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PREoperative intraVENous iron To Treat anaemia in major surgery (PREVENTT)

Submission date
08/10/2012

Recruitment status
No longer recruiting

Registration date
09/10/2012

Overall study status
Completed

Last Edited
01/03/2021

Condition category
Haematological Disorders

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

Plain English summary of protocol

Background and study aims
Anaemia is a common problem in patients undergoing surgery. About half of patients undergoing a major operation have anaemia (low blood count), often a consequence of the disease requiring surgery. Anaemia causes patients to feel tired and unwell. At the time of surgery having preoperative anaemia increases the need for a blood transfusion (50% if anaemic compared to only 15% without anaemia). Both anaemia and blood transfusions can be an extra risk, associated with increased complications from surgery, delayed recovery and prolonged hospital stay. We propose that giving intravenous (given directly into a vein) iron before operation can be used to correct anaemia in these patients. Consequently if patients are not anaemic they are less likely to need blood transfusion. This may make patients feel better and improve their health before their operation so that they are more likely to tolerate the surgery, recover faster, be less likely to have complications from surgery and return home sooner. This will have benefits to the individual patient and also to the NHS by reducing costs. The main aim of this study is to assess if intravenous iron will reduce the need for blood transfusion in the time period around the operation. We will further document; patient-reported quality of life, complications, length of hospital stay, and cost. Outcomes will be assessed both during hospital stay and after the patient has been discharged.

Who can participate?
Patients with anaemia undergoing major abdominal surgery (at least 18 years of age)

What does the study involve?
Patients will randomly be allocated to one of two treatment groups: iron or placebo (dummy). Both groups will receive the treatment as an intravenous infusion over 15 minutes; either normal saline (placebo) or normal saline with iron (ferric carboxymaltose). The treatment will be given 10 days-6 weeks before the planned surgery. Patients will be followed-up at 8 weeks and 6 months after the date of the surgery.

What are the possible benefits and risks of participating?
Potential benefits to the patients include correction of anaemia and restoration of iron levels with potential improvements in fatigue symptoms. The risks of participating are the possible side effects of receiving intravenous iron. The most common reported side effects are nausea

and headache. Other known side effects, which may occur, are dizziness, high blood pressure, and/or injection site reactions.

Where is the study run from?
The study will be run in about 40 hospitals in the UK

When is the study starting and how long is it expected to run for?
September 2013 to August 2019 (as of 04/10/2018)

Who is funding the study?
National Institute for Health Research Health Technology Assessment (NIHR HTA) (UK)

Who is the main contact?
Laura Van Dyck
laura.vandyck@lshtm.ac.uk

Contact information

Type(s)
Scientific

Contact name
Mr Toby Richards

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Additional identifiers

Clinical Trials Information System (CTIS)
2012-002786-35

ClinicalTrials.gov (NCT)
NCT01692418

Protocol serial number
HTA 10/104/06, sponsor protocol no.: 12/0246

Study information

Scientific Title

A randomised double-blind controlled phase III study to compare the efficacy and safety of intravenous ferric carboxymaltose with placebo in patients with anaemia undergoing major open abdominal surgery

Acronym
PREVENTT

Study objectives
To determine if a single dose of intravenous iron (ferric carboxymaltose; 1000 mg) given to patients with anaemia prior to major open abdominal surgery reduces the need for peri-operative blood transfusion.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/1010406
Protocol can be found at: http://preventt.lshtm.ac.uk/files/2016/09/PREVENTT-protocol_version-6_2016_07_25-signed.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee East of England - Welwyn; East of England Research Ethics Committee Centre, 05/11/2012, REC ref: 12/EE/0445

Study design
Multicentre phase III randomised double-blind controlled trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Patients will be randomised to receive either intravenous iron (ferric carboxymaltose) or placebo. The treatment will be a one-off infusion.

Ferric Carboxymaltose group:
For all patients the total iron dose will be 1000 mg as a one off infusion in 100 ml normal saline administered over a minimum of 15 minutes.

Placebo group:
Placebo patients will receive the same volume of normal saline without the trial drug; 100 ml normal saline administered over a minimum of 15 minutes.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Iron (ferric carboxymaltose)

Primary outcome(s)
The co-primary outcomes are:
1. Risk of blood transfusion or death from randomisation until 30-days following the index operation.
2. Blood transfusion rate (including repeat transfusions) from randomisation until 30-days following the index operation.

Key secondary outcome(s))
Current secondary outcome measures as of 24/01/2014:
1. Change in haemoglobin levels from randomisation to day of index operation, 8-weeks post index operation and 6 months post index operation
2. Total number of units of blood or blood products cross matched, total number of packed red cells and any blood products transfused from randomisation to 30 days post index operation
3. Post Operative Morbidity Survey outcome at days 3, 5, 7 and 14 following the index operation. Outcomes will be presence of morbidity defined by the domains of the POMS (e.g., gastrointestinal, cardiovascular)
4. Health-related quality of life outcome:
4.1. Change in The Multidimensional Fatigue Inventory (MFI) questionnaire total score from baseline to the 10 days assessment and at 8 weeks and 6 months postoperatively
4.2. Change in European Quality of Life: 5 Dimensions-5 Levels (EQ-5D-5L) questionnaire total score from baseline to the 10 days assessment and at 8 weeks and 6 months postoperatively
4.3. Change in Single Question Outcome Measure (SQOM)
5. Health-economics outcome:
5.1. Health resource utilisation at each assessment time point
5.2. Calculated direct, indirect and total costs for the NHS from two perspectives (payers and societal perspective)
5.3. Cost effectiveness of treatment options using relevant effectiveness parameters
6. Safety and related efficacy outcomes:
6.1. Any reaction or side effect from trial therapy
6.2. Any reaction or side effect from whole blood or blood product, transfusion reaction
6.3. Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reactions (SUSARs)
6.4. Length of hospital stay
6.5. Mortality at 8 weeks and 6 months post-operatively.
6.6. Readmission within 8 weeks and within 6 months of the index operation
6.7. Blood transfusion from randomisation to 8 weeks and 6 months post-operatively
6.8. Change in estimated glomerular filtration rate (e-GFR)
6.9. Vital signs
6.10. Laboratory data

Previous secondary outcome measures:
1. Change in haemoglobin levels from randomisation to day of index operation, 8-weeks post index operation and 6 months post index operation
2. Total number of units of blood or blood products cross matched, total number of packed red cells and any blood products transfused from randomisation to 30 days post index operation

3. Post Operative Morbidity Survey outcome at days 3, 7 and 14 following the index operation. Outcomes will be presence of morbidity defined by the domains of the POMS e.g. gastrointestinal, cardiovascular.
4. Health-related quality of life outcome:
4.1. Change in The Multidimensional Fatigue Inventory (MFI) questionnaire total score from baseline to the two week assessment and at 8 weeks and 6 months post operatively.
4.2. Change in European Quality of Life: 5 Dimensions-5 Levels (EQ-5D-5L) questionnaire total score from baseline to the two week assessment and at 8 weeks and six months post operatively.
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6.8. Change in estimated glomerular filtration rate (e-GFR)
6.9. Vital signs
6.10. Laboratory data

Completion date
20/05/2019

Eligibility

Key inclusion criteria
Current inclusion criteria as of 23/04/2015:
1. At least 18 years of age and signed written informed consent
2. Patients undergoing elective major open abdominal surgery
2.1. The Indication for operation may be for benign or malignant disease
2.2 Major Surgery is defined as an operation of anticipated duration more than one hour
3. Screening haemoglobin (Hb) greater than or equal to 90 g/L (9.0 g/dL) but below or equal to 120 g/L (12.0 g/dL) in women or 130 g/L (13.0 g/dL) in men within four weeks of randomisation
4. Randomisation and administration of study infusion a minimum of 10 days and maximum 42 days before planned operation
5. Negative pregnancy test for women of childbearing potential (within last 7 days), and agree to use effective form of contraception until 6 weeks post treatment
6. Laboratory data used for determination of eligibility at the baseline visit must not be older than four weeks

Previous inclusion criteria from 24/01/2014 to 23/04/2015:
1. At least 18 years of age and signed written informed consent
2. Patients undergoing elective major open abdominal surgery
2.1. The Indication for operation may be for benign or malignant disease

2.2. Major Surgery is defined as an operation of anticipated duration more than one hour where all or part of an abdominal organ is to be removed (hepatectomy, pancreatectomy procedure, gastrectomy, oesophagectomy, colectomy (total/partial), nephrectomy, cystectomy, hysterectomy).
3. Screening haemoglobin (Hb) greater than or equal to 90 g/L (9.0 g/dL) but below or equal to 120 g/L (12.0 g/dL) within four weeks of randomisation
4. Randomisation and administration of study infusion a minimum of 10 days and maximum 42 days before planned operation
5. Negative pregnancy test for women of childbearing potential (within last 7 days), and agree to use effective form of contraception until 6 weeks post treatment
6. Laboratory data used for determination of eligibility at the baseline visit must not be older than four weeks

Original inclusion criteria:
1. At least 18 years of age and signed written informed consent
2. Patients undergoing elective major open abdominal surgery
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2.2. Major Surgery is defined as an operation of anticipated duration more than one hour where all or part of an abdominal organ is to be removed (hepatectomy, pancreatectomy procedure, gastrectomy, oesophagectomy, colectomy (total/partial), nephrectomy, cystectomy, hysterectomy).
3. Screening haemoglobin (Hb) greater than or equal to 9.0 g/dL but below or equal to 12.0 g/dL within four weeks of randomisation
4. Randomisation and administration of study infusion a minimum of 14 days and maximum 42 days before planned operation
5. Negative pregnancy test for women of childbearing potential (within last 7 days), and agree to use effective form of contraception until 6 weeks post treatment
6. Laboratory data used for determination of eligibility at the baseline visit must not be older than four weeks

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
487

Key exclusion criteria
Current exclusion criteria as of 30/09/2016:
1. Patients undergoing laparoscopic surgery

2. Body weight under 50kg
3. Known history of acquired iron overload, or family history of haemochromatosis or thalassemia or TSAT >50%
4. Known reason for anaemia (e.g. untreated B12 or folate deficiency or haemoglobinopathy)
5. Known hypersensitivity to ferric carboxymaltose (Ferinject®) or its excipients
6. Temperature > 37.5 degrees C or patient on non-prophylactic antibiotics
7. Known chronic liver disease
8. If clinically indicated for the patient to have LFT's as part of pre-assessment for surgery and this screening alanine transaminase (ALT) or aspartate transaminase (AST) is above three times the upper limit of the normal range
9. Received erythropoietin or i.v. iron therapy in the previous 12 weeks
10. Immunosuppressive therapy (for organ transplantation) or renal dialysis (current or planned within the next 12 months)
11. Patients with severe asthma or severe allergy (requiring hospitalisation within the last 12 months)
12. Unfit for elective surgery
13. Pregnancy or lactation
14. Inability to fully comprehend and/or perform study procedures in the investigator's opinion
15. Patient involvement in another IMP trial within the previous 4 weeks, prior to randomisation. Involvement in another IMP trial, following randomisation, that may impact on the results of the PREVENTT trial

Previous exclusion criteria from 23/04/2015 to 30/09/2016:
1. Patients undergoing laparoscopic surgery
2. Body weight under 50kg
3. Known history of acquired iron overload, or family history of haemochromatosis or thalassemia or TSAT >50%
4. Known reason for anaemia (e.g. untreated B12 or folate deficiency or haemoglobinopathy)
5. Known hypersensitivity to ferric carboxymaltose (Ferinject®) or its excipients
6. Temperature > 37.5 degrees C or patient on non-prophylactic antibiotics
7. Chronic liver disease and/or screening alanine transaminase (ALT) or aspartate transaminase (AST) above three times the upper limit of the normal range
8. Received erythropoietin, i.v. iron therapy or blood transfusion in the previous 12 weeks
9. Immunosuppressive therapy (for organ transplantation) or renal dialysis (current or planned within the next 12 months)
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9. Immunosuppressive therapy (for organ transplantation) or renal dialysis (current or planned within the next 12 months)
10. Patients with severe asthma or severe allergy
11. Unfit for elective surgery
12. Pregnancy or lactation
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7. Chronic liver disease and/or screening alanine transaminase (ALT) or aspartate transaminase (AST) above three times the upper limit of the normal range
8. Received erythropoietin, i.v. iron therapy or blood transfusion in the previous 12 weeks
9. Immunosuppressive therapy or renal dialysis (current or planned within the next 12 months)
10. Pregnancy or lactation
11. Inability to fully comprehend and/or perform study procedures in the investigator's opinion
12. Patient involvement in another Investigational Medicinal Product (IMP) trial within the previous 4 weeks, prior to randomisation. Involvement in another IMP trial, following randomisation, that may impact on the results of the PREVENTT trial

Date of first enrolment
01/09/2013

Date of final enrolment
30/09/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University College Hospital
London
United Kingdom
NW1 2BU

Study participating centre
39 other hospitals
United Kingdom
-

Sponsor information

Organisation
University College London (UK)

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
NIHR - Health Technology Assessment (HTA) (UK) ref:10/104/06

Results and Publications

Individual participant data (IPD) sharing plan
Research data will be made available to the scientific community with as few restrictions as possible so as to maximise the value of the data for research and for eventual patient and public benefit. All data requests should be submitted to the Chief Investigator (Toby Richards, toby.richards@uwa.edu.au) for consideration

(updated 15/10/2020, previously:
IPD sharing statement:
The data sharing plans for the current study are unknown and will be made available at a later date)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
	results				

Results article		01/10/2020	23/09/2020	Yes	No
Results article	results	01/02/2021	01/03/2021	Yes	No
Protocol article	protocol	04/06/2015		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes