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Intravenous ferric carboxymaltose versus iron sucrose in the treatment of iron deficiency anaemia in patients with chronic renal failure undergoing haemodialysis: a randomised trial

Submission date
28/11/2008

Registration date
23/01/2009

Last Edited
14/02/2020

Recruitment status
No longer recruiting

Overall study status
Completed

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

Protocol serial number
VIT-IV-CL-015

Study information

Scientific Title

A multicentre, controlled phase III study to compare the efficacy and safety of VIT-45 and Venofer® in the treatment of iron deficiency anaemia associated with chronic renal failure in patients on haemodialysis

Study objectives
The primary objective was to compare the efficacy of VIT-45 (ferric carboxymaltose) injections and Venofer® injections in patients on haemodialysis with iron deficiency anaemia (IDA) associated with chronic renal failure.

Ethics approval required
Old ethics approval format

Ethics approval(s)
At each study centre, the protocol (dated 30 January 2004) and informed consent form for this study were reviewed and approved by a duly constituted Independent Ethics Committee (IEC) and approval in writing provided to PAREXEL before initiation of the study. Amendments to the protocol (amendment 1, dated 28 July 2004 and amendment 2, dated 20 October 2004) were reviewed and approved in the same manner before being implemented.

Primary study design
Interventional

Study design
Multicentre open-label randomised parallel group phase III study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Iron deficiency anaemia

Interventions
VIT-45 (ferric carboxymaltose) injections and Venofer® (Iron sucrose) injections:

Ferric carboxymaltose:
Aqueous solution containing 50 mg/mL iron administered by dilution by intravenous bolus injection directly into the haemodialysis venous line 1 hour after the start of the dialysis session.
Dose: 200 mg iron (or 100 mg for last dose if needed according to individual iron requirement).

Iron sucrose:
Aqueous solution containing 20 mg/mL iron administered without dilution by intravenous injection over 10 minutes directly into the haemodialysis venous line 1 hour after the start of a dialysis session. The final dose was administered over 5 minutes if it was 100 mg iron.
Dose: 200 mg iron (or 100 mg for the last dose if needed according to individual iron requirement).

There was a 2 week screening period prior to the starting of dosing. Dosing started on day 1, week 0 for both treatment arms and continued two or three times weekly until the individual cumulative dose was reached (week 4). Follow up was 4 weeks (+/- 4 days after the final dose of study medication).

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Venofer®, VIT-45

Primary outcome(s)
The percentage of patients reaching an increase in Hb of greater than or equal to 10 g/L at 4 weeks after baseline.

Key secondary outcome(s)
1. Maximum increase in Hb, ferritin and TfS during study participation
2. Change from baseline levels of Hb, serum ferritin, and TfS, at weeks 1, 2 and 4 and the follow-up visit
3. The number and proportion of patients who, at weeks 1, 2, and 4, and the follow-up visit, achieved target levels of:
3.1. Hb: greater than or equal to 110 g/L in patients with a baseline Hb greater than or equal to 100 g/L or less than or equal to 120 g/L in patients with a baseline Hb greater than 100 g/L to less than or equal to 115 g/L
3.2. Serum ferritin: 200 to 800 µg/L
3.3. TfS: 20 to 50%
4. The individual area under the plasma concentration time curve (AUC) of change from baseline levels of Hb, serum ferritin and TfS, standardised per day of study participation

Safety:
5. Adverse events (AEs): type, nature, incidence and outcome
6. Vital signs (axillary temperature, blood pressure and heart rate) and weight (added by Amendment no 1)
7. 12-lead electrocardiogram (ECG) including documentation of QT and RR intervals
8. Physical examinations
9. Clinical laboratory panels (haematology/coagulation and clinical chemistry)
10. Discontinuation of treatment due to AEs

Completion date
18/01/2005

Eligibility

Key inclusion criteria
1. Adult, male or female, between the ages of 18 and 80 years (inclusive) requiring haemodialysis /haemodiafiltration with iron deficiency secondary to chronic renal failure
2. IDA defined as haemoglobin (Hb) less than or equal to 115 g/L and at least one of the following:
2.1. Transferrin saturation (TfS) less than 20%
2.2. Serum ferritin less than 200 µg/L
Initially, a total of 120 patients (60 in each treatment group) were enrolled with a Hb value of less than or equal to 100 g/L. Following amendment 2, this was adjusted such that in each

treatment group at least 50% of patients (at least 60 in each treatment group) were enrolled with a Hb value of less than or equal to 100 g/L
3. Patients treated with EPO (including epoetin alfa, epoetin beta, and darbepoetin alfa) must have received this treatment for at least 8 weeks prior to inclusion in the study. The EPO dose may have been decreased during the study at the discretion of the investigator; increases in the dose of EPO were not permitted.
4. Permanent vascular access appropriate for haemodialysis/haemodiafiltration
5. Females of childbearing potential must have had a negative serum pregnancy test at screening and agreed to practise an acceptable method of birth control during the study and for up to one month after the last dose of the study medication. Acceptable methods of birth control included barrier methods (including male and female condoms), diaphragms (cervical caps) with intravaginal spermicide (including jellies, foams and suppositories), intra-uterine devices or hormonal contraceptives. Non-childbearing potential included being 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. Fertile males agreed to ensure that they use adequate contraception during the study.
6. Demonstrated the ability to understand the requirements of the study, willingness to provide written informed consent, abide by the study restrictions, and agree to return for the required assessments

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
183

Key exclusion criteria
1. Body weight less than 40 kg
2. Blood transfusion or oral or parenteral iron treatment within 30 days prior to enrolment, or anticipated need for a blood transfusion during the study
3. Documented hypersensitivity to components of VIT-45 or Venofer®
4. Other types of anaemia (especially haemolytic, macrocytic, hypoplastic, or sideroblastic anaemia)
5. Haemochromatosis or other iron storage disorders. Addition of haemodiafiltration was introduced following protocol amendment 1.
6. Untreated vitamin B12 or folic acid deficiency (deficiency defined as below the normal range). Patients with subnormal vitamin B12 levels were included if all of the following criteria are met:
6.1. No suspicion of atrophic gastritis
6.2. No history of resection of large parts of the stomach or upper intestine

6.3. Treatment of vitamin B12 deficiency was started prior to randomisation
7. Treatment with an investigational drug within the 30 days prior to enrolment
8. History of addiction to drugs or chronic alcohol abuse
9. Prior use of VIT-45 or prior participation in other studies of VIT-45
10. Myelosuppressive therapy or need for surgery
11. Active severe infection or malignancy other than carcinoma in situ of the cervix and non-melanoma skin cancer
12. Active liver disease. Patients who were positive for hepatitis B surface-antigen (HbsAg) or hepatitis C virus antibody (anti-HCV) were excluded if they had abnormal liver function test (LFT) results
13. Significant cardiovascular disease, including myocardial infarction within 12 months prior to study inclusion, congestive heart failure (New York Heart Association grade III or IV), or poorly controlled hypertension according to the judgement of the investigator
14. Positive for human immunodeficiency virus-1 (HIV)-1/HIV-2 antibodies (anti-HIV)
15. Pregnant women or nursing mothers
16. Endocrinologic or metabolic disorders that were not controlled

Date of first enrolment
01/07/2004

Date of final enrolment
18/01/2005

Locations

Countries of recruitment
Belgium

Bulgaria

Poland

Romania

Russian Federation

Slovakia

Ukraine

Study participating centre
National Medical Surgery Centre
Moscow
Russian Federation
105203

Sponsor information

Organisation
Vifor Pharma (Switzerland)

ROR
https://ror.org/0185z7g17

Funder(s)

Funder type
Industry

Funder Name
Vifor Pharma (Switzerland)

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?
Abstract results	conference abstract	01/06/2008	14/02/2020	No	No