RECAST-3 FAQs

V4.0, 17 Oct 2024

Contents

General

How many participants are you expecting each site to recruit?
Sites should recruit approximately 21 patients over the 2 years of recruitment (less than 1 per month).

What is the planned recruitment end date?
30th June 2026

Do you allow non-medic PIs? Yes, research nurses can be PI. Where a site has a research nurse PI, a medic needs to take on the deputy PI role to assist with reviewing and signing off SAEs.

When exactly does each day start and end with regards to reporting and completing CRFs? E.g. Day 1 start time is it randomisation or 00:00 of the same day? Each day starts and ends at 00:00. So, for the day 1 follow up form, the start time is 00:00 of that day as opposed to the time of randomisation. If for example you were to randomise a patient at 2pm this afternoon, the day 1 follow up data (including baseline/pre-randomisation data) would include data up to the end of today at midnight. If necessary, you can complete some of the answers on the day 1 follow-up form retrospectively, but the data itself should relate to day 1 and not day 2 onwards.

Who will conduct the day 90 follow-up?
The day 90 follow-ups will be conducted centrally by the Follow-up Coordinator in Nottingham. Participants will be contacted by telephone with a postal back-up form if the participant cannot be contacted.

Is it a requirement for only manual BP readings to be taken within the first 24 hours following thrombolysis? No, automated BP monitoring can be used.

Do clinical scans need to be uploaded? Yes, in addition to the baseline scan, please upload any additional clinical scans for the participant.

Eligibility

Is there a maximum BP for inclusion? No

For wake up stroke, is the 24 hour inclusion window to be taken from time last seen well or wake up time? Symptom discovery - wake up time. Please note that the allowance for 24 hours since symptom discovery is intended to capture those who wake up with stroke having been well the night before (and not those who live alone and may not have been found for a prolonged, unknown, period of time).

If someone has had previous breast cancer or axillary node clearance, are we only going to apply the intervention to one arm? Previous axillary node clearance isn't on the list of exclusion criteria but it will be down to the discretion of the site investigator as to whether they feel it appropriate to include the patient in the trial with the planned bilateral treatment. It won't be an option to enrol on the basis that the intervention will be delivered only on one arm.

Can we recruit a participant who has a normal baseline scan (no evidence of ischemic stroke) but they have a clinical diagnosis of stroke? Patients that don't have radiological evidence of stroke on their baseline scan but are treated in accordance with a clinical diagnosis of stroke will be considered eligible for the trial if all other criteria are met.

Who can confirm eligibility? Eligibility can be confirmed and consent obtained by members of the research team (which may include research nurses, research practitioners, research associates and research coordinators) who have local approval to do so and are authorised onto the delegation log with the consent taking role. A medically qualified doctor will be available to answer participant queries on their medical care if needed. If the research team member is unsure on eligibility, it’s good practice to check with the medical team [who don’t have to be on the delegation log].

Would a patient be deemed ineligible if they are suspected to have dementia? Patient would be deemed ineligible if they have a formal diagnosis or were already undergoing an assessment prior to their stroke.

Can prisoners or offenders be recruited? We do not currently have approval for prisoners or offenders supervised by the probation service to be able to take part in the trial. We are planning to submit an amendment to allow prisoners and offenders to take part in the trial and will update sites when the necessary approvals are in place.

For patients planned for thrombectomy, can they be consented and randomised before the procedure as opposed to waiting to do eligibility checks afterwards? So if NIHSS score was 5-25 before thrombectomy they would be eligible and randomised at that point, and if it dropped to 4 following the procedure, delivery of the intervention can continue? Eligibility is at the time of randomisation. We recommend starting RIC/sham as soon as practically possible after randomisation. If the patient isn't randomised prior to the NIHSS falling outside of the window, then they would have become ineligible.

If an eligible patient has capacity but there is a language barrier, is it acceptable for the family to translate? Yes, family can assist to explain the study - if the participant has capacity, participant consent form to be used. If don't have capacity, relative can provide proxy consent.

How can overseas patients that have a stroke when visiting the UK be recruited? What steps need to be put in place for the follow up data to be collected? Patient can be recruited if:

(i) NOK can complete follow up: Patient has a NOK in the UK who can be contacted on their behalf to provide follow up information if for example there is a language barrier or ppt doesn't have capacity. Permission to contact them directly (without prior alive and well check with GP) to be confirmed by site before recruitment. Site to also provide ppt with copy of the GP letter to take home.

OR

(ii) Participant follow up: If no language barrier, participant has capacity and provides a phone number, site to print GP letter for ppt to take home with them and ask the ppt for permission to contact them directly to complete FU rather than GP first for alive and well.

Consent & randomisation

Does oral consent need to be witnessed? When obtaining oral consent from a participant, this must be fully documented in the medical notes and followed up with written consent within 24 hours (or as soon as is practicable). A witness is not required. When obtaining oral consent from a consultee/legal representative, the process is the same as for participant oral consent (document in the medical notes and follow up with written consent as soon as possible). Oral consent can be obtained from a consultee/legal representative via telephone/video link, in which case the telephone consent form should be used (this doesn't need to be witnessed).

Which consent form should be used when obtaining independent physician consent? Please use the consultee declaration form. Independent physician consent cannot be used by Scottish sites.

Are the research team able to obtain consent? Yes, we do not need a medic to take consent. Consent can be obtained by members of the research team (which may include research nurses, research practitioners, research associates and research coordinators) who have local approval to do so and are authorised onto the delegation log with the consent taking role.

If a patient (who has capacity) gives verbal consent but is unable to sign/mark the consent form, who initials the individual boxes on the consent form? Is this done by the person taking consent, or done by the witness? Either the witness or the person taking consent, but they put the initials of the participant in the boxes and the form is then signed/dated by the witness, which documents the participant gave informed consent. When a witness is used for consent the independent observer can be anyone, they should not be on the delegation log, it could be one of the ward staff, for example.

Do we need to print and file a copy of the randomisation result? You do not need to print a screenshot of the randomisation result as you will be able to access this information for the duration of the trial period via the participant list on the trial database for RECAST-3. When a participant is randomised, please ensure that you record the randomisation result in the medical notes. The delivery of each dose of the intervention needs to be documented on the daily treatment log and in the medical notes. We have a sticker template that can be used when adding this information to the medical notes.

Repatriation

For repatriated participants, who will complete outstanding CRFs after their transfer? When a participant is repatriated to another RECAST-3 site, the recruiting site will need to complete the 'site-to-site transfer' CRF. The recipient RECAST-3 site will then have access to the participants record on the database. The recipient site will be required to complete remaining RIC/sham doses and complete all outstanding CRFs form that point onwards. The recruiting site will still be able to access and enter data on the database after repatriation.

When a participant is repatriated to another RECAST-3 site, how will the recipient site be informed about the group (RIC or sham) to which the participant was randomised? Once the site-to-site transfer CRF has been completed on the database, a member of the research team at the recruiting site should hand over this information to a member of the research team at the recipient site who should then record this information in the medical notes.

Safety reporting

For how long should SAEs be reported? Sites should report all SAEs for 20 days following the start of intervention delivery, regardless of the duration of 'treatment' given. The database has been set up to indicate that this is the requirement. After day 20, please report all fatal SAEs and safety outcomes through until day 90.

Do we need to report AEs or ADEs? Please document AEs and ADEs in the medical notes. We only need SAEs, SADEs and safety outcomes to be reported using the SAE CRF for the first 20 days post randomisation. After day 90, please report fatal SAEs and safety outcomes through until day 90.

In the previous studies, were there any reports of increased bruising with the trial intervention for those patients who had received thrombolysis? A degree of petechiae is not unusual (even when a BP is taken). This did not raise any safety concerns in RECAST-2

in terms of neurovascular compromise of the limb. We will still be monitoring safety events, but we will only require the events reporting that meet the seriousness criteria.

Would bruising or skin redness be classed as an adverse device effect? If an adverse event interferes with the treatment regimen (e.g. intervention changed from bilateral to unilateral), then it can be considered medically important, and therefore meeting SAE criteria such that an SAE CRF would need to be submitted on the database. Redness on the arms not deemed clinically significant does not need to be reported and the intervention can continue.

Device and intervention

Which devices are being used for the remote ischaemic conditioning?
Anetic Aid AT4 Tourniquet – these devices are currently used in A&E departments for Biers Block procedures. The Anetic Aid AT4 Tourniquet is CE marked.

Will there be a sham device?
No, the AT4 Tourniquet will perform both the intervention and the sham

When will the device be delivered to sites and how many per site will we receive?
The devices will be delivered to sites in batches relating to when the site get their approvals in place/green light to start recruiting. Each site will receive one device which can be used for the sham and intervention.

Will we be restricted to only recruiting Monday to Thursday, if research nurses do not work at the weekend and will therefore be unable to deliver the intervention if a patient is recruited on a Friday?
As long as the ward staff (band 2 and above) have been trained in trial procedures by the research team and have watched a shortened GCP training video which we will produce and upload to the trial website, they can apply the device out of hours/weekends. **Please Note:** ward staff will not be able to obtain consent or randomise patients.

Sites who are unable to deliver the intervention during the weekend must give at least 4 doses pre-weekend to be able to miss the weekend. If weekends are missed, the intervention will be continued over a period greater than 14 days in order to deliver the 28 doses.

Do you anticipate any problems with compliance due to the length of time and repetitiveness of the intervention, especially in cognitively impaired patients?
We have trialled devices in 2 separate studies and there have been no issues with compliance. However, this larger study will look at whether the device is well-tolerated in stroke patients.

Does the person delivering the intervention need to remain with the patient for the duration of the treatment (approx. 40 mins)?
Yes - the participant should not be left alone. The investigator should be in the local vicinity, i.e. in the bay and be able to view the participant at all times while receiving the treatment.

Additional notes regarding repatriation and intervention delivery:

- Whilst we are keen for patients to receive the full 14 days, we appreciate that it can be difficult to predict how long a participant will stay on site. Therefore, as long as patients meet all eligibility criteria, they can be recruited to the trial and the intervention should be delivered for as long as possible, up to a maximum of 14 days (28 doses).
- Sites that routinely discharge patients to a rehabilitation centre within the 14 days post stroke can join the trial and should aim to deliver the intervention to participants for as long as possible (up to a maximum of 14 days/28 doses) before they are moved.
- Patients that have an NIHSS score towards the lower end of the 5-25 inclusion range should still be approached to take part in the trial if all other eligibility criteria are met. Again, the intervention should be delivered for as long as possible up to 14 days/28 doses maximum.
- For the following exclusion criteria: 'expected repatriation of the participant to another hospital not participating in RECAST-3 where RIC or sham cannot continue', this will be applicable when it is known that a patient will be repatriated early on, for example in comprehensive centres that receive out of region patients who are due to be moved within ~72 hours.
- A patient admitted to a hospital outside of their locality (for example when they are on holiday) can still be recruited unless it is known that they are planned for repatriation to their local hospital within ~72 hours.

What are the timings for delivering the intervention?

Up to 28 doses of the intervention will be delivered in total (2 per day), with each dose consisting of 4 cycles:

- On day 1, the first dose must be delivered within 24 hours of the onset of the stroke, which is then followed by the 2nd dose >4 hours after the end of the first dose.
- On day 2 - 14, two doses of the RIC or sham are applied - once in the morning and once in the afternoon (there is no specified time from randomisation). There should be a gap of at least 4 hours between doses.

What do we need to complete on the database if a participant withdraws from treatment before the 28 doses are delivered? In this situation, ensure all treatment log CRFs documenting treatments delivered are completed on the database. Please also complete the 'end of treatment' CRF. The death or discharge CRF should not be completed until one of these events takes place.

For participants who have had thrombectomy or thrombolysis who have started the intervention but their follow up scan shows a haemorrhagic transformation of infarction P2 - should the intervention continue or stop at that point? The trial intervention can continue, assuming it's clinically appropriate (i.e. active medical treatment is ongoing). The decision will be down to the treating clinician.

Cuff orientation - tubing hanging down from cuff or exiting upwards (as in the training video)? It is acceptable to use the cuff with either orientation, Anetic Aid advised that having the tubing coming upwards helps to keep them out of the way. The pressure delivered is the same regardless of whether the cuff is placed with tubes coming out the top or bottom.

What should we do if a participant decides to continue with either once daily and/or unilateral treatment part way through the trial? It will be acceptable for participants to receive unilateral and/or once daily interventions if making this change enables them to continue in the trial (on the basis that 'some treatment may be better than no treatment'). Should this happen, please ensure that this is documented on a file note and treatment log CRFs are completed to make it clear what treatment the participant has received. It will not be necessary to submit a protocol violation under these circumstances.

Can we continue with intervention if patients who were initially treated as a clinical stroke but turned out to not be a stroke? It is at the Investigator's discretion, there is no harm in continuing. If it is absolutely not a stroke e.g. confirmed brain tumour, the treating clinician is likely to recommend stopping; if the diagnosis is uncertain and stroke remains within the differential diagnosis e.g. functional neurological disorders versus stroke, then consider continuing treatment.

During the last cycle of deflation, do the cuffs need to stay on the patient for the 5 minutes? Removing the cuffs after the final deflation is acceptable but please stay with the participant until the end of the 5 minutes to ensure they are ok. You could for example use this time to clean the equipment and ensure the treatment log form is completed.

Participant tolerated only 2/4 cycles on one arm but all 4 on the other. How should the treatment log be completed to reflect this? C5a/b or E5a/b (*'If cycles not completed, please indicate reason' and 'If cycles not completed, please give details'*) should be marked as not applicable. C6a/b or E6a/b (*'Please indicate any other deviation from the intended intervention – e.g. interruptions, delayed start'* and *'If such a deviation occurred, please give details'*) should be completed to document this as 'any other deviation'

Can the intervention be delivered when a participant is receiving IV fluids/meds? The intervention can be delivered with a cannula in the antecubital vein as long as it is closed off such that no meds/fluid is going through during intervention/sham. It is acceptable to temporarily interrupt 24 hour IV fluids to deliver the intervention - this is the only situation in which an IV infusion should be interrupted (don't interrupt meds). For non-continuous med infusions, please deliver the intervention once the infusion has finished. Please don't interrupt continuous insulin infusion. It is OK to deliver the intervention on the other arm only.

Funding FAQs

What is the payment per participant?
£40 per participant
£200 per site for archiving at the end of the trial