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

Study website http://preventt.lshtm.ac.uk/

Contact information

Type(s) Scientific

Contact name Mr Toby Richards

Contact details

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Additional identifiers

EudraCT/CTIS number 2012-002786-35

IRAS number

ClinicalTrials.gov number NCT01692418

Secondary identifying numbers 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 perioperative 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/PREVENTTprotocol_version-6_2016_07_25-signed.pdf

Ethics approval required Old ethics approval format

Old ethics approval forma

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

Secondary study design Randomised controlled trial

Study setting(s) Hospital

Study type(s) Treatment

Participant information sheet

Patient information can be found at: http://preventt.lshtm.ac.uk/files/2014/06 /PREVENTT_Information-sheet_version-4_2013-Dec-16.pdf

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 measure

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.

Secondary outcome measures

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

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
 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. 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 (payer's 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

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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.

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6.8. Change in estimated glomerular filtration rate (e-GFR)

6.9. Vital signs

6.10. Laboratory data

Overall study start date

01/09/2013

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

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 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

Age group

Adult

Lower age limit 18 Years

Sex

Both

Target number of participants 500

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)

10. Patients with severe asthma or severe allergy (requiring hospitalisation within the last 12 months)

11. Unfit for elective surgery

12. Pregnancy or lactation

13. Inability to fully comprehend and/or perform study procedures in the investigator's opinion 14. 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 24/01/2014 to 23/04/2015:

1. Patients undergoing laparoscopic surgery

2. Body weight under 50kg

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4. Known reason for anaemia (e.g. 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)

10. Patients with severe asthma or severe allergy

11. Unfit for elective surgery

12. Pregnancy or lactation

13. Inability to fully comprehend and/or perform study procedures in the investigator's opinion

14. 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.

Original exclusion criteria:

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. 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 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 England

United Kingdom

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

Study participating centre 39 other hospitals United Kingdom

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Sponsor information

Organisation University College London (UK)

Sponsor details Joint UCLH/UCL Biomedical Research Unit 1st Floor Maple House 149 Tottenham Court Road London England United Kingdom W1T 7NF

Sponsor type University/education

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

Publication and dissemination plan

Planned publication in a high-impact peer-reviewed journal

Intention to publish date

31/08/2020

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?
Protocol article	protocol	04/06/2015		Yes	No
<u>Results article</u>	results	01/10/2020	23/09/2020	Yes	No
<u>Results article</u>	results	01/02/2021	01/03/2021	Yes	No
HRA research summary			28/06/2023	No	No