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Red blood cell transfusion schedule in myelodysplastic syndromes

Submission date
22/01/2021

Recruitment status
No longer recruiting

Registration date
20/09/2023

Overall study status
Ongoing

Last Edited
18/06/2025

Condition category
Cancer

[ ] 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
Current 3-4 weekly RBC transfusion schedules are largely historical and have never been tested in clinical trials. These arrangements are often characterised by delays in the patient pathway (e. g. planning transfusion in busy day units, requirements of pre-transfusion testing within 72 hours prior to planned transfusion) which may further impact on patient care. It is plausible that weekly transfusions of lower dose RBCs, aiming for a more stable Hb level in between transfusion episodes, may be more effective and acceptable.

Aims:
1. Establish the feasibility of delivering weekly RBC transfusions using matched RBCs rather than waiting for results of contemporaneous cross-matching.
2. Explore patient and staff experiences of the new weekly transfusion schedule including: potential enablers, barriers, positive and negative experiences, acceptability and comparison to the standard transfusion schedule. This will provide greater in-depth understanding of the weekly transfusion schedule and provide information to develop future clinical transfusion trials.

Who can participate?
Patients aged over 18 years who have a Myelodysplastic Syndrome (MDS) and receive regular blood transfusions.

What does the study involve?
You will be in the study for 12 weeks, during which you will need to come to the see the study team every 3 weeks for study visits. During the visits the study doctor will ask you about your health do a basic examination and also check your blood results. While on your normal transfusion regime, the number of clinic visits and transfusion visits is unlikely to be increased. On the weekly arm you will attend for a transfusion on the day unit each week but we are aiming for these visits to be complete within 2-3 hours.
At each study visit a routine blood sample will be carried out to check your blood counts and for transfusion testing. In addition, 5ml of blood (approximately one teaspoon) will be taken to measure your iron levels at 3 visits: the beginning of the trial, once in Arm A (before and 2 hours after transfusion) and once in Arm B (before and 2 hours after transfusion).
The doctor/research nurse will give you four short questionnaires asking about you and your

health. A copy of these questionnaires is available if you wish to look at them prior to taking part. You will also be asked to do a six-minute walking test (which checks how far you can walk on flat ground for six minutes) and also a handgrip strength test which checks how strong your handgrip is. You will also be given a wrist-worn device (like a Fitbit) during the trial, to measure your physical activity, the wrist-worn device will be provided to you at the beginning of the study and will be returned when you reach your final study visit.
When you visit for a transfusion appointment, you will have routine transfusion-related tests such as: blood count, blood group and testing for antibodies. Your Hb level will be monitored during the trial and recorded on the study form, but you will not be told what the result is - this is called 'blinding' and allows more accurate assessing of the study results.
After the research is completed you will receive a phone call within 3 months of your trial treatment finishing. During the call there will be a short interview with a researcher to ask about your experience. Your most recent routine blood tests will also be checked for your Hb and transfusion-related tests.
At the end of the 12-week study period, you will return to your usual doctor for ongoing treatment. As you will have experienced both Arm A and Arm B, you can discuss with your doctor which treatment you prefer and continue on that treatment if desired.

What are the possible benefits and risks of participating?
Patients with Myelodysplastic Syndromes (MDS) are currently receiving transfusion care by Red Blood Cell transfusions that are typically 2-4 units every 3-4 weeks. The purpose of this study is to compare your usual transfusion schedule against a new weekly transfusion schedule using matched red blood cells. It is possible that another strategy of lower doses and weekly transfusions of red cells is more effective and acceptable than the current standard of transfusion care.
We need to compare different treatments and their results to see which one is better by comparing your usual transfusion schedule (Arm A) with a weekly transfusion schedule (Arm B). Both schedules will be personalised for your individual requirements, as each patient with MDS is different and has different transfusion needs. All participants will receive both treatment arms. You will be randomly started in either Arm A or Arm B. After 6 weeks, you will switch to the other arm.

Where is the study run from?
The Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
August 2020 to March 2027

Who is funding the study?
1. Newcastle Hospitals Charity (UK)
2. Activinsights Limited (UK)

Who is the main contact?
Dr Andrew Charlton, Andrew.Charlton1@nhs.net

Contact information

Type(s)
Principal investigator

Contact name

Dr Andrew Charlton

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
265147

Protocol serial number
CPMS 45145, IRAS 265147

Study information

Scientific Title
A randomised feasibility n-of-1 trial of weekly-interval red cell transfusion in myelodysplastic syndromes

Acronym
REDDS: study 2

Study objectives
Current standard of transfusion care in transfusion-dependent MDS is based on a policy for regular RBC transfusions that is typically multiple (2-4) units every 3-4 weeks. However, it is equally plausible that an alternative strategy, specifically lower dose and weekly transfusions of red cells, is more effective and acceptable, avoiding the Hb peaks, and particularly the troughs, of the current strategy.

Current transfusion schedules are also characterised by multiple delays in the intended sequence (e.g. planning transfusion in busy hospital units, requirements of comprehensive pre-transfusion testing). To facilitate timely delivery of weekly RBC transfusion, we will provide phenotype or genotype-matched RBCs, without the delays of awaiting prospective crossmatching on the day of transfusion. Routine pre-transfusion testing results will inform the following week's transfusion strategy.

This study will address weekly transfusions with the use of matched RBCs and without the delays involved in waiting for results of contemporaneous antibody screening/cross-matching.

Ethics approval required

Ethics approval required

Ethics approval(s)
approved 18/08/2020, North East – Newcastle & North Tyneside 2 Research Ethics Committee (NHS BT Blood Donor Centre, Holland Drive, Newcastle, NE2 4NQ, United Kingdom; +44 207 1048091; newcastlenorthtyneside2.rec@hra.nhs.uk), ref: 20/NE/0097

Study design
Randomised; Both; Design type: Treatment, Complex Intervention, Qualitative

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Myelodysplastic syndromes

Interventions
All eligible, informed and consented patients will receive the following two transfusion treatment interventions as below, with randomised allocation of the treatment sequence (i.e. AB or BA).

Arm A (usual transfusion schedule given by treating clinician)
Patients will receive red cell transfusions as per their usual schedule for a 6-week treatment period, with all aspects of their transfusion treatment (including Hb threshold, number of RBC units and frequency of transfusion) directed by their usual treating physician. As per standard clinical practice, patients will have pre-transfusion samples taken for routine compatibility testing and transfusion within 72 hours.

Arm B (weekly transfusion using individualised schedules)
Patients will receive weekly red cell transfusions for a 6-week treatment period. The weekly transfusion schedule will be fixed and outpatients will be seen at a defined weekly appointment in the hospital day unit. Patients will have an HB and pre-transfusion sample for routine compatibility testing taken as usual. Patients will receive a transfusion with matched red cells based on their red cell phenotype/genotype. This will enable timely delivery of a weekly transfusion, without the delays due to waiting for results of contemporaneous cross-matching (often several to many hours). Antibody screening and cross-matching will still be performed, and results will be reviewed and recorded, in accordance with national guidelines.

The design of the study is termed "N-of-1" trials, which are individualised trials of single patients, treated with two or more treatments, with the trial design controlled by the patient and/or clinician. They offer more individualised and personalised treatments for trial participants, and reflect experiences and outcomes which are directly relevant to each participant, which may be better for the outcomes we wish to determine.

A second part of the study will explore the experiences of patients and clinicians about the study. At the time of recruitment for the trial, patients will be approached by their treating nurse or clinician and asked if they are interested in taking part in this qualitative study to share their experiences of the new proposed strategy. If the express interest, a study research nurse

of investigator will visit and explain the study information and consent process. Staff members from each participating hospital site will also be invited to participate in the focus groups to evaluate their experiences with eh different transfusion schedules and use of matched red cells. At the commencement of the trial, information
regarding the focus group sessions will be distributed to staff from the relevant medical, nursing, and administrative and blood bank departments at each hospital site.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Time interval between transfusions measured using patient records. The feasibility of delivering a weekly transfusion schedule is defined by a difference in median time between transfusions of >7 days between the two treatment arms

Key secondary outcome(s))
1. Number of RBC units transfused per arm measured using lab IT system at end of 12 weeks study period
2. Proportion of transfusions in the weekly arm provided with fully matched RBC units measured using lab IT system at end of 12 weeks study period
3. Proportion of Hb measures falling below, within, and above the target range (to ensure the transfusion strategy maintains Hb levels in the target ranges) measured using blood test at 3 month follow up
4. Time from patient admission to the transfusion centre until the commencement of RBC transfusion measured using trial worksheet timings at end of 12 weeks study period
5. Quality of life measured at randomisation & pre-transfusion
5.1. QUALMS-1
5.2. EQ-5D-5L
5.3. EORTC-QLQ-C30
6. Outcomes of rehabilitation measured using CIQ-R at randomisation & study visit 2 (week 6)
7. Functional activity thresholds and measures (via 6-minute walk test, handgrip strength and accelerometer):
7.1. Accelerometer: at enrolment visit, study visit 1 (week 3), study visit 3 (week 9)
7.2. Functional test (6MWT & Grip): Using Dynamometer and tape measure at enrolment visit, randomisation, pre-transfusion at last transfusion visits in each arm.
8. Numbers of adverse events, including transfusion reactions, per arm, and others e.g. disease progression measured using participant notes/review appointments at Randomisation, Study visit 1 (week 3), study visit 2 (week 6), 3 month follow up
9. Number of patients developing new RBC alloantibodies measured using lab IT system at end of 12 weeks study period
10. Enrolment rates; number of screening failures measured using As and when using Enrolment log
11. Effect of more frequent transfusions on iron biomarker assays measured using stored biomarker samples at future time
12. Estimates of carryover effect between different transfusion treatments measured using statistical analysis at trial end
13. Exploring patient and staff experiences of the weekly transfusion strategy measured using structured interview at agreed timepoints with staff and patients

Completion date
31/03/2027

Eligibility

Key inclusion criteria
1. All patients aged >=18 years with WHO-defined MDS or mixed myeloproliferative /myelodysplastic neoplasm overlap. syndromes (MPN/MDS)
2. Transfusion-dependent: on average at least 1 RBC transfusion episode per month in the last 8 weeks (at least two transfusion episodes, each with at least two units of RBCs during the 16 weeks prior to study entry).
3. Continuing transfusion requirement expected for at least 6 months.
4. Life expectancy >= 6 months.
5. No new treatments likely to affect transfusion requirements during the study period.
6. Able to attend hospital to receive weekly transfusions.
7. Able to complete QoL questionnaires.
8. Able to participate in physical function tests (6-minute walk test, accelerometer to measures steps taken per day.)
9. Red cell phenotyping and/or genotyping results available.
10. For the qualitative study, able to understand and converse in conversational English for purposes of interviews.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Unable to tolerate a weekly transfusion schedule as determined by the attending clinician
2. Poor performance/functional status (Eastern Cooperative Oncology Group system; ECOG >=3)
3. Patients on Erythropoietic-Stimulating Agent (ESA) or disease modifying agents for their MDS (such as Enalidomide, Azacitidine, Hydroxycarbamide, experimental agents), as these may exert their own effects on the patients' QoL and transfusion requirements.
4. Patients with myelofibrosis
5. Patients presenting with active bleeding or evidence of significant haemolysis
6. Splenomegaly >5cm below the costal margin
7. Patients with >2 known RBC alloantibodies, and/or patients with rare antigen types which complicate cross-matching

Date of first enrolment
01/09/2021

Date of final enrolment

30/11/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

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

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

Study participating centre
North Tyneside General Hospital
Rake lane
North Shields
United Kingdom
NE29 8NH

Study participating centre

Uclh
250 Euston Road
London
United Kingdom
NW1 2PQ

Sponsor information

Organisation
Monash University

ROR
https://ror.org/02bfwt286

Funder(s)

Funder type
Industry

Funder Name
Activinsights Limited

Results and Publications

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

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?
Participant information sheet	version 3.0	14/08/2020	22/08/2023	No	Yes