ISRCTN68321818 https://doi.org/10.1186/ISRCTN68321818

Safety and efficacy of subcutaneous HMR4396 for the management of anaemia in subjects with chronic renal failure

Submission date	Recruitment status	[_] Prospectively registered
25/05/2007	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
02/07/2007	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
04/01/2021	Urological and Genital Diseases	

Plain English summary of protocol
Not provided at time of registration and not expected to be available in the future

Contact information

Type(s)
Scientific

Contact name
Dr Chris Freitag

Contact details
Shire Pharmaceuticals contact for trial
Hampshire International Business Park
Lime Tree Way
Basingstoke
United Kingdom
RG24 8EP

Additional identifiers

Protocol serial number
HMR4396A/3002

Study information

Scientific Title
Safety and efficacy of subcutaneous HMR4396 for the management of anaemia in subjects with chronic renal failure

Study objectives
Chronic Kidney Disease (CKD) is often associated with severe anaemia, which is primarily the result of reduced erythropoietin production. Anaemia in patients with CKD is associated with increased morbidity and mortality, and reduced quality of life. Recombinant human erythropoietins can be used to treat anaemia, but existing agents are produced in Chinese Hamster Ovary (CHO) cell lines, leading to a hamster glycosylation profile different from that of endogenous human erythropoietin. HMR4396 is produced in a human cell line, and thus offers a glycosylation profile that differs from that of conventional epoetins.

The primary objective was to evaluate the safety and efficacy of subcutaneous HMR4396 in the management of anaemia in subjects with chronic renal failure.

Ethics approval required
Old ethics approval format

Ethics approval(s)
This was a multi-national, multi-centre trial with 21 centres in the European Union and 27 centres in the United States. The independent ethics committee from each of the sites approved the study before the start date of 1st October 1998.

Study design
Phase III open-label uncontrolled international multicentre study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic Kidney Disease (CKD)

Interventions
The intervention was administration of HMR4396, given subcutaneously 1, 2, or 3 times weekly for up to 52 weeks, starting at the same dose as the previous epoetin in three patient groups:
1. CKD not on dialysis (pre-dialysis)
2. CKD on haemodialysis
3. CKD on peritoneal dialysis

The main comparison was the ability to maintain the Haemoglobin (Hb) concentration over the duration of the trial.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
HMR4396, a gene-activated erythropoietin

Primary outcome(s)
The primary efficacy endpoint in this study was the determination of each subjects average haemoglobin concentration (avHGB) over weeks 12, 16, 20, and 24. The primary efficacy analysis of avHGB was performed using the modified Intent-To-Treat (mITT) population. Additional analyses of the primary efficacy endpoint were conducted using the ITT and per-protocol populations.

Efficacy analyses were conducted using haematology data collected up to seven days after the last held or received dose of study medication.

Key secondary outcome(s))
Secondary efficacy endpoints included:
1. Mean treatment dose
2. Mean haematocrit
3. Percentage of haemoglobin values above 10 g/dL
4. Percentage of haematocrit values above 30%
5. Changes in weekly profiles of haemoglobin and haematocrit
6. Counts of red blood cells and reticulocytes

Analyses of non-primary endpoints were conducted using both the modified Intent-To-Treat (mITT) and Intent-To-Treat (ITT) populations.

Completion date
07/06/2000

Eligibility

Key inclusion criteria
1. Men or women, 18 years of age or older, with chronic renal failure
2. Evidence of anaemia (haemoglobin less than 11.0 g/dL) in medical history
3. Subjects receiving hemodialysis must have been prescribed to receive epoetin two or three times weekly by subcutaneous (s.c.) administration for at least 30 days immediately before signing informed consent
4. Predialysis subjects and subjects receiving peritoneal dialysis must have been prescribed to receive epoetin at least once weekly by s.c. administration for at least 30 days immediately before signing informed consent
5. Dose of epoetin not changed by more than 50% (increase or decrease) in the 30 days before signing informed consent
6. Haemoglobin 10.0 to 12.0 (±0.4) g/dL for the two weeks before receiving the first dose of HMR4396 as determined by one measurement per week
7. For predialysis subjects, serum creatinine greater than 2 mg/dL or creatinine clearance less than 45 mL/min as estimated by 24-hour urine collection or Cockcroft and Gault formula
8. Serum ferritin greater than or equal to 90 ng/mL and transferrin saturation greater than or equal to 18% as determined by the pre-study measurement

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
478

Key exclusion criteria
1. Uncontrolled hypertension
2. For haemodialysis subjects, missed more than three dialysis sessions in the 30 days before signing informed consent
3. One or more doses of epoetin missed or withheld by physician order in the 14 days before signing informed consent
4. Concomitant unrelated illness that could reduce life expectancy to less than 12 months (such as malignancy, immune deficiency, myocardial infarction or cerebrovascular accident within 30 days before signing informed consent)
5. Thrombocytopenia (platelet count less than 75,000/mm^3)
6. Active bleeding
7. Treatment with immunosuppressive drugs (other than corticosteroids for a chronic condition) within 30 days before signing informed consent
8. Androgen therapy within 30 days before signing informed consent
9. Current drug abuse
10. Known Human Immunodeficiency Virus (HIV) infection from medical history
11. Treatment with any investigational drug within 30 days before signing informed consent
12. Breastfeeding
13. Pregnancy at enrolment or plans to become pregnant during the study. It was required that absence of pregnancy be documented by serum test before exposure to HMR4396 or any other study procedure with potential risk to a foetus
14. Childbearing potential. Absence of childbearing potential was defined as being surgically sterile, at least one year post-menopausal, or using a medically accepted (prescription or nonprescription) method of contraception
15. History of hypersensitivity to HMR4396 or to drugs with similar chemical structures
16. Impaired hepatic function, defined as a pre-study value for Aspartate Aminotransferase (AST) (Serum Glutamic Oxaloacetic Transaminase [SGOT]) or Alanine Aminotransferase (ALT) (Serum Glutamic Pyruvic Transaminase [SGPT]) exceeding three times the upper limit of the normal range for the central laboratory
17. Clinically relevant haematologic, cardiovascular, hepatic, neurologic, endocrine, infectious, inflammatory or other major systemic disease making implementation of the protocol or interpretation of the study results difficult
18. Mental condition rendering the subject unable to understand the nature, scope and possible consequences of the study
19. Subject unlikely to comply with protocol, e.g., uncooperative attitude, inability to return for follow-up visits, or unlikely to complete the study
20. Likelihood that the subject would require treatment during the study period with drugs not permitted by the protocol
21. Previous treatment with HMR4396

Date of first enrolment
01/10/1998

Date of final enrolment
07/06/2000

Locations

Countries of recruitment
United Kingdom

England

France

Germany

United States of America

Study participating centre
Shire Pharmaceuticals contact for trial
Basingstoke
United Kingdom
RG24 8EP

Sponsor information

Organisation
Hoechst Marion Roussel (Shire Pharmaceuticals) (France)

ROR
https://ror.org/02n6c9837

Funder(s)

Funder type
Industry

Funder Name
Hoechst Marion Roussel (France)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	25/02/2009	04/01/2021	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes