ISRCTN62713985 https://doi.org/10.1186/ISRCTN62713985

A double-blind, placebo-controlled, parallel-arms dose response study of two doses of HRM4396 versus placebo for anaemia in subjects treated with chemotherapy

Submission date
12/06/2007

Registration date
19/07/2007

Last Edited
15/08/2008

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Haematological Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Contact details
Shire contact for trial - no PI was identified
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

HMR4396B/3001

Study information

Scientific Title

Study objectives
Advanced cancer is frequently associated with significant anaemia. The causes of this anaemia are multi-factorial and may include the cytotoxic effects of chemotherapeutic agents on bone marrow.

Primary objective was to determine in anaemic cancer subjects treated with chemotherapy, the efficacy of 150 and 300 U/kg of subcutaneously injected HMR4396 compared to placebo based on haemoglobin and the percent of these subjects requiring red blood cell transfusions.

Ethics approval required
Old ethics approval format

Ethics approval(s)
This was a multi-national, multi-centre trial with 49 centres in the United States. The independent ethics committee from each of the sites approved the study before subjects were enrolled.

Study design
Phase III, randomised, multinational, double-blind, placebo-controlled, parallel arm study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Anaemia

Interventions
The intervention was administration of HMR4396 at a dose of 150 U/kg or 300 U/kg compared to placebo. All study treatments were given three times weekly subcutaneously for 12 weeks.

Quality of life was evaluated using the Functional Assessment of Cancer Therapy - Anaemia (FACT-An) questionnaire.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
HMR4396

Primary outcome measure
The co-primary efficacy endpoints in this study were the determination of each subjects change in haemoglobin from baseline to week 12 and the occurrence of red blood cell transfusions during week 5 to 12 (yes/no). The primary analysis was based on the Intent-To Treat (ITT) population.

Secondary outcome measures
Secondary efficacy endpoints were:
1. Change in FACT-An fatigue subscale from baseline to week 12
2. Number of RBC transfusions received during weeks 5 - 12 (expressed as a rate per 28 days)
3. Number of RBC units transfused during weeks 5 - 12 (expressed as a rate per 28 days)
4. Change in Haematocrit (Hct) at week 12 when compared to baseline
5. Average Hgb during weeks 5 - 12
6. Rate of change of Hgb from baseline to first treatment interruption or to when a blood transfusion (red cell or whole blood) was first received
7. Average Hct during weeks 5 - 12
8. Rate of change of Hct from baseline to first treatment interruption or to when a blood transfusion (red cell or whole blood) was first received
9. Change in the total FACT-An score from baseline to week 12
10. Change in each non-fatigue subscale from baseline to week 12

Overall study start date
18/05/2000

Completion date
20/06/2002

Eligibility

Key inclusion criteria
1. Men or women, 18 years of age or older, with cancer except for acute leukaemias, malignancies of the myeloid cell line and myelodysplasia
2. Receiving cancer chemotherapy with at least two cycles remaining when randomised to study medication
3. Eastern Cooperative Oncology Group (ECOG) performance score of zero, one or two
4. Life expectancy of three months or greater
5. Haemoglobin (Hgb) less than or equal to 10.5 g/dL
6. Women were to be surgically sterile, post-menopausal (greater than one year) or using an effective method of birth control and were to have had a negative serum pregnancy test (quantitative human chorionic gonadotropin radioimmunoassay test) prior to study medication
7. Men had to agree to an effective method of contraception

8. Laboratory values within the following parameters:
8.1. Neutrophils greater than 500 cells/mm^3 (absolute value = 0.5 x 1000/mm^3 [as per Amendment 1])
8.2. Platelets greater than 75,000 cells/mm^3
8.3. Creatinine less than 2.0 mg/dL
8.4. Serum calcium less than 12 mg/dL
9. Serum ferritin at least 12 mg/mL and transferrin saturation at least 15% as determined by the prestudy evaluation
10. Stool occult blood (negative)
11. A desire and competence to self-administer the study drug or willing to come to the clinic three days each week for the duration of the study to receive study medication
12. Informed consent was obtained for subjects before enrolment in the study

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
575 subjects were screened of which 313 were randomised

Key exclusion criteria
Subjects meeting any of the following criteria were not to be included in the study:
1. History of any primary non-malignant heamatologic disease
2. Clinically significant disease/dysfunction of the pulmonary, cardiovascular, endocrine, neurological, gastrointestinal, or genitourinary systems not attributable to underlying malignancy and making implementation of the protocol or interpretation of the study results difficult
3. Uncontrolled hypertension (i.e. diastolic Blood Pressure [BP] greater than 100 mmHg) at the prestudy evaluation
4. Evidence of folate or B12 deficiency defined as below the lower standard value for the central laboratory
5. Androgen therapy within two months of randomisation to study medication
6. Known hypersensitivity to erythropoietin
7. Known hypersensitivity to products derived from mammalian cell-culture systems
8. Experimental drug administered or experimental device used within 30 days prior to randomisation to study medication
9. Radiation therapy completed within four weeks before randomisation to study medication or extensive radiation therapy defined as more than 40% of marrow exposed in the radiation field completed within six weeks before randomisation to study medication
10. A malignancy requiring bone marrow transplant or stem cell transplant in the forthcoming 24 weeks (six months)
11. Bone marrow transplant or stem cell transplant recipients
12. Loss of blood requiring Red Blood Cell (RBC) transfusion within the last 30 days

13. Subjects known to be Human Immunodeficiency Virus (HIV) positive
14. Blood (500 ml) or equivalent serum donation during the last three months (as per Amendment 1)
15. Pregnant
16. Breast feeding
17. Treatment with other erythropoietins within the last 12 weeks before randomisation to study medication
18. Likelihood of requiring treatment during the study period with drugs not permitted by the study protocol
19. Clinically relevant cardiovascular disease requiring treatment, including but not limited to:
19.1. Myocardial infarction in the preceding six months
19.2. Cardiac arrhythmia
19.3. Unstable angina
20. Current drug abuse
21. Impaired hepatic function, defined as prestudy value for Aspartate Transaminase (AST [SGOT]) or Alanine Transaminase (ALT [SGPT]) exceeding twice the upper limit of normal of the central laboratory values
22. A mental condition rendering the subject unable to understand the nature, scope and possible consequences of the study
23. Subjects unlikely to comply with protocol, e.g. uncooperative attitude, inability to return for follow-up visits, and unlikely to complete the study

Date of first enrolment
18/05/2000

Date of final enrolment
20/06/2002

Locations

Countries of recruitment
England

United Kingdom

United States of America

Study participating centre
Shire contact for trial - no PI was identified
Basingstoke
United Kingdom
RG24 8EP

Sponsor information

Organisation

Hoechst Marion Roussel (Shire Pharmaceuticals) (France)

Sponsor details
102 Route de Noisy
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France
93235

Sponsor type
Industry

Website
http://www.shire.com/shire/

ROR
https://ror.org/02n6c9837

Funder(s)

Funder type
Industry

Funder Name
Hoechst Marion Roussel (Shire Pharmaceuticals) (France)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration