ISRCTN16403302 https://doi.org/10.1186/ISRCTN16403302

Intravenous iron treatment in patients with heart failure and iron deficiency: IRONMAN

Submission date
28/11/2016

Recruitment status
No longer recruiting

Registration date
15/12/2016

Overall study status
Completed

Last Edited
08/09/2023

Condition category
Circulatory System

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

Plain English summary of protocol

Current plain English summary as of 16/03/2022:
Background and study aims
Chronic heart failure (CHF) is a long-term condition where the heart has become weakened and isn't able to pump blood around the body effectively. Chronic heart failure (CHF) is a very common problem. Despite improvements in treatment, many patients suffer limiting symptoms of shortness of breath and fatigue (extreme tiredness). Many patients with CHF have iron deficiency, meaning that the iron levels in their blood are too low or they are unable to utilise iron properly. This is associated with poor health outcomes, as iron is vital for the transport of oxygen around the body by red blood cells. The aim of this study is to find out whether treating iron-deficient CHF patients with intravenous (through a vein) iron is an effective way of reducing death due to circulatory system problems, and hospitalisation due to heart failure.

Who can participate?
Adults with chronic heart failure and iron deficiency.

What does the study involve?
Participants are randomly allocated to one of two groups. On the formal study visit, those in the first group receive iron through a trip at an individual dosage calculated from their height, weight and current iron levels. This takes around 15-30 minutes and participants need to stay in the clinic for around 30 minutes before going home. The whole visit takes between 1.5-2 hours. Those in the second group do not receive any iron and have blood tests at the formal study visit only. This takes between 1-1.5 hours. For those in both groups, subsequent study visits are arranged at 4 weeks and then three times a year for the rest of the study (between 3 months and 5.5 years). At these follow-up visits, participants undergo a clinical assessment (including checking weight, blood pressure and pulse) and are asked about their symptoms, medication and any medical problems since the last visit as well as completing a quality of life questionnaire.

What are the possible benefits and risks of participating?
If the iron treatment is successful and iron deficiency improves or is completely resolved, participants may feel better. There is no guarantee that a benefit will be felt by participants, however. Nevertheless, results from this study may provide information which will help us to treat heart failure patients with iron deficiency more successfully in the future. Participants may

experience side effects related to the iron therapy but these are rare. Initial screening tests may reveal a medical problem which may mean the participant can't be entered into the study. Blood sampling is a part of this study and may cause minor discomfort and bruising.

Where is the study run from?
Queen Alexandra Hospital (lead site) and around 64 other NHS hospitals (UK)

When is the study starting and how long is it expected to run for?
July 2015 to August 2022

Who is funding the study?
1. British Heart Foundation (UK)
2. Pharmacosmos UK Ltd. (UK)

Who is the main contact?
Ms Elizabeth Thomson
elizabeth.thomson@glasgow.ac.uk

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Previous plain English summary:
Background and study aims
Chronic heart failure (CHF) is a long-term condition where the heart has become weakened and isn't able to pump blood around the body effectively. Chronic heart failure (CHF) is a very common problem. Despite improvements in treatment, many patients suffer limiting symptoms of shortness of breath and fatigue (extreme tiredness). Many patients with CHF have iron deficiency, meaning that the iron levels in their blood are too low or they are unable to utilise iron properly. This is associated with poor health outcomes, as iron is vital for the transport of oxygen around the body by red blood cells. The aim of this study is to find out whether treating iron-deficient CHF patients with intravenous (through a vein) iron is an effective way of reducing death due to circulatory system problems, and hospitalisation due to heart failure.

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What are the possible benefits and risks of participating?
If the iron treatment is successful and iron deficiency improves or is completely resolved, participants may feel better. There is no guarantee that a benefit will be felt by participants, however. Nevertheless, results from this study may provide information which will help us to treat heart failure patients with iron deficiency more successfully in the future. Participants may experience side effects related to the iron therapy but these are rare. Initial screening tests may

reveal a medical problem which may mean the participant can't be entered into the study. Blood sampling is a part of this study and may cause minor discomfort and bruising.

Where is the study run from?
Queen Alexandra Hospital (lead site) and around 64 other NHS hospitals (UK)

When is the study starting and how long is it expected to run for?
July 2015 to March 2022

Who is funding the study?
1. British Heart Foundation (UK)
2. Pharmacosmos UK Ltd. (UK)

Who is the main contact?
Ms Elizabeth Thomson
elizabeth.thomson@glasgow.ac.uk

Study website
https://www.ironmanstudy.co.uk/

Contact information

Type(s)
Public

Contact name
Ms Elizabeth Thomson

Contact details
Institute of Health and Wellbeing
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elizabeth.thomson@glasgow.ac.uk

Additional identifiers

EudraCT/CTIS number
2015-004196-73

IRAS number

ClinicalTrials.gov number
NCT02642562

Secondary identifying numbers
31982

Study information

Scientific Title
Effectiveness of intravenous iron treatment vs standard care in patients with heart failure and iron deficiency: a randomised, open-label multicentre trial (IRONMAN)

Acronym
IRONMAN

Study objectives
The aim of this study is to establish in patients with chronic heart failure and iron deficiency whether treatment with intravenous iron is effective in reducing death due to cardiovascular problems, and hospitalisation due to heart failure.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East Midlands - Leicester South Research Ethics Committee, 25/02/2016, ref: 15/EM/0551

Study design
Randomized interventional

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Heart failure and iron deficiency

Interventions
Current intervention as of 16/03/2022:
Participants are randomised to one of two groups. All participants will be involved in the study for an average approximately 4 years (event driven trial, expected maximum around 5.5 years, minimum around 3 months – anticipated 5 years recruitment and a projected further minimum 3

months of treatments/assessments, giving a range of projected patient participation of around 3 months – 5.5 years). All participants will be seen at 4 weeks and then every 4 months for study duration.

Intervention arm: Participants will receive an injection at the first formal study visit. The iron (ferric derisomaltose) is given intravenously as an infusion over 15-30 minutes and the dosage that is required is calculated according to participant weight and blood tests (calculated by electronic case record form, eCRF). The participant will then need to stay in the clinic for another 30 minutes before going home. This whole visit will take around 1.5 to 2 hours. Subsequent study visits will be arranged at around 4 weeks and then every 4 months (that is three times a year) until the study finishes. Blood will be tested at, or before, each study visit. At each visit there will be a clinical assessment (including checking weight, blood pressure, pulse) and the research team will ask about symptoms, medication and any medical problems since the last visit. A quality of life questionnaire will be completed (a second questionnaire and a walking test for 6 minutes will be offered at two further time points during the study). Each visit will last around 1 hour.
An iron infusion will only be required if iron levels are found to be low; on average we expect this to be around once a year (this will vary between participants – some needing it more often and others less often). The iron injection (Monofer®) will normally be given at a separate appointment although it may sometimes be possible for this to be given on the same day as the study visit. It is anticipated that participants will be in the clinic for around 1.5 to 2 hours for each iron injection.

Standard arm: Participants will not receive the intervention (intravenous iron). Blood will be tested at the formal study visit. This visit will take approximately 1 – 1.5 hours. Subsequent study visits will be arranged at convenient times at around 4 weeks and then every 4 months (that is three times a year) until the study finishes. Blood will be tested at, or before, each study visit. At each visit there will be a clinical assessment (including checking weight, blood pressure, pulse) and the research team will ask about symptoms, medication and any medical problems since the last visit. A quality of life questionnaire will be completed (a second questionnaire and a walking test for 6 minutes will be offered at two further time points during the study). Each visit will last around 1 hour.

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Previous intervention:
Participants are randomised to one of two groups. All participants will be involved in the study for an average of 3 years (event driven trial, expected maximum 4.5 years, minimum 2.5 years – anticipated 2 years recruitment and a projected further 2 years of treatments/assessments, and a further closeout visit giving a range of projected patient participation of 2.5 – 4.5 years). All participants will be seen at 4 weeks and then every 4 months for study duration.

Intervention arm: Participants will receive an injection at the first formal study visit. The iron (iron isomaltoside 1000) is given intravenously as an infusion over 15-30 minutes and the dosage that is required is calculated according to participant weight and blood tests (calculated by electronic case record form, eCRF). The participant will then need to stay in the clinic for another 30 minutes before going home. This whole visit will take around 1.5 to 2 hours. Subsequent study visits will be arranged at around 4 weeks and then every 4 months (that is three times a year) until the study finishes. Blood will be tested at, or before, each study visit. At each visit there will be a clinical assessment (including checking weight, blood pressure, pulse) and the research team will ask about symptoms, medication and any medical problems since the last visit. A quality of life questionnaire will be completed (a second questionnaire and a walking test for 6 minutes will be offered at two further time points during the study). Each visit will last

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An iron infusion will only be required if iron levels are found to be low; on average we expect this to be around once a year (this will vary between participants – some needing it more often and others less often). The iron injection (Monofer®) will normally be given at a separate appointment although it may sometimes be possible for this to be given on the same day as the study visit. It is anticipated that participants will be in the clinic for around 1.5 to 2 hours for each iron injection.

Standard arm: Participants will not receive the intervention (intravenous iron). Blood will be tested at the formal study visit. This visit will take approximately 1 – 1.5 hours. Subsequent study visits will be arranged at convenient times at around 4 weeks and then every 4 months (that is three times a year) until the study finishes. Blood will be tested at, or before, each study visit. At each visit there will be a clinical assessment (including checking weight, blood pressure, pulse) and the research team will ask about symptoms, medication and any medical problems since the last visit. A quality of life questionnaire will be completed (a second questionnaire and a walking test for 6 minutes will be offered at two further time points during the study). Each visit will last around 1 hour.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Monofer (ferric derisomaltose/iron isomaltoside 1000)

Primary outcome measure
Current primary outcome measure as of 07/09/2022:
CV mortality or hospitalisation for worsening heart failure is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow-up period (minimum of 3 months follow-up from last patient recruited)

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Previous primary outcome measure as of 16/03/2022:
Cardiovascular CV mortality or hospitalisation for worsening heart failure is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 3 months - 5.5 years or 4 years on average)

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Previous primary outcome measure:
Cardiovascular CV mortality or hospitalisation for worsening heart failure is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average).

Secondary outcome measures
Current secondary outcome measures as of 07/09/2022:
1. Hospitalisation for worsening heart failure (recurrent events) [Time Frame: Minimum of 3 months follow-up from last patient recruited]
2. CV hospitalisation (first event) [Time Frame: Minimum of 3 months follow-up from last patient recruited]

3. CV death or hospitalisation for heart failure analysed as time to first event [Time Frame: Minimum of 3 months follow-up from last patient recruited]
4. Overall Score from Minnesota Living with Heart Failure [Time Frame: At 4 months]
5. Cardiovascular mortality [Time Frame: Minimum of 3 months follow-up from last patient recruited]
6. Overall EQ-5D VAS [Time Frame: At 4 months]
7. Overall EQ-5D index [Time Frame: At 4 months]
8. CV mortality or hospitalisation for major CV event (stroke, MI, heart failure) (first event) [Time Frame: Minimum of 3 months follow-up from last patient recruited]
9. All-cause mortality [Time Frame: Minimum of 3 months follow-up from last patient recruited]
10. All-cause hospitalisation (first event) [Time Frame: Minimum of 3 months follow-up from last patient recruited]
11. Combined all-cause mortality or first all-cause unplanned hospitalisation [Time Frame: Minimum of 3 months follow-up from last patient recruited]
12. Physical domain of QoL (Minnesota Living With Heart Failure) [Time Frame: At 4 months]
13. Physical domain of QoL (Minnesota Living With Heart Failure) [Time Frame: At 20 months]
14. Overall EQ-5D VAS [Time Frame: At 20 months]
15. Overall EQ-5D index [Time Frame: At 20 months]
16. Overall Score from Minnesota Living With Heart Failure [Time Frame: At 20 months]
17. Days dead or hospitalised [Time Frame: At 36 months]
18. Quality-adjusted days alive and out of hospital [Time Frame: At 12 months]
19. 6 minute walk test [Time Frame: At 4 months]
20. 6 minute walk test [Time Frame: At 20 months]
21. Death due to infection [Time Frame: Minimum of 3 months follow-up from last patient recruited]
22. Hospitalisation primarily for infection (first event) [Time Frame: Minimum of 3 months follow-up from last patient recruited]

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Previous secondary outcome measures as of 16/03/2022:

1. CV mortality is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 3 months - 5.5 years or 4 years on average)
2. Hospitalisation for worsening heart failure (analysis will include first and recurrent hospitalisations) and is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 3 months - 5.5 years or 4 years on average)
3. All-cause mortality is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 3 months - 5.5 years or 4 years on average)
4. CV mortality or first hospitalisation for major CV event (stroke, myocardial infarction [MI], heart failure). Days dead or hospitalised is assessed through review of case notes and reporting of patient, relative, carer or clinician
5. Physical domain of QoL (Minnesota Living With Heart Failure) – this will be the difference between groups at 4 months and also at 20 months. Minnesota Living with Heart Failure is used at these time points to measure QoL.
6. Overall QoL assessment (Minnesota Living With Heart Failure, EQ-5D index and EQ-5D VAS) – this will be the difference between groups at 4 months and also at 20 months. Minnesota Living with Heart Failure and EQ-5D are used at these time points to measure QoL.
7. Combined all-cause mortality or first all-cause unplanned hospitalization is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 3 months - 5.5 years or 4 years on average)

8. Days dead or hospitalised at 3 years (minimum duration of follow-up) is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period
9. Quality-adjusted days alive and out of hospital at 3 years assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period
10. CV hospitalisation (first event) assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 3 months - 5.5 years or 4 years on average)
11. All-cause hospitalisation (first event) is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 3 months - 5.5 years or 4 years on average)
12. 6-minute walk test - this will be the difference between groups at 4 months and also at 20 months.
13. (Secondary safety) Death due to infection is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 3 months - 5.5 years or 4 years on average)
14. (Secondary safety) Hospitalisation primarily for infection is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 3 months - 5.5 years or 4 years on average)

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Previous secondary outcome measures as of 31/12/2019:

1. CV mortality is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
2. Hospitalisation for worsening heart failure (analysis will include first and recurrent hospitalisations) and is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
3. All-cause mortality is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
4. CV mortality or first hospitalisation for major CV event (stroke, myocardial infarction [MI], heart failure). Days dead or hospitalised is assessed through review of case notes and reporting of patient, relative, carer or clinician at 2.5 years of follow up.
5. Physical domain of QoL (Minnesota Living With Heart Failure) – this will be the difference between groups at 4 months and also at 20 months. Minnesota Living with Heart Failure is used at these time points to measure QoL.
6. Overall QoL assessment (Minnesota Living With Heart Failure, EQ-5D index and EQ-5D VAS) – this will be the difference between groups at 4 months and also at 20 months. Minnesota Living with Heart Failure and EQ-5D are used at these time points to measure QoL.
7. Combined all-cause mortality or first all-cause unplanned hospitalization is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
8. Days dead or hospitalised at 2.5 years (minimum duration of follow-up) is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
9. Quality-adjusted days alive and out of hospital at 2.5 years) is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
10. CV hospitalisation (first event)) is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
11. All-cause hospitalisation (first event) is assessed through review of case notes and reporting

of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
12. 6-minute walk test - this will be the difference between groups at 4 months and also at 20 months.
13. Death due to infection is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
14. Hospitalisation primarily for infection is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)

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Previous secondary outcome measures as of 31/05/2018:

1. CV mortality is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
2. Hospitalisation for worsening heart failure (analysis will include first and recurrent hospitalisations) and is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
3. All-cause mortality is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
4. CV mortality or first hospitalisation for major CV event (stroke, myocardial infarction [MI], heart failure). Days dead or hospitalised is assessed through review of case notes and reporting of patient, relative, carer or clinician at 2.5 years of follow up.
5. Physical domain of QoL (Minnesota Living With Heart Failure) – this will be the difference between groups at 4 months and also at 20 months. Minnesota Living with Heart Failure is used at these time points to measure QoL.
6. Overall QoL assessment (Minnesota Living With Heart Failure, EQ-5D index and EQ-5D VAS) – this will be the difference between groups at 4 months and also at 20 months. Minnesota Living with Heart Failure and EQ-5D are used at these time points to measure QoL.
7. Combined all-cause mortality or first all-cause unplanned hospitalization is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
8. Days dead or hospitalised at 2.5 years (minimum duration of follow-up) is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
9. Quality-adjusted days alive and out of hospital at 2.5 years) is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
10. CV hospitalisation (first event)) is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
11. All-cause hospitalisation (first event) is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
12. 6-minute walk test - this will be the difference between groups at 4 months and also at 20 months.
13. Death due to sepsis is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
14. Hospitalisation primarily for infection is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)

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4. CV mortality or first hospitalisation for major CV event (stroke, myocardial infarction [MI], heart failure). Days dead or hospitalised is assessed through review of case notes and reporting of patient, relative, carer or clinician at 2.5 years of follow up.
5. Physical domain of Quality of Life (QoL) - this will be the difference between groups at 4 months and also at 20 months. Minnesota Living with Heart Failure and EQ-5D are used at these time points to measure QoL.
6. Overall QoL assessment - this will be the difference between groups at 4 months and also at 20 months Minnesota Living with Heart Failure and EQ-5D are used at these time points to measure QoL.
7. Combined all-cause mortality or first all-cause unplanned hospitalization is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
8. Days dead or hospitalised at 2.5 years (minimum duration of follow-up) is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
9. Quality-adjusted days alive and out of hospital at 2.5 years) is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
10. CV hospitalisation (first event)) is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
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12. Death due to sepsis is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)
13. Hospitalisation primarily for infection is assessed through review of case notes and reporting of patient, relative, carer or clinician throughout the follow up period (range 2.5 – 4.5 years or 3 years on average)

Overall study start date
08/07/2015

Completion date
31/08/2022

Eligibility

Key inclusion criteria

Current inclusion criteria as of 31/05/2018:
1. Aged ≥18 years
2. LVEF <45% within the prior two years using any conventional imaging modality (this should be the most recent assessment of LVEF)
3. New York Heart Association (NYHA) class II – IV
4. Iron deficient - defined as TSAT <20% and/or ferritin <100 mcg/l
5. Evidence of being in a higher risk HF group:
5.1. Current (with the expectation that patient will survive to discharge) or recent (within 6 months) hospitalisation for HF (as of 08/10/2018), or
5.2. Out-patients with NT-proBNP >250 ng/l in sinus rhythm or >1,000 ng/l in atrial fibrillation (or BNP of >75 pg/ml or 300 pg/ml, respectively)
6. Able and willing to provide informed consent

Previous inclusion criteria:
1. Age ≥18 years
2. LVEF <45% within the last 6 months using any conventional imaging modality
3. New York Heart Association (NYHA) class II – IV
4. Iron deficient defined as a TSAT<20% and/or ferritin >100 mcg/l
5. Evidence of being in a higher risk heart failure group:
5.1. Current (with intention to discharge in next 48 hours) or recent (within 6 months) hospitalisation for heart failure, or
5.2. Outpatients with NTproBNP >250 ng/l in sinus rhythm or >1,000 ng/l in atrial fibrillation (or BNP of > 75 pg/ml or 300 pg/ml, respectively)
6. Able and willing to provide informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 1300; UK Sample Size: 1300

Total final enrolment
1137

Key exclusion criteria
Current exclusion criteria as of 31/12/2019:

1. Haematological criteria: ferritin >400ug/l; haemoglobin <9.0, or >13 g/dl in women or >14 g/dl in men; (B12 or folate deficiency should be corrected but do not exclude the patient)
2. MDRD/CKD-EPI estimated glomerular filtration rate (eGFR) <15ml/min/1.73m²
3. Already planned to receive IV iron
4. Likely to need or already receiving erythropoiesis stimulating agents (ESA)

5. Any of the following apply:
5.1. Planned cardiac surgery or revascularisation
5.2. Within 3 months of any of the following: a primary diagnosis of type 1 myocardial infarction (excluding small troponin elevations in the context of heart failure admissions), cerebrovascular accident (CVA), major CV surgery or percutaneous coronary intervention (PCI), or blood transfusion
5.3. On active cardiac transplant list
5.4. Left ventricular assist device implanted
6. Any of the following comorbidities: active infection (if the patient is suffering from a significant ongoing infection as judged by the investigator recruitment should be postponed until the infection has passed or is controlled by antibiotics), other disease with life expectancy of <2 years, active clinically relevant bleeding in the investigator's opinion, known or suspected gastro-intestinal malignancy
7. Pregnancy, women of childbearing potential (i.e. continuing menstrual cycle) not using effective contraception or breast-feeding women
8. Contraindication to IV iron in the investigator's opinion according to current approved Summary of Product Characteristics:
8.1. Hypersensitivity to the active substance, to Monofer® or any of its excipients (water for injections, sodium hydroxide (for pH adjustment), hydrochloric acid (for pH adjustment))
8.2. Known serious hypersensitivity to other parenteral iron products
8.3. Non-iron deficiency anaemia (e.g. haemolytic anaemia)
8.4. Iron overload or disturbances in utilisation of iron (e.g. haemochromatosis, haemosiderosis)
8.5. Decompensated liver disease
9. Participation in another intervention study involving a drug or device within the past 90 days (co-enrolment in observational studies is permitted)

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Previous exclusion criteria as of 08/10/2018:

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5.3. On active cardiac transplant list
5.4. Left ventricular assist device implanted
6. Any of the following comorbidities: active infection (if the patient is suffering from a significant ongoing infection as judged by the investigator recruitment should be postponed until the infection has passed or is controlled by antibiotics), other disease with life expectancy of <2 years, active clinically relevant bleeding in the investigator's opinion, known or suspected gastro-intestinal malignancy
7. Pregnancy, women of childbearing potential (i.e. continuing menstrual cycle) not using effective contraception or breast-feeding women
8. Contraindication to IV iron in the investigator's opinion according to current approved Summary of Product Characteristics:
8.1. Hypersensitivity to the active substance, to Monofer® or any of its excipients (water for injections, sodium hydroxide (for pH adjustment), hydrochloric acid (for pH adjustment))

8.2. Known serious hypersensitivity to other parenteral iron products
8.3. Non-iron deficiency anaemia (e.g. haemolytic anaemia)
8.4. Iron overload or disturbances in utilisation of iron (e.g. haemochromatosis, haemosiderosis)
8.5. Decompensated liver disease
9. Participation in another intervention study involving a drug or device within the past 90 days (co-enrolment in observational studies is permitted)

_____
Previous exclusion criteria (as of 31/05/2018):

1. Haematological criteria: ferritin >400ug/l; haemoglobin <9.0, or >13 g/dl in women or >14 g/dl in men; (B12 or folate deficiency should be corrected but do not exclude the patient)
2. MDRD estimated glomerular filtration rate (eGFR) <15ml/min/1.73m2
3. Chronic defined need for IV iron therapy
4. Likely to need or already receiving erythropoiesis stimulating agents (ESA)
5. Any of the following apply: (a) planned cardiac surgery or revascularisation or cardiac device implantation; (b) within 3 months of any of the following: a primary diagnosis of type 1 myocardial infarction (excluding small troponin elevations in the context of heart failure admissions), cerebrovascular accident (CVA), major CV surgery or percutaneous coronary intervention (PCI), or blood transfusion; (c) on active cardiac transplant list; (d) left ventricular assist device implanted.
6. Any of the following comorbidities: active infection (if the patient is suffering from a significant ongoing infection as judged by the investigator recruitment should be postponed until the infection has passed or is controlled by antibiotics), other disease with life expectancy of <2 years, active clinically relevant bleeding in the investigator's opinion, known or suspected gastro-intestinal malignancy
7. Pregnancy, women of childbearing potential (i.e. continuing menstrual cycle) not using effective contraception or breast-feeding women
8. Contra-indication to IV iron in the investigator's opinion according to current approved Summary of Product Characteristics: hypersensitivity to the active substance, to Monofer® or any of its excipients (water for injections, sodium hydroxide (for pH adjustment), hydrochloric acid (for pH adjustment)); known serious hypersensitivity to other parenteral iron products; non-iron deficiency anaemia (e.g. haemolytic anaemia); iron overload or disturbances in utilisation of iron (e.g. haemochromatosis, haemosiderosis); decompensated liver cirrhosis and hepatitis
9. Participation in another intervention study involving a drug or device within the past 90 days (co-enrolment in observational studies is permitted)

Previous exclusion criteria:
1. Haematological criteria: ferritin >400ug/L; haemoglobin <9.0 or >13 g/dL in women or >14g/dL in men; (B12 or folate deficiency should be corrected but do not exclude the patient)
2. MDRD estimated glomerular filtration rate (eGFR) <15ml/min/1.73m2
3. Chronic defined need for IV iron therapy
4. Likely to need or already receiving erythropoiesis stimulating agents (ESA)
5. Planned cardiac surgery or revascularisation or cardiac device implantation; within 3 months of a primary diagnosis of type 1 myocardial infarction (excluding small troponin elevations in the context of heart failure admissions), cerebrovascular accident (CVA), major CV surgery or percutaneous coronary intervention (PCI), cardiac device implantation or blood transfusion; on active cardiac transplant list; left ventricular assist device implanted
6. Any of the following comorbidities: active infection (if the patient is suffering from a significant ongoing infection as judged by the investigator recruitment should be postponed until the infection has passed or is controlled by antibiotics), other disease with life expectancy of <2 years, active clinically relevant bleeding in the investigators opinion, known or suspected gastrointestinal malignancy

7. Pregnancy or women of childbearing potential (i.e. continuing menstrual cycle) not using effective contraception
8. Contraindication to IV iron in the investigator's opinion according to current approved Summary of Product Characteristics: hypersensitivity to the active substance, to Monofer® or any of its excipients (water for injections, sodium hydroxide (for pH adjustment), hydrochloric acid (for pH adjustment)); known serious hypersensitivity to other parenteral iron products; noniron deficiency anaemia (e.g. haemolytic anaemia); iron overload or disturbances in utilisation of iron (e.g. haemochromatosis, haemosiderosis); decompensated liver cirrhosis and hepatitis
9. Participation in another intervention study involving a drug or device within the past 90 days (coenrolment In observational studies is permitted)

Date of first enrolment
25/08/2016

Date of final enrolment
15/10/2021

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
Queen Alexandra Hospital
Portsmouth Hospitals NHS Trust
Southwick Hill Road
Cosham
Portsmouth
United Kingdom
PO6 3LY

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
Glasgow
United Kingdom
G4 0ET

Study participating centre
Golden Jubilee National Hospital
Agamemnon Street
Clydebank
United Kingdom
G81 4DY

Study participating centre
Queen Elizabeth University Hospital
1345 Govan Road,
Govan
Glasgow
United Kingdom
G51 4TF

Study participating centre
Salford Royal Hospital
Stott Lane
Salford
United Kingdom
M6 8HD

Study participating centre
Glenfield Hospital
University of Leicester
Clinical Science Wing
Leicester
United Kingdom
LE3 9QP

Study participating centre
Royal Sussex County Hosptial
Eastern Road
Brighton
United Kingdom
BN2 5BE

Study participating centre

Great Western Hospital
Marlborough Road
Swindon
United Kingdom
SN3 6BB

Study participating centre
Ninewells Hospital and Medical School
Division of Cardiovascular & Diabetes Medicine
Mailbox 2
Dundee
United Kingdom
DD1 9SY

Study participating centre
Basingstoke and North Hampshire Hospital
Aldermaston Rd
Basingstoke
United Kingdom
RG24 9NA

Study participating centre
Raigmore Hospital
Old Perth Road
Inverness
United Kingdom
IV2 3UJ

Study participating centre
Aintree University Hospital
Longmoor Lane
Liverpool
United Kingdom
L9 7AL

Study participating centre
Royal Glamorgan Hospital
Ynysmaerdy
Llantrisant
United Kingdom
CF72 8XR

