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The safety and efficacy of intravenous ferric carboxymaltose in patients with anaemia receiving haemodialysis: a multicentre, open-label, clinical study

Submission date
08/12/2008

Recruitment status
No longer recruiting

Registration date
05/01/2009

Overall study status
Completed

Last Edited
28/11/2019

Condition category
Haematological Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

53214

Study information

Scientific Title
A multicentre, open-label, single-arm study to investigate the safety and efficacy of intravenous ferric carboxymaltose in haemodialysis patients with anaemia

Study objectives
The primary objective was to assess the safety of intravenous ferric carboxymaltose therapy in patients with haemodialysis associated anaemia (HDAA).

Ethics approval required
Old ethics approval format

Ethics approval(s)
The final, approved protocol (dated 7 February 2003), amendments 1, 2 and 3 (dated 16 April 2003, 12 September 2003 and 19 December 2003 respectively) were approved by the Medicines Control Council (MCC) in South Africa, Medicines Control Agency at the Ministry of Health of Lithuania and the National Drug Agency in Romania and the Independent Ethic Committee (IECs) for the relevant study centres.

Study design
Multicentre, open-label, single-arm, multiple-dose, phase II study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Haemodialysis associated anaemia

Interventions
Ferric carboxymaltose as an infusion solution in 2 ml ampoules containing 100 mg iron per ampoule. Patients received study medication during their individually scheduled haemodialysis sessions (two to three sessions per week). Patients received 200 mg iron (ie. 4 ml of ferric carboxymaltose) at the applicable haemodialysis session. The cumulative dosage was determined according to the patient's individual potential iron requirement using the Ganzoni formula. The maximal cumulative dose was limited to 2400 mg of iron. Treatment lasted a maximum of 6 weeks. An observation period of one month followed the last haemodialysis

session of the study (i.e. the last study medication administration) during which patients were monitored for safety.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Ferric carboxymaltose

Primary outcome measure
Efficacy, assessed by correction of patients iron stores and haemoglobin levels. Treatment responders were defined as patients who exhibited an increase of greater than or equal to 1.0 g /dL Hb from baseline at any point during the study. Haemoglobin was taken at screening and on days 0, 2 weeks, 4 weeks, 6 weeks, 8 weeks and 12 weeks.

Secondary outcome measures
1. Safety and tolerability of the study medication, assessed by the incidence of treatment-emergent adverse events (TEAEs), recorded by the investigator from the first dose of FCM. TEAEs were defined as mild, moderate or severe; the causality of which was judged by the investigator to be unrelated, related, possibly related, probably related or certainly related to the use of study medication.
2. Routine clinical laboratory safety parameters, vital signs and physical parameters (including 12-lead electrocardiogram [ECG] measurements)
3. Pre- and post-dialysis serum urea values

Safety investigations were determined every 2 weeks (+/- 1-2 days) from baseline (the first study medication administration) until the end of the observation. Blood samples for haematology and clinical chemistry (including iron status) were taken before each dialysis session, while only a clinical chemistry sample for post-dialysis serum urea was taken immediately after the dialysis session.

Overall study start date
16/07/2003

Completion date
11/05/2004

Eligibility

Key inclusion criteria
1. Male and female HDAA patients undergoing maintenance haemodialysis (two to three haemodialysis sessions per week)
2. Aged 18 - 65 years of age (inclusive) (the upper limit of the age was changed from 60 years according to amendment no 2, dated 12 September 2003), either sex
3. Iron deficiency anaemia defined as:
3.1. Haemoglobin (Hb) equals 11 g/dl
3.2. Serum transferrin saturation (TfS) less than 20% or serum ferritin equals 200 ng/ml (changed

according to amendment no 2, dated 12 September 2003)
4. Clinically stable, without a history of admission to hospital due to renal decompensation during the 4 weeks preceding the inclusion date
5. Patients who were being treated with EPO, were to have received this treatment for at least one month prior to inclusion in the study, and had to remain on stable doses during participation in the study
6. Patients voluntarily signed an informed consent form at the screening visit, after being informed of the purpose, aims, benefits and risks of the study
7. Females of childbearing potential had to use reliable forms of contraception (barrier methods, including male and female condoms, and diaphragms [cervical caps] with intravaginal spermicide [including jellies, foams and suppositories], intra-uterine device or hormonal contraceptives) in the study and up to one month after the last dose of the study medication. Non-childbearing potential would include surgically sterilised at least 6 months prior to the study or post-menopausal with no menstrual bleeding for at least 2 years prior to the study.
8. Permanent vascular access appropriate for haemodialysis

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
163 patients (safety set); 162 patients (ITT set); 157 patients (PP set)

Key exclusion criteria
1. Known hypersensitivity to iron polysaccharide complexes and compounds of ferric carboxymaltose
2. Ferritin greater than 500 ng/ml, TfS greater than 50%, Hb less than 6.5 g/dl, serum albumin less than 2.5 g/dl (changed according to amendment no 2, dated 12 September 2003)
3. Vitamin B12 or folic acid deficiency
4. Types of anaemia other than anaemia associated with chronic renal failure and iron deficiency anaemia (especially haemolytic, macrocytic, hypoplastic, or sideroblastic anaemia)
5. Any history or clinical findings of iron storage conditions/disorders such as haemochromatosis
6. Active or acute infection or malignancy
7. Active peptic ulcer, asthma, or rheumatoid arthritis
8. Treatment with an investigational drug within the 30 days prior to enrolment
9. Patients positive for hepatitis B surface antigen (HBsAg), or anti-hepatitis C virus (HCV) (for Romania only there was an addition of '...and evidence for acute hepatitis, i.e. abnormal liver function test [LFT] results' according to amendment no 3, dated 19 December 2003). Justification for performing HBsAg, or anti-HCV tests on patients was that LFTs were closely monitored as a possible sign of iron toxicity. Patients with hepatitis B or C infection were

excluded because of difficulties to distinguish changes in liver function due to iron toxicity from symptoms of hepatitis.
10. Active liver disease
11. Significant cardiovascular disease, including myocardial infarction within 6 months prior to study inclusion, congestive heart failure New York Heart Association (NYHA) grade III or IV, or poorly controlled hypertension according to judgement of the investigator
12. Endocrinologic or metabolic disorders that were not controlled according to judgement of the investigator
13. Blood transfusion or treatment with intravenous (i.v.) iron preparations within 4 weeks before inclusion into the study (oral iron was not allowed)
14. Patients who needed a blood transfusion within 2 months of the start of the study
15. Anticipated surgery with the exception of surgery related to vascular access
16. Known history of drug or alcohol abuse
17. Pregnancy or lactation
18. Patients with a body mass index (BMI) higher than 15% above the normal BMI (this criterion was deleted by amendment no 2, dated 12 September 2003)

Date of first enrolment
16/07/2003

Date of final enrolment
11/05/2004

Locations

Countries of recruitment
Lithuania

Romania

South Africa

Study participating centre
Dialysis and Transplantation Center
La°i
Romania
6600

Sponsor information

Organisation
Vifor Pharma (UK)

Sponsor details
c/o Kate Freeman
The Old Stables

Bagshot Park
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United Kingdom
GU19 5PJ

Sponsor type
Industry

Website
http://www.aspreva.com

ROR
https://ror.org/01hfdsp13

Funder(s)

Funder type
Industry

Funder Name
Vifor Pharma (Switzerland)

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2010	28/11/2019	Yes	No