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

Submission date	Recruitment status  No longer recruiting	Prospectively registered		
25/05/2007		☐ 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 ( $\pm$ 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