RECAST-3 FAQs

V3.0, 16 April 2024

General FAQs

When are you expecting to set-up sites?
Due to an issue with the original devices, we are now on board with a new company providing an alternative RIC device and the first delivery of devices arrived in January 2024. We have REC approval but do not need MHRA approval as the device is CE marked for remote ischaemic conditioning. We are now setting up sites and started recruitment in February 2024.

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

Are the research team able to obtain consent?
Yes, we do not need a medic to take consent. Research nurses trained in GCP and the trial procedure, and on the delegation log can take consent. Research assistants and coordinators who are not professionally registered cannot obtain consent. 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.

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).

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.

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.

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

<u>Device FAQs</u>

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 will get their approvals in place/green light to start recruiting. We will have the first 10 devices ready for shipping at the end of January 2024 and another 10 at the end of February 2024.

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.

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.

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.

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.

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.

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.

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.

Eligibility FAQs

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.

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.

Funding FAQs

What is the payment per participant?

£40 per participant

£200 per site for archiving at the end of the trial