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INTACT2: Improving ICU outcomes by treating anaemia

Submission date
23/01/2025

Recruitment status
Recruiting

Registration date
31/03/2025

Overall study status
Ongoing

Last Edited
29/10/2025

Condition category
Haematological Disorders

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Anaemia (low blood count) is common in patients who survive ICU. It makes them feel weak and tired. This can lead to longer hospital stays, difficulty in coping at home after leaving hospital and poor quality of life. Expert committees and patient groups have called for research to find the best way to treat anaemia in ICU survivors. We want to see if treating anaemia improves patients' health after they leave ICU. Our research will test if two treatments – iron (infused into the veins) and a man-made version of a hormone normally produced by the body (recombinant EPO, given as an injection under the skin) – can successfully treat anaemia and improve physical aspects of health-related quality of life. These treatments are safe and are already used in the NHS to treat anaemia in heart and kidney disease.

Who can participate?
Anaemic survivors of critical illness defined as patients aged 16 years and over who have received Intensive Care Society Level 2 or 3 care and who are ready for discharge from Critical Care (i.e. an ICU or HDU in the UK) who have mild or moderate anaemia (plasma haemoglobin ≤100 g/L before ICU/HDU discharge)

What does the study involve?
We will split people into two groups at random ('by chance'): half will get iron and rHuEPO and half will get identical-looking placebos (dummy drugs). These dummy drugs will contain salt water but no "active" drugs. We will then measure physical health using a reliable questionnaire that has been used in many ICU studies. It will give us important information about ICU survivors' quality of life including their ability to carry out essential activities of daily living (bathing, dressing, eating, shopping), and how much they are able to walk, exercise, return to work and enjoy life in general. We will also collect blood samples to understand how the treatments work, information about how much time patients spend at home after leaving the hospital, and their overall health at 30 and 90 days after entering the study. We will also collect routine NHS electronic clinical information to help us work out how much the treatments cost the NHS and how much they save. We have an experienced team running the study. They include doctors, scientists, former patients, health economists and statisticians. Together they will make sure the study runs smoothly and finishes on time.

What are the possible benefits and risks of participating?
Taking part in this study may help improve the healthcare of patients who are recovering from intensive care in the future. A small study showed that patients who had their anaemia treated went home from hospital quicker and were less likely to return to hospital afterwards. There are no direct benefits of taking part in this study.
The treatments used are given to many patients with different medical conditions in hospitals in the UK. The medical and research teams will work together and check the patient's medical records for any known health conditions that put them at risk for developing any severe treatment-related side effects. If this is the case, we will not include you in the study.
We will monitor the patient's safety during and after the infusion and we will review their medical notes to check for any other problems that might be associated with the treatments.
As with all injections or infusions through drips, the patient may experience some short-term minor discomfort at the site where the infusion is given. Taking the blood samples may cause some local discomfort or bruising.
The iron infusion we are using is generally very safe and well tolerated. Over 9000 patients have already received this medication in clinical studies. However, there are some side effects associated with its use, most of which are mild and disappear once the infusion is complete. These are: nausea, strange taste for a short time, headache, flushing and high blood pressure. Severe and allergic reactions are very rare.
The hormone we are using is also generally very safe. Common side effects, most of which are mild, include rashes and swelling, raised blood pressure and discomfort at the injection site. There is a small risk of blood clots associated with the hormone, but this is more common in patients with kidney problems, certain types of cancer and in those who receive very high doses of the drug. However, in all clinical studies reported to date in ICU patients (around 5500 patients), there has been no report of increased blood clots in patients who have received hormone compared with those who have received a placebo. The administration of the infusion and injection will take place in hospital and the patient will be monitored by a member of the research team during and after the infusion.
Safety: All research teams will record adverse events that they become aware of, and promptly report SARs and SUSARs to the study
Sponsor. The trial will have a Data Monitoring Committee that will monitor safety throughout the study.
Questionnaires: Patients will complete questionnaires as part of the study outcome. This will take time and may be inconvenient. We will give different options to complete the questionnaires so the patient can choose the method that suits them best e,g, by telephone, in person, by post or online.
their representatives to consider this and if participation will affect any insurance they have and encourage them to seek advice if necessary.

Where is the study run from?
University of Edinburgh (UK)

When is the study starting and how long is it expected to run for?
August 2024 to November 2027

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

Who is the main contact?
INTACT2.trial@ed.ac.uk

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1011145

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
AC24041

Study information

Scientific Title
INtravenous iron and eryThropoietin to treat Anaemia following CriTical care 2: a multi-centre, randomised, parallel-group, double-blind, placebo-controlled, clinical efficacy trial (INTACT2)

Acronym
INTACT-2

Study objectives
Primary objective:
To determine whether treating anaemia using a combined intervention of IV iron and subcutaenous darbepoetin alfa results in an improvement in physical function at 90 days after ICU discharge, compared with placebo.

Secondary objectives:
1. To determine the effect of treating anaemia with IV iron and subcutaneous darbepoetin alfa on important patient-centred outcomes such as fatigue, quality of life, requirement for blood transfusion and the amount of time spent outside of hospital within the first 90 days (days alive and at home), compared with placebo.
2. To determine the safety of IV iron and subcutaneous darbepoetin alfa compared with placebo.
3. To determine whether pre-specified subgroups of ICU survivors with anaemia have different responses to IV iron and SC recombinant human erythropoietin (rHuEpo).
4. To determine the mechanisms of action of IV iron and rHuEPO on PCS, compared to placebo, in ICU survivors with anaemia using intermediate endpoints measured at 30 days post-randomisation.
5. To determine whether treatment of anaemia in ICU survivors with IV iron and SC rHuEPO is cost-effective from the NHS perspective.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 28/03/2025, Scotland A REC (Mainpoint 102, Westport, Edinburgh, EH3 9ND, United Kingdom; +44 (0)781 460 9032; Loth.sesres@nhs.scot), ref: 25/SS/0019

Study design
Double-blind randomized placebo-controlled parallel-group trial

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Anaemic survivors of critical illness defined as patients who have received Intensive Care Society Level 2 or 3 care who are ready for discharge from Critical Care (i.e. an ICU or HDU in the UK) who are have mild or moderate anaemia (plasma haemoglobin ≤100 g/L prior to ICU/HDU discharge)

Interventions
Participants will be randomised using an online database to the intervention intravenous ferric carboxymaltose 1000 mg and subcutaneous darbepoetin alfa 150 mcg) or the comparator (equal volume of 0.9% sodium chloride solution). The duration of the treatment phase will be 30-60 minutes, including a period of clinical observation.

Participants will be followed up via questionnaire at 7 days/hospital discharge (whichever comes first), 30 days (questionnaire and blood samples) and 90 days via questionnaire post-randomisation. These time points cover the period of greatest morbidity, resource use, and steepest recovery trajectory for physical function in ICU survivors and provide the optimal window to detect relevant treatment effects. For the primary outcome at 90 days, participants will be offered several options to complete a follow-up questionnaire: online, telephone, postal and in person. When feasible we will obtain follow-up data at post-ICU follow-up services to reduce patient burden and increase completeness.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Ferric carboxymaltose, darbepoetin alfa

Primary outcome(s)
Physical aspects of health-related quality of life measured using the physical component summary of the SF-36 health-related quality of life (HRQoL) questionnaire (PCS) completed by patients at 90 days post-randomisation.

Key secondary outcome(s))
Current secondary outcome measures as of 29/10/2025:
Patient-centred outcomes:

1. The physical health components of health-related quality of life are measured using the PCS completed by patients at 30 days post-randomisation.
2. The mental health components of health-related quality of life are measured using the mental component summary of the SF-36 health-related quality of life (HRQoL) questionnaire (MCS) completed by patients at 30 and 90 days post-randomisation.
3. Fatigue is measured using the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) questionnaire completed by patients at 7 and 90 days post-randomisation.
4. Days spent by patients outside a healthcare facility measured using Days Alive and at Home (DAH) at 30 and 90 days post-randomisation which will be calculated from vital status, date of death, days spent in hospital prior to discharge and hospital readmission days at 30 and 90 days post-randomisation.
5. Red blood cell transfusion measured by totalling the number of red blood cell units transfused during the first 90 days post-randomisation.
6. Hospital readmissions measured using medical records and include the number of hospital readmissions and the total number of days during hospital readmissions.
7. Mortality ascertained from medical records at 30 and 90 days.

Safety outcomes:
1. New clinically important infection up to hospital discharge: new post-ICU infection (new initiation of IV antibiotics or IV antivirals for suspected or confirmed infection between ICU and hospital discharge) ascertained from medical records.
2. Clinically important infection after hospital discharge up to 90 days: new initiation of IV antibiotics or IV antivirals between hospital discharge and the 90-day follow-up mentioned by patients in a safety questionnaire administered at 30 and 90 days after randomisation.
3. Thromboembolic event up to hospital discharge: clinically diagnosed deep vein thrombosis (DVT) or pulmonary embolism (PE) ascertained from medical records.
4. Thromboembolic event after hospital discharge up to 90 days: clinically diagnosed DVT or PE reported by patients in a safety questionnaire administered at 30 and 90 days after randomisation.

Previous secondary outcome measures:
Patient-centred outcomes:
1. The physical health components of health-related quality of life are measured using the PCS completed by patients at 30 days post-randomisation.
2. The mental health components of health-related quality of life are measured using the mental component summary of the SF-36 health-related quality of life (HRQoL) questionnaire (MCS) completed by patients at 30 and 90 days post-randomisation.
3. Fatigue is measured using the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) questionnaire completed by patients at 7 and 90 days post-randomisation.
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Completion date
30/11/2027

Eligibility

Key inclusion criteria
1. Adults (≥16 years) who required ≥24 hours critical care (defined as requiring level 3 or level 2* care at ICU admission) and are considered fit for ICU or HDU discharge by caring consultant /clinician.
2. Most recently available laboratory Hb ≤100 g/L prior to ICU/HDU discharge.
3. Provision of informed consent.
*Levels of Adult Critical Care, Consensus Statement, Intensive Care Society https://ics.ac.uk /resource/levels-of-care.html

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 29/10/2025:
1. Acute uncontrolled infection – defined as ongoing bacteraemia and/or patient expected to be on non-prophylactic antibiotics for greater than 14 days from the date of eligibility assessment.
2. Cancer (known or suspected malignant disease and has not completed a course of curative treatment).
3. IV iron and/or rHuEPO in the last 30 days.
4. Severe chronic liver disease (defined by a Child-Pugh grade of C).
5. Patient is known to be pregnant. (a pregnancy test in individuals with childbearing potential will be performed prior to enrolment and patients who are pregnant will be excluded).
6. Diagnosis of haemochromatosis or secondary iron overload disorder.

7. Immunosuppression for organ transplant.
8. Primary neurological diagnosis and/or severe traumatic brain injury.
9. Admission to ICU following elective cardiac surgery.
10. Known hypersensitivity to iron and/or rHuEPO.
11. History of pure red cell aplasia following erythropoietin therapy.
12. Thromboembolism chemoprophylaxis is contraindicated.
13. Patient receiving palliative or end-of-life care.
14. Known allergy to derivative of latex.

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2. Cancer (known or suspected malignant disease and has not completed a course of curative treatment).
3. IV iron and/or rHuEPO in the last 30 days.
4. Severe chronic liver disease (defined by a Child-Pugh score of 3).
5. Patient is known to be pregnant. (a pregnancy test in individuals with childbearing potential will be performed prior to enrolment and patients who are pregnant will be excluded).
6. Diagnosis of haemochromatosis or secondary iron overload disorder.
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12. Thromboembolism chemoprophylaxis is contraindicated.
13. Patient receiving palliative or end-of-life care.

Date of first enrolment
06/10/2025

Date of final enrolment
30/11/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Royal Infirmary of Edinburgh
51 Little France Crescent
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Sponsor information

Organisation
University of Edinburgh & NHS Lothian ACCORD

ROR
https://ror.org/01nrxwf90

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date