Study participating centre
West Middlesex University Hospital
Twickenham Rd
Isleworth
United Kingdom
TW7 6AF

Study participating centre
Manchester Royal Infirmary
Oxford Rd
Manchester
United Kingdom
M13 9WL

Study participating centre
Royal Alexandra Hospital
Corsebar Road
Paisley
United Kingdom
PA2 9PN

Study participating centre
St Bartholomew's Hospital
W Smithfield
London
United Kingdom
EC1A 7BE

Study participating centre
University College Hospital
35 Euston Rd
Bloomsbury
London
United Kingdom
NW1 2BU

Study participating centre

Castle Hill Hospital
Castle Rd
Cottingham
United Kingdom
HU16 5JQ

Study participating centre
University Hospital Monklands
Monkscourt Ave
Airdrie
United Kingdom
ML6 0JS

Study participating centre
Royal Infirmary of Edinburgh
51 Little France Cres
Edinburgh
United Kingdom
EH16 4SA

Study participating centre
Liverpool Heart and Chest Hospital
Thomas Dr
Liverpool
United Kingdom
L14 3PE

Study participating centre
Royal Bournemouth Hospital
Castle Ln E
Bournemouth
United Kingdom
BH7 7DW

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Health Campus
Foresterhill Rd
Aberdeen
United Kingdom
AB25 2ZN

Study participating centre
Royal Devon and Exeter Hospital
Barrack Rd
Exeter
United Kingdom
EX2 5DW

Study participating centre
University Hospital Coventry
Clifford Bridge Rd
Coventry
United Kingdom
CV2 2DX

Study participating centre
King's College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Morriston Hospital
Heol Maes Eglwys
Morriston
Cwmrhydyceirw
Swansea
United Kingdom
SA6 6NL

Study participating centre
University Hospital Crosshouse
Kilmarnock Rd
Crosshouse
Kilmarnock
United Kingdom
KA2 0BE

Study participating centre
Wythenshawe Hospital
Southmoor Rd
Wythenshawe
Manchester
United Kingdom
M23 9LT

Study participating centre
Harefield Hospital
Hill End Rd
Harefield
Uxbridge
United Kingdom
UB9 6JH

Study participating centre
Ulster Hospital
Upper Newtownards Rd
Dundonald
Belfast
United Kingdom
BT16 1RH

Study participating centre
Eastbourne District General Hospital
Kings Dr
Eastbourne
United Kingdom
BN21 2UD

Study participating centre
North Middlesex University Hospital
Sterling Way
London
United Kingdom
N18 1QX

Study participating centre
Royal Gwent Hospital
Cardiff Rd

Newport
United Kingdom
NP20 2UB

Study participating centre
University Hospital Llandough
Penlan Rd
Llandough
Penarth
United Kingdom
CF64 2XX

Study participating centre
University Hospital Southampton
Tremona Rd
Southampton
United Kingdom
SO16 6YD

Study participating centre
Barnet Hospital
Wellhouse Ln
Barnet
United Kingdom
EN5 3DJ

Study participating centre
Antrim Area Hospital
Bush Rd
Antrim
United Kingdom
BT41 2RL

Study participating centre
Blackpool Teaching Hospitals
Whinney Heys Rd
Blackpool
United Kingdom
FY3 8NR

Study participating centre
Bradford Royal Infirmary
Duckworth Ln
Bradford
United Kingdom
BD9 6RJ

Study participating centre
Chesterfield Royal Hospital
Chesterfield Rd
Calow
Chesterfield
United Kingdom
S44 5BL

Study participating centre
Darlington Memorial Hospital
Hollyhurst Rd
Darlington
United Kingdom
DL3 6HX

Study participating centre
Forth Valley Royal Hospital
Stirling Rd
Larbert
United Kingdom
FK5 4WR

Study participating centre
Hammersmith Hospital
72 Du Cane Rd
White City
London
United Kingdom
W12 0HS

Study participating centre
New Cross Hospital
Wolverhampton Rd

Heath Town
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
Nottingham University Hospital
Hucknall Rd
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Poole Hospital
Longfleet Rd
Poole
United Kingdom
BH15 2JB

Study participating centre
Northern General Hospital
Herries Rd
Sheffield
United Kingdom
S5 7AU

Study participating centre
Southend University Hospital
Prittlewell Chase
Westcliff-on-Sea
United Kingdom
SS0 0RY

Study participating centre
Wansbeck General Hospital
Woodhorn Ln
Ashington
United Kingdom
NE63 9JJ

Study participating centre
Wycombe General Hospital
Queen Alexandra Rd
High Wycombe
United Kingdom
HP11 2TT

Study participating centre
Sunderland Royal Hospital
Kayll Rd
Sunderland
United Kingdom
SR4 7TP

Study participating centre
Torbay Hospital
Newton Rd
Torquay
United Kingdom
TQ2 7AA

Study participating centre
Royal Victoria Hospital
Holtye Rd
East Grinstead
United Kingdom
RH19 3DZ

Study participating centre
Guy's and St Thomas' Hospital
Westminster Bridge Rd
Lambeth
London
United Kingdom
SE1 7EH

Study participating centre
Doncaster Royal Infirmary
Thorne Rd
Doncaster

United Kingdom
DN2 5LT

Study participating centre
Royal Stoke University Hospital
Newcastle Rd
Stoke-on-Trent
United Kingdom
ST4 6QG

Study participating centre
St George's Hospital
Blackshaw Rd
Tooting
London
United Kingdom
SW17 0QT

Study participating centre
Broomfield Hospital
Court Rd
Broomfield
Chelmsford
United Kingdom
CM1 7ET

Study participating centre
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Salisbury District Hospital
Odstock Rd
Salisbury
United Kingdom
SP2 8BJ

Study participating centre
Kingston Hospital
Galsworthy Rd
Kingston upon Thames
United Kingdom
KT2 7QB

Study participating centre
Royal Oldham Hospital
Rochdale Rd
Oldham
United Kingdom
OL1 2JH

Study participating centre
Basildon University Hospital
Nether Mayne
Basildon
United Kingdom
SS16 5NL

Study participating centre
Watford General Hospital
Vicarage Rd
Watford
United Kingdom
WD18 0HB

Study participating centre
St Richard's Hospital
Spitalfield Ln
Chichester
United Kingdom
PO19 6SE

Study participating centre
Princess of Wales Hospital
Coity Rd
Bridgend

United Kingdom
CF31 1RQ

Study participating centre
Bristol Royal Infirmary
Marlborough St
Bristol
United Kingdom
BS2 8HW

Study participating centre
Royal Cornwall Hospital
Treliske
Truro
United Kingdom
TR1 3LQ

Study participating centre
Hairmyres Hospital
Eaglesham Road
East Kilbride
United Kingdom
G75 8RG

Study participating centre
Dumfries and Galloway Royal Infirmary
Bankend Road
Dumfries
Dumfries and Galloway
United Kingdom
DG1 4AP

Study participating centre
Princess Royal Hospital
Apley Castle
Grainger Drive
Apley
Telford
United Kingdom
TF1 6TF

Study participating centre
The Queen Elizabeth Hospital
Gayton Road
Kings Lynn
United Kingdom
PE30 4ET

Study participating centre
Croydon Health Services NHS Trust
Croydon University Hospital
530 London Road
Thornton Heath
United Kingdom
CR7 7YE

Study participating centre
University Hospital Ayr
Dalmellington Road
Ayr
United Kingdom
KA6 6DX

Sponsor information

Organisation
University of Glasgow

Sponsor details
University Avenue
Glasgow
Scotland
United Kingdom
G12 8QQ
+44 141 232 1798
Debra.Stuart@glasgow.ac.uk

Sponsor type
University/education

Organisation

NHS Greater Glasgow & Clyde Research and Development

Sponsor details
R&D Management Office
Clinical Research & Development
NHS Greater Glasgow & Clyde
Ward 11, Dykebar Hospital
Grahamston Road
Paisley
Scotland
United Kingdom
PA2 7DE
+44 (0)141 232 1813
maureen.travers@ggc.scot.nhs.uk

Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Pharmacosmos UK Ltd.

Results and Publications

Publication and dissemination plan

Current publication and dissemination plan as of 07/09/2022:
The study protocol and a description of the recruitment experience and participant baseline characteristics will be published before study completion. On completion of the trial, the database will be locked and analysed by the staff of the Robertson Centre for Biostatistics, University of Glasgow. A final study report will be prepared and the results will be published in a major medical journal by the end of 2022.

Previous publication and dissemination plan:
The study protocol and a description of the recruitment experience and participant baseline characteristics will be published before study completion. On completion of the trial, the database will be locked and analysed by the staff of the Robertson Centre for Biostatistics, University of Glasgow. A final study report will be prepared and the results will be published in a major medical journal in January 2021.

Intention to publish date

31/12/2022

Individual participant data (IPD) sharing plan

The data sharing plans for the current study are not fully formulated and will be made available at a later date. However they will be based on the following strategy:
The study database will be held at the Robertson Centre for Biostatistics University of Glasgow. After planned publications have been completed, the study Publications Committee will review applications for additional data analyses, data access, collaborative analyses (eg meta-analyses and pooling projects). In considering these requests, the Publications Committee will take into account the cost of meeting requests, the scientific validity of the requests, overlap with other requests, other legal and ethical issues, patient consent issues and information governance issues.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Results article		17/12/2022	08/09/2023	Yes	No