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RElated haplo-DonoR haematopoietic stEm cell transplantation for adults with Severe Sickle cell disease

Submission date 10/10/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 25/10/2022	**Overall study status** Ongoing	
Last Edited 04/10/2024	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Sickle Cell Disease (SCD) is a serious inherited condition, in which red blood cells become an abnormal sickle shape under stressful conditions causing blood vessels to be easily blocked. This leads to health problems such as sickle cell crises (painful episodes around the body), a higher risk of stroke, heart issues and many other complications.

People with SCD need treatment throughout their lives. Currently available treatments for SCD include regular blood transfusions (when blood from a donor is given to replace a patient's red blood cells) and a medicine called hydroxycarbamide. Sometimes painkillers are given to manage painful episodes. These treatments are not sufficient because some people may not respond well or fully. Stem Cell Transplant (SCT) is a procedure that may cure SCD. This process destroys damaged blood cells and replaces them with stem cells from the blood or bone marrow of a genetically matched family donor.

Unfortunately, many patients do not have a fully matched donor available. Research has shown that SCT from haploidentical (half-matched) family donors has the same potential to cure severe SCD, but this is only approved for use in children due to concerns about side effects in adults. New transplant protocols mean it is now possible for haploidentical SCT to be done safely in adults. This treatment is expensive, so it is important to show that this is good value for money for the NHS.

The aim is to carry out a clinical trial to find out whether haploidentical SCT is safe, effective, and cost-worthy in treating adults with severe SCD. We will invite participants; assigned by chance to receive either haploidentical SCT or standard of care. We will monitor participants for 2 years to see if haploidentical SCT cures people of SCD and is a good value for the NHS.

Who can participate?
Adults aged 18 years old and over with severe SCD with a first-degree relative that is eligible as a haploidentical (half-matched) donor

What does the study involve?
Participants will be assigned to one of two groups at random (decided by chance by a computer, like at the flip of a coin). The first is the standard of care group. Participants in this group will receive standard medical care including any currently available treatment for SCD. The second is the haploidentical stem cell transplant group. Participants in this group will receive a stem cell transplant from a haplo-matched family donor. Participants will be in the study for around 2 years.

At a minimum, this will involve initial screening and baseline visits then, depending on the arm randomised to, preparation and admission for stem cell transplant with regular visits until 3 months post-transplant. Participants will then have set study visits after 6 months, 12 months and 24 months. These visits will be scheduled at the same time as standard hospital visits as much as possible. We will also ask for information about participants' general well-being every 3 months, either in person or over the phone. In the first 3 months of the study, the frequency at which participants will need to come for hospital visits will depend on the treatment arm they are in.

We will collect the following: demographic information (age, sex ethnicity etc.), medical history, information from a physical examination (health check that participant is fit for transplant procedure), blood, urine, data from lung function test, data from echocardiogram (heart) scan, MRI and MRA scan, FerriScan & FibroScan (liver scans) and questionnaire on quality of life.

What are the possible benefits and risks of participating?
We cannot guarantee or promise that the participant will receive any benefits from this research. However, the procedure is potentially curative of sickle cell disease. The tests provided may also help participants learn about their general health. This study may help doctors and scientists to better understand the treatments for sickle cell disease. Therefore, participation may have an indirect benefit to science and society in the future to help people suffering from sickle cell disease.

There are important potential side effects from a bone marrow transplant and this is why only those with severe SCD are currently being considered for this treatment. The main risks of the trial for participants randomised to the transplant arm relate to the medical risks of the transplant procedure. These include side effects of chemotherapy drugs, infection related to immune suppression required for the transplant procedure and graft versus host disease. Side effects of chemotherapy are minimised by supportive care measures such as anti-emetics. Risks of infection are minimised by the use of infection prevention such as anti-bacterial, anti-fungal and antiviral preventative medicines. Patients will be monitored regularly as part of routine transplant care for infection and therefore the development of any infection can be treated promptly. Graft versus hosts disease is minimised by the use of immune suppression medicines to continue for one year after transplant. Similarly, regular monitoring of patients allows for early detection and treatment of graft versus host disease while symptoms are minimal.

Participants who do not receive a transplant will continue with their regular sickle cell care. The main issue here is that while they would not be exposed to the adverse effects of a transplant, they will not receive a potentially curative transplant and continue with sickle cell disease. This may be distressing for some participants. We aim to minimise this via good information prior to and regular review with the sickle teams within the Haemoglobinopathy coordinating centres. Participants will be routinely offered psychological support. If the trial proves successful, then these participants would be offered a transplant in the future.

Where is the study run from?
The study is lead by researchers at King's College Hospitals NHS Foundation Trust, Guy's and St Thomas' Hospitals NHS Foundation Trust and King's College London. The trial is being coordinated by the King's Clinical Trials Unit (KCTU) at King's College London.

When is the study starting and how long is it expected to run for?
March 2022 to June 2027

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

Who is the main contact?
Mr Daryl Hagan (REDRESS Trial Manager((UK)
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
312212

ClinicalTrials.gov (NCT)
NCT05392894

Protocol serial number
CPMS 54147, IRAS 312212

Study information

Scientific Title
A multi-centre open randomised controlled trial to assess the effect of related haplo-donor haematopoietic stem cell transplantation versus standard of care (no transplant) on treatment failure at 24 month in adults with severe sickle cell disease (REDRESS V1.0)

Acronym
REDRESS V1.0

Study objectives
Haematopoietic stem cell transplantation from haploidentical donors is a clinically and cost-effective treatment for adults with severe sickle cell disease as measured by treatment failure or mortality (clinical effectiveness) and healthcare resource use (cost-effectiveness) after 24 months.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved pending at time of registration, London – Chelsea Research Ethics Committee (REC) (c/o. Gemma Oakes, Approvals Specialist, REC London Centre, 2 Redman Place, London, E20 1JQ, UK; +44 (0)207 104 8029; chelsea.rec@hra.nhs.uk), ref: 22/LO/0702

Study design
Multicentre open-label randomized controlled study

Primary study design
Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied
Sickle cell disease

Interventions
This is a multi-centre, open-label, randomised controlled trial to assess the effect of haploidentical stem cell transplant compared to standard of care (no transplant) on treatment failure in adults with severe sickle cell disease over 2 years. 120 participants will be assigned at random using the King's Clinical Trials Unit randomisation system online tool to receive a transplant or standard of care in a 1:1 ratio. We will collect data from participants at 6, 12, 18 and 24 months after randomisation on their response to treatment. We will also collect data on quality of life and healthcare service use every 3 months from the point of randomisation.

Intervention Type
Other

Primary outcome(s)
Treatment failure or mortality, defined as occurrence of vaso-occlusive crisis, or transfusion from 6 months post-randomisation, measured by accessing medical records by 24 months post-randomisation

Key secondary outcome(s))
Current secondary outcome measures as of 04/10/2024:

1. Health-related quality of life (QoL) measured using the EQ-5D-5L questionnaire at 3, 6, 9, 12, 15, 18, 21 and 24 months
2. Healthcare utilisation: Frequency of hospital admissions and opiate use in haploidentical SCT and standard of care groups measured using participant reporting in a questionnaire at 3, 6, 9, 12, 15, 18, 21 and 24 months
3. Employment status of participants at 24 months
4. All-cause mortality from randomisation, defined as death from any cause, measured by accessing medical records within 24 months
5. Sickle Cell Disease-related mortality (excluding transplant-related complications): defined as death due to any sickle cell disease-related cause, measured by accessing medical records within 24 months
6. Sickle-type haemoglobin percentage (HbS%) as measured using haemoglobin electrophoresis at 6, 12 and 24 months
7. SCD-related complications (transfusion requirement, painful VOC, stroke, pulmonary hypertension) measured by accessing medical records within 24 months
8. Haemoglobin levels, reticulocyte count, LDH, and bilirubin measured by accessing medical records for standard lab blood tests at 6, 12, and 24 months
9. Pulmonary function measured using FEV1 %, FEV1/FVC ratio, and transfer capacity of the lung, for the uptake of carbon monoxide (TLCO) % at 12 months and 24 months
10. Renal function measured using urea, creatinine and eGFR levels measured by accessing medical records for standard urine tests at 6, 12 and 24 months
11. Iron overload measured using serum ferritin level with FerriScan (R2-MRI-based method) at 24 months
12. Cardiac function and pulmonary hypertension measured using echocardiogram/tricuspid regurgitation velocity (TRV) at 12 and 24 months
13. Cerebrovascular progression measured using a clinical stroke or evidence of progression on

MRI/MRA at 24 months
14. Evidence of hepatic progression measured using a liver function (ALT, AST, ALP, GGT, Bilirubin levels in blood samples) and FibroScan liver elastography at 24 months
15. Percentage of participants requiring opioid use for pain related to the vaso-occlusive sickle-related crisis measured by accessing medical records at 12 months and 24 months

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Completion date
30/06/2027

Eligibility

Key inclusion criteria
Current exclusion criteria as of 04/10/2024:

1. Adult patients aged > = 18 years
2. Confirmed haploidentical donor

3. Severe SCD phenotype who are at high risk for morbidity and mortality. Severe SCD is defined by at least one of the following:
3.1. Clinically significant neurologic event (stroke) or deficit lasting > 24 hours
3.2. History of > = 2 acute chest syndromes in a 2-year period preceding enrolment despite optimum treatment, e.g. with hydroxycarbamide (HC)
3.3. History of > = 3 severe pain crises per year in a 2-year period preceding enrolment despite the institution of supportive care measures (e.g. optimum treatment with HC)
3.4. Administration of regular transfusion therapy (=8 packed red blood transfusions per year for 1 year to prevent vaso-occlusive complications).
3.5. Patients assessed as requiring transfusion but with red cell alloantibodies/very rare blood type, rendering it difficult to continue/commence chronic transfusion
3.6. Patients requiring HC/transfusion for treatment of SCD complications who cannot tolerate either therapy due to significant adverse reactions
3.7. Established end organ damage relating to SCD, including but not limited to progressive sickle vasculopathy and hepatopathy.
4. Patients must be fit to proceed to Haploidentical SCT as defined below:
4.1. Karnofsky score > = 60
4.2. Cardiac function: LVEF > = 45% or shortening fraction > = 25%
4.3. Lung Function: FEV1, FVC and TLCO > = 50%
4.4. Renal function: EDTA GFR > = 40 ml/m2/1.73m²
4.5. Hepatic function: ALT < x3 ULN and bilirubin < x2 the upper limit of normal, those with hyperbilirubinemia due to sickle-related haemolysis will not be excluded. No radiological evidence of cirrhosis.
5. Written informed consent

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3.3. History of > = 3 severe pain crises per year in a 2-year period preceding enrolment despite the institution of supportive care measures (e.g. optimum treatment with HC)
3.4. Administration of regular transfusion therapy (=8 packed red blood transfusions per year for 1 year to prevent vaso-occlusive complications).
3.5. Patients assessed as requiring transfusion but with red cell alloantibodies/very rare blood type, rendering it difficult to continue/commence chronic transfusion
3.6. Patients requiring HC/transfusion for treatment of SCD complications who cannot tolerate either therapy due to significant adverse reactions
3.7. Established end organ damage relating to SCD, including but not limited to progressive sickle vasculopathy and hepatopathy. End-organ sufficient for entry to this trial shall be ratified at the UK NHP.
4. Patients must be fit to proceed to Haploidentical SCT as defined below:
4.1. Karnofsky score > = 60
4.2. Cardiac function: LVEF > = 45% or shortening fraction > = 25%
4.3. Lung Function: FEV1, FVC and TLCO > = 50%
4.4. Renal function: EDTA GFR > = 40 ml/m2/1.73m²

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5. Written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Fully matched sibling donor.
2. Previous bone marrow transplant.
3. Pregnancy or breast feeding.
4. Participants who are able to conceive a child and are unprepared to use effective contraception.
5. Clinically significant donor-specific HLA antibodies.
6. HIV infection or active Hepatitis B or C.
7. Uncontrolled infection including bacterial, fungal and viral.
8. Participation in another interventional trial in the last three months.
9. Pre-existing condition deemed to significantly increase the risk of Haploidentical SCT by the local Principal Investigator.

Date of first enrolment
23/02/2023

Date of final enrolment
30/06/2025

Locations

Countries of recruitment
United Kingdom

Study participating centre
King’s College Hospital
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Study participating centre
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Study participating centre
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M13 9WL

Study participating centre
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SW17 0QT

Study participating centre
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E1 2ES

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S5 7AU

Study participating centre
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B71 4HJ

Study participating centre
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Study participating centre
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Sponsor information

Organisation
King's College Hospital NHS Foundation Trust

ROR
https://ror.org/01n0k5m85

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 datasets generated and/or analysed during the current study will be published as a supplement to the results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes