical evidence of acute infection or history of infection requiring intravenous (IV) antibiotic therapy within the 8 weeks prior to Week -4 Screening through Day 1 (randomization). NOTE: IV antibiotics as prophylaxis are allowed.

- Malignancy: Subjects with a history of malignancy within the prior 5 years, who

receiving treatment for cancer, or who have a strong family history of cancer (e.g., familial cancer disorders); with the exception of squamous cell or basal cell carcinoma of the skin that has been definitively treated prior to Week -4 Screening through Day 1 (randomization).

- Concomitant medication and other Investigational Product-related criteria

- Severe allergic reactions: History of severe allergic or anaphylactic reactions or hypersensitivity to excipients in the investigational product.

- Drugs and supplements: Use of any prescription or non-prescription drugs or dietary supplements that are prohibited from Week -4 Screening until the Follow-up Visit.

- Prior investigational product exposure: The Subject has participated in a clinical trial and has received an experimental investigational product within the prior 30 days from Week -4 Screening through Day 1 (randomization).

- General health-related criteria

- Other Conditions: Any other condition, clinical or laboratory abnormality, or examination finding that the Investigator considers would put the subject at unacceptable risk.

- Pregnancy or Lactation: Pregnant females as determined by positive serum human chorionic gonadotropin (hCG) test OR women who are lactating at Week -4 Screening or during the trial.

- Other Eligibility Criteria Considerations

- Laboratory eligibility criteria will be assessed according to the central laboratory results for the screening samples.

- Subjects who fail screening may be rescreened as soon as the investigator feels they may have become eligible. However, an individual subject may not rescreen more than twice. There is no predetermined amount of time that the investigator needs to wait to rescreen a previously ineligible subject, except those excluded for Hgb or folate who may only rescreen in 2 and 4 weeks, respectively, and those excluded for Vitamin

B12 who may rescreen in 8 weeks

Addresses

- **Primary Sponsor**

  GlaxoSmithKline

  Telephone: **[---]***
  Fax: **[---]***
  E-mail: **[---]***
  URL: **[---]***
- **Contact for Scientific Queries**

  GlaxoSmithKline
  GSK Clinical Trials

  Telephone: **[---]***
  Fax: **[---]***
  E-mail: **[---]***
  URL: **[---]***
- **Contact for Public Queries**

  US GSK Clinical Trials Call Center

  Telephone: **877-379-3718**
  Fax: **[---]***
  E-mail: **GSKClinicalSupportHD at gsk.com**
  URL: **[---]***

Sources of Monetary or Material Support

- **[---]***

  Bitte wenden Sie sich an den Sponsor / Please refer to primary sponsor

  Telephone: **[---]***
  Fax: **[---]***
  E-mail: **[---]***
  URL: **[---]***

Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

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Trial Publications, Results and other documents

The parameters in ClinicalTrials.gov and DRKS are not identical. Therefore the data import from ClinicalTrials.gov required adjustments. For full details please see the DRKS FAQs.

- Translation on version: 1

- Last processed date by ClinicalTrials.gov: 2014/07/16

* *This entry means the parameter is not applicable or has not been set.*

*** *This entry means that data is not displayed due to insufficient data privacy clearing.*