ISRCTN13370767 https://doi.org/10.1186/ISRCTN13370767

# Intravenous iron for cancer-related anaemia symptoms

**Submission date**
03/09/2018

**Recruitment status**
No longer recruiting

**Registration date**
05/09/2018

**Overall study status**
Completed

**Last Edited**
28/02/2024

**Condition category**
Haematological Disorders

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

## Plain English summary of protocol

Background and study aims
Fatigue is the most common symptom in palliative cancer care patients occurring in up to 80% of individuals. The causes of fatigue are multi-factorial. Anaemia (low red blood count) is an important and common cause of fatigue, occurring in over two-thirds of patients in palliative care. Up to 50% of this anaemia may be related to iron deficiency. Studies have shown that correcting anaemia improves quality of life. Currently neither fatigue nor anaemia in palliative cancer care have specific treatments, other than treating the underlying cancer when possible. The standard management of anaemia is with oral iron supplementation or blood transfusion from a donor. Oral iron supplementation is cheap and easily dispensed. However, it corrects anaemia slowly. Furthermore, there are issues with adherence as certain patients are unable to tolerate oral iron supplementation due to the gastrointestinal side-effects such as diarrhoea or constipation. For severe anaemia the mainstay of treatment is blood transfusion but this carries high costs, has limited supply and can lead to potential complications. New intravenous (injected) iron products are safe to deliver and offer the potential for an effective treatment to be applied where currently no treatment is given. Studies have shown that intravenous iron results in a quicker rise in haemoglobin (in red blood cells). Intravenous iron has also been shown to be better tolerated than the oral formulation because it has fewer gastrointestinal side-effects. Currently there is no evidence relating to the use of intravenous iron in palliative cancer care to treat anaemia-related symptoms and its effects on the patient's immune system response, tumour spread and gut bacteria. The aim of this study is to explore its use in the treatment of anaemia and the impact on fatigue and quality of life in such patients and to inform the design of a larger study.

Who can participate?
Patients aged 18 and over with solid cancer, anaemia and fatigue who are being supported with palliative care

What does the study involve?
Participants are randomly allocated to receive the same volume of either intravenous iron or placebo (dummy injection). Participants in the iron group receive a dose according to the manufacturer's guidance based on their existing haemoglobin and body weight. In a small proportion of patients it is anticipated that they will require two infusions with a 7-10 day

interval. the other group are given a placebo at the same dose and may therefore also be required to receive two infusions.

What are the possible benefits and risks of participating?
Participants may benefit from the additional blood tests allowing for the earlier detection of any changes. Patients receiving intravenous iron may, based on results from similar studies in the non-palliative setting, benefit from a reduced need for blood transfusion and an improved quality of life. Patients will be required to visit the hospital for a first visit, one or two infusion visits and for two follow-up visits. Where possible these will be linked to existing clinical visits. The study carries the burden of additional blood tests for the patient. Where possible existing results from clinical blood samples will be used after obtaining full informed consent from patients and the clinical team in order minimise the inconvenience and discomfort of additional blood tests. Side effects of intravenous iron infusion can include local skin reactions and gastrointestinal side effects or headache. In extremely rare cases severe anaphylactic reactions can occur. Patients will be fully informed of this during the consent process. Infusions will be given in a facility with all of the necessary resuscitation facilities available. Adverse reactions will be monitored carefully and patients will be given full details of who to contact in the event of an adverse reaction. It is anticipated that a small group of participants may already be taking oral iron supplementation to treat anaemia and will be required to stop this as part of the trial. All patients will have their anaemia carefully monitored as part of the trial and if the research or clinical team deem it necessary to intervene, including withdrawal from the trial, due to concerns relating to worsening anaemia they will do so.

Where is the study run from?
1. Nottingham University Hospitals NHS Foundation Trust (UK)
2. Royal Wolverhampton Hospital NHS Trust (UK)

When is the study starting and how long is it expected to run for?
March 2018 to December 2020

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

Who is the main contact?
Mr Edward Dickson, Edward.dickson@nhs.net

# Contact information

### Type(s)
Scientific

### Contact name
Mr Edward Dickson

### Contact details
Department of GI Surgery
Queens Medical Centre
Nottingham
United Kingdom

NG7 2UH
+44 (0)1158231143
edward.dickson@nhs.net

# Additional identifiers

### Clinical Trials Information System (CTIS)
2018-001669-17

### Protocol serial number
38409

# Study information

### Scientific Title
ICaRAS (IV Iron for Cancer-Related Anaemia Symptoms) – a feasibility study of intravenous iron therapy for anaemia in palliative cancer care

### Acronym
ICaRAS

### Study objectives
Currently there is no evidence relating to the use of intravenous iron in palliative cancer care to treat anaemia related symptoms and its effects on the patients immune system response, tumour spread and the gut bacteria. This feasibility study aims to explore its use in the treatment of anaemia and the impact on fatigue and quality of life in such patients and to inform the design of a large definitive study.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
East Midlands – Nottingham 2, 28/08/2018, ref: 18/EM/1096

### Study design
Randomised; Interventional; Design type: Treatment, Drug

### Primary study design
Interventional

### Study type(s)
Treatment

### Health condition(s) or problem(s) studied
Anaemia in patients with cancer

### Interventions
This study has been designed to assess the feasibility of a larger definitive trial investigating the efficacy of intravenous iron for fatigue and anaemia in palliative cancer care. This feasibility study is a double blind randomised controlled trial. Local audit data suggests that around 100

patients would be eligible for the trial per year. This trial will recruit 40 patients to assess feasibility of recruitment and retention. 40 patients with a proven diagnosis of a solid cancer who are suffering from fatigue and anaemia (haemoglobin <130g/L men and <120 g/L women) will be randomised to receive the same volume of either intravenous iron (iron isomaltoside, 20 patients) or placebo (normal saline 0.9%, 20 patients). Patients in the intervention arm will receive a dose of intravenous iron according to the manufacturers guidance based on their existing haemoglobin and body weight. A maximum dose of 20 mg/kg iron isomaltoside 1000 can be administered weekly therefore in a small proportion of patients it is anticipated that they will require two infusions with a 7-10 day interval. In order to maintain blinding patients in the control arm will be administered a placebo at the same dose and may therefore also be required to receive two infusions.

Patients will be identified at multidisciplinary team meetings, the palliative care day therapy unit and palliative outpatient clinics. Patients will initially be approached by a member of their clinical care team who, with permission, will introduce them to a member of the research team. Where possible this discussion will be held in person but an information sheet may be posted to the patient if this is not possible. Patients will be given at least 24 hours to consider participation in the trial. If a patient agrees to participate they will be invited for a formal screening visit and, if appropriate, they will be consented for participation in the trial. Patients will then be randomised to one of the two treatment arms and baseline data will be collected. A visit will then be scheduled for them to receive their allocated treatment. Where possible this will coincide with a scheduled appointment with their clinical team.

### Intervention Type
Drug

### Phase
Phase IV

### Drug/device/biological/vaccine name(s)
Iron as iron(III) isomaltoside 1000 (Monofer, ferric derisomaltose)

### Primary outcome(s)
Feasibility assessed based on patient numbers for:
1. Inclusion eligibility
2. Willingness to be recruited (acceptability)
3. Willingness to be randomised (concordance)
4. Study exclusion (screen failures)
5. Numbers withdrawn (non-concordance)
6. Study retention
Timepoint(s): Baseline to end of trial participation

### Key secondary outcome(s))
1. Quality of life and fatigue measured using the questionnaires FACIT-F fatigue score, EQ-5D and EORTC QLQc30 at baseline, 4 weeks and 8 weeks post infusion
2. Blood transfusion rate recorded by number of units transfused at 4 week and 8 weeks post infusion
3. Haemoglobin levels and body iron stores measured in blood samples taken at baseline, 4 weeks and 8 weeks post infusion
4. Gut microbiome measured by stool sample analysis at baseline, 4 weeks and 8 weeks
5. Activity levels measured using number of daily steps recorded on a pedometer for 7 days prior

to the baseline visit, the 4 and 8 week follow up visits
6. Physical condition assessed by scores for the Short Physical Performance Battery (SPPB) protocol at baseline, 4 weeks and 8 weeks post infusion
7. Change in blood markers to analyse the immune response to iron including hepcidin and cytokine activity measured at baseline, 4 weeks and 8 weeks follow up

### Completion date
01/12/2020

## Eligibility

### Key inclusion criteria
1. Age ≥18 years
2. Histologically proven solid tumour
3. Haemoglobin < 130g/L men and <120 g/L women
4. ECOG (Eastern Cooperative Oncology Group, Oken 1982) performance status 0-2
5. Moderate to severe fatigue (numeric rating scale score ≥ 4 out of 10)
6. Cancer not amenable to curative treatment

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
18 years

### Sex
All

### Total final enrolment
34

### Key exclusion criteria
1. Evidence of iron overload or disturbance of iron utilisation e.g. haemachromotosis
2. Previous allergy to iron or related iron products
3. Evidence of active bleeding or untreated infection
4. Concurrent anti-cancer chemotherapy and/or immunotherapy and/or radiotherapy (within 8 weeks)
5. Untreated haematological malignancy
6. Female participants who are pregnant, lactating or planning a pregnancy during the course of the study
7. Patients who are unable to consent
8. Any other significant disease or disorder which, in the opinion of the Investigator, may either

put the participants at risk because of participation in the study, or may influence the result of the study, or the participant's ability to participate in the study
9. Thromboembolic event within 3 months unless ongoing treatment with anticoagulation

### Date of first enrolment
01/10/2018

### Date of final enrolment
01/10/2020

## Locations

### Countries of recruitment
United Kingdom

England

### Study participating centre
**Nottingham University Hospitals NHS Foundation Trust**
Queens Medical Centre
Nottingham
United Kingdom
NG7 2UH

### Study participating centre
**Royal Wolverhampton Hospital NHS Trust**
New Cross Hospital
Wolverhampton Road
Wolverhampton
United Kingdom
WV10 0QP

## Sponsor information

### Organisation
Nottingham University Hospitals NHS Foundation Trust

### ROR
https://ror.org/05y3qh794

## Funder(s)

### Funder type
Government

### Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: PB-PG-0816-20017

# Results and Publications

### Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

### IPD sharing plan summary
Other

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | | 06/01/2023 | 09/01/2023 | Yes | No |
| Other unpublished results | | | 28/02/2024 | No | No |
| Participant information sheet | version v1.3 | 30/08/2018 | 05/09/2018 | No | Yes |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |