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ISRCTN97695350

TRANEXAMIC ACID FOR INTRACEREBRAL HAEMORRHAGE: TICH-3 TRIAL

INVESTIGATOR MEETING

Professor Nikola Sprigg and Brittany Hare

On behalf TICH-3 Trial Team

Wednesday 19th July 2023 1.30 – 2.30pm

Agenda

1. Drug expiry and destruction logs
2. UK Recruitment update
3. Congratulations
4. Recruitment options
5. Pilot Progression Review
6. Reporting SAEs
7. Co-enrolment with TICH-3
8. Upcoming events
9. Thank you
10. Questions?

Drug expiry and destruction logs (1)

- The current TICH-3 treatment packs that you have on site expire 31/07/2023.
- New treatment packs are in manufacture and will be manufactured by 24th July.
- Aiming to have new treatment packs on site before the expiry of current treatment packs.

On arrival on the new treatment packs on site please process them as you have done with the previous treatment packs:

1. Mark the treatment packs as received on the TICH-3 website
2. Complete accountability and inventory logs for the new treatment packs
3. Place the new treatment packs in the secure storage location
4. Mark the new treatment packs as available for randomisation on the TICH-3 website
   - Note: please continue to select the next lowest numbered treatment pack within each block to randomise any eligible consenting participants

Drug expiry and destruction logs (2)

After arrival of the new treatment packs on site and before or on 31st July 2023

1. Please quarantine the old treatment packs to be destroyed as per your local procedure
2. Process the treatment packs for destruction as soon as possible
3. Send us a copy of the destruction log **(this is an essential document we require)**
4. Update accountability and inventory logs for the expired treatment packs

PLEASE TAKE EXTRA CARE TO NOT USE ANY EXPIRED TREATMENT PACKS TO RANDOMISE A PARTICIPANT

The co-ordinating centre will disable all of the expired treatment packs on the TICH-3 website on 1st August 2023, you do not need to action anything on the TICH-3 website.

UK Recruitment Update

Site Status	Number
Sites open to recruitment Recruited *(286 participants in total)* Not recruited	56 51 5
In set up	13
Initial feasibility assessments	7
Declined for now (capacity issues)	8
Withdrawn	10

Congratulations

TICH-3 has recruited a further 133 UK participants since April 2023, thank you so much for your continued support! Some highlights…..

St George's Hospital, London has recruited 7 participants since April
Queens Medical Centre, Nottingham recruited 6 participants since April
UCLH, London recruited 6 participants since April
Royal Hallamshire Hospital, Sheffield recruited 4 participants since April
Ninewells Hospital, Scotland recruited 2 participants since April
Lincoln County Hospital recruited their first participant in April
Luton and Dunstable recruited their first participant in May
Antrim Area Hospital, Northern Ireland recruited their first participant in May
Leeds General Infirmary has recruited 3 participants since May
Cheltenham General Hospital recruited their first participant in May
Hull Royal Infirmary recruited their first participant within 3 weeks of receiving greenlight
Dorset County Hospital recruited their first 2 participants in June
South West Acute, Northern Ireland recruited their first participants in June
Peterborough Hospital recruited their first participant in July

REPORTING SAEs (1)

Assessing relation to the study drug

When submitted SAEs or safety events please select possible only if you suspect the IMP may be related to the event. If you think it is unlikely but cannot absolutely exclude a relationship, please select improbable. All events that are reported as probable need to have causality assessed as could be a SAR or SUSAR. If in doubt, please speak to your PI, site medic or contact the coordinating centre.

A10a Relationship to study drug	☐ Not related ☐ Improbable ☐ Possible ☐ Probable ☐ Definite

Event classification

MHRA guidelines are that if you suspect an event to be possibly/probably/defiantly related that the event categorisation must be a SAR or a SUSAR, if you think it is unlikely to be related to the study drug (not related/improbable) then this is an SAE.

A10b Please classify the event	☐ SAR ☐ SAE ☐ SUSAR **Please assess if expected according to SmPC.** Expectedness should only be assessed in events that are thought to be possibly/probably/definitely related to the IMP.

REPORTING SAEs (2)

Ongoing SAEs

If an ongoing SAE submitted e.g. seizure/PE and then patient dies, unless you think the death was related to this event please complete a data correction that this event was resolved and then submit a new SAE for the fatal event.

A12a	Clinical outcome of this event	☐ Resolved ☐ Event ongoing ☐ Recovered with sequelae ☐ Died
A12b	If event ongoing or recovered with sequelae, please provide details	

Cause of death

Please make sure you always provide details in question A4 of what was the cause of death

A4	Please describe the event, e.g. new limb weakness, crushing chest pain, bleeding gums, rash **Note: Death is an end result, not an independent event**	

Suspected SUSARs

If you are suspecting a SUSAR please call the emergency helpline phone numbers.

For urgent medical enquiries (including unblinding), and for randomisation problems, you can contact the following emergency mobile numbers.

+44 (0)7725 580 092 +44 (0)7736 843 592

+44 (0)7798 670 726 +44 (0)7810 540 604

Recruitment options

Recruited out of hours:

- Saturday 20
- Sunday 21
- Evenings/overnight 44

Patients on DOACS = 19
Patients on antiplatelets = 63

Types of consent:

- Participant consent 123
- Relative consent 183
- Independent doctor consent 19
- No consent 6

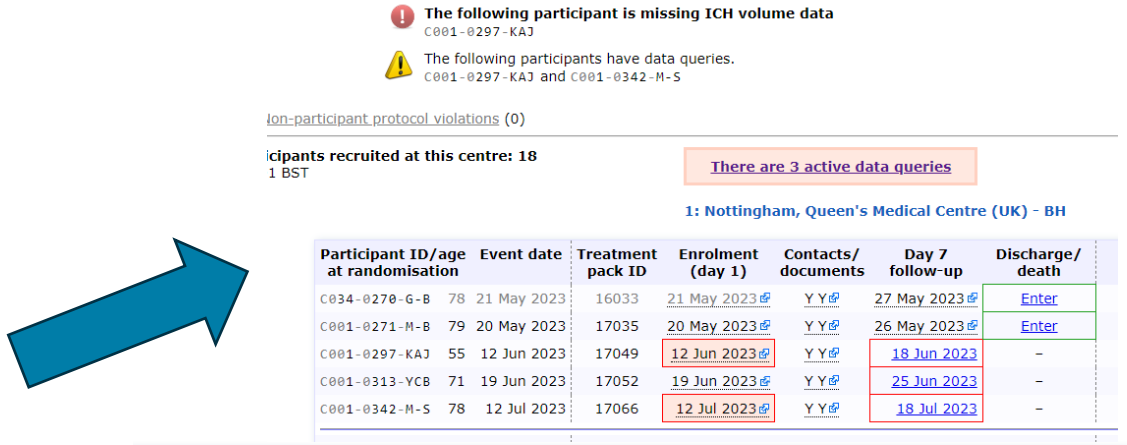
Protocol violations – so far

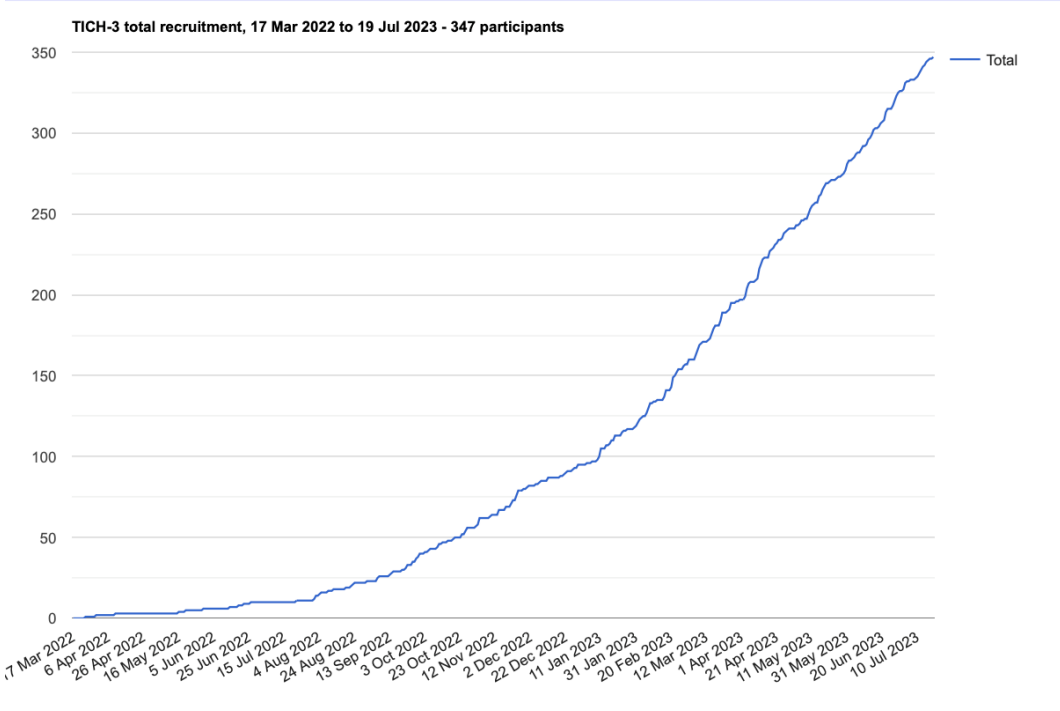
- Not all IMP given – 2nd dose not prescribed
- Tranexamic acid given as part of standard of care
- 100mls infusion given as 10ml bolus
- IMP administered late (4hrs 56 minutes) due to difficulty to get IV access
- 2 patients massive ICH (considerably > 60 mls)
- 1 treatment pack given to non trial participants

Pilot Progression Review

Upcoming committee meetings
DMC 14/09/2023
TSC 19/09/2023

Outstanding data
Please can you ensure any data queries have been completed prior to the upcoming DMC meeting.
> You can review if your site has any data queries by going to the ‘participant list’ on the TICH-3 website





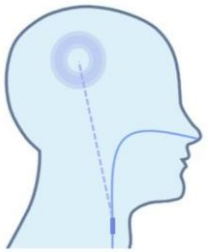
There is guidance available on the TICH-3 documents page for completing data correction requests https://stroke.nottingham.ac.uk/docs/TICH-3/UK_site_training/TICH-3%20Data%20corrections%20guidance%20Final%20v1.0%2007.03.2023.pdf

Please also remember to complete the death/discharge eCRF when appropriate.

Co-enrolment with TICH-3

Co-enrolment is permitted, and sponsor approved for the following University of Nottingham sponsored trials (contract with site not required)

- MAPS-2 (IC now up-to 24 hours to enrol)
- PhEAST



Co-enrolment has been agreed with the following non-University of Nottingham sponsored CTIMPs (contract with site REQUIRED before co-enrolment is permitted)

- TRIDENT
- ENRICH-AF (MASTER CONTRACT NOW AGREED)

If you are taking part in either trial, please let us know so your site (PI and R&I) can document they agree to co-enrolment at your site.

Please let us know if there are any other trials you may wish to co-enrol with so that we can begin the contracts process.

There is a co-enrolment log on the TICH-3 documents page
https://stroke.nottingham.ac.uk/sif/docs/?sid=TICH-3

Upcoming events

It was good to see some of you at ESOC in Munich!

- World Stroke Congress, Toronto (10-12 October 2023)
- UKSF ICC, Birmingham (4 to 6 December 2023)

Acknowledgements

TICH-3 would not be possible without:

All our participants and their families – we thank them for agreeing to take part and help us try to find better treatments for stroke due to intracerebral haemorrhage.

Thank you also to:

- TICH-3 Investigators
- TICH-3 staff Nottingham Stroke Trials Unit, Nottingham Clinical Trials Unit
- TICH-3 co-applicants
- Collaborators including Andrew Willis
- Nottingham Stroke Research Partnership Group - PPIE
- TICH-3 trial steering committee, data monitoring committee
- Funders – NIHR HTA

The Centre for Ethnic Health Research
national centre for tackling health inequalities

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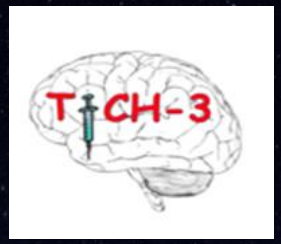

Any questions?

Question and answers (Eligibility and consent)

Does eligibility have to be confirmed by a medic?

Confirming eligibility is defined as a medical decision, so must be undertake by a medically qualified doctor under the clinical trials regulations, they do not need to be on the TICH-3 delegation log to confirm eligibility. Anyone who if taking oral or written consent must be on the TICH-3 online delegation log to take consent.

What is appropriate training to have code J enrolment consent for CTIMPs to be applied to non-consultants?

As long as it is evidenced in their CV or a certificate that the team member has had appropriate training (incase of MHRA audit) e.g. the NIHR Informed Consent training course, to take enrolment consent for CTIMPs and the PI agrees they have had appropriate training or experience then code J can be delegated to the team member. Please check with your local trust that they allow non-consultants to take enrolment consent for CTIMPs.

Does IMP have to be administered within 4.5 hours?

Patient is eligible to be included if present within 4.5 hours of symptom onset, if there are then problems with drug administration i.e. cannulation problems, develop clinical reason for drug not to be administered after randomisation, the treatment should still be administered (unless participant has deteriorated in the delay) then this would be protocol violation and needs to be reported.

Question and answers (Out of hours recruitment)

What steps are in place to allow out of hours recruitment?

- Prescribing of the IMP can be completed by anyone licensed to prescribe they do not need to be on the TICH-3 delegation log or GCP trained.
- Administration of the IMP can be completed by anyone qualified to give IVs e.g. nurse, they do not need to be on the TICH-3 delegation log or GCP trained.
- Person confirming eligibility does not need to be on the delegation log and this can be done remotely over the phone or telemedicine.
- Anyone will code J delegated to them on the online TICH-3 delegation log can take oral enrolment consent.
- Verbal permission can be given over the phone or telemedicine.
- QR code recruitment alert can be completed by anyone, they do not need a log in for the TICH-3 website, this alert lets everyone in the team know a recruitment has taken place and paperwork e.g. consent form, collecting contact details can be completed the next day.
- All consent processes should be documented in the participants medical notes, the person on site can do this or some sites can do electronic notes remotely.

Question and answers (Co-enrolment)

Is co-enrolment with FASTEST permitted?

No, if your site is taking part in FASTEST and the patient is within 2 hours from symptom onset and fits the FATEST pathway then enrol into FASTEST but you cannot then co-enrol with TICH-3. If the patient presents between 2 hours and 4.5 hours from symptom onset then then can be enrolled into TICH-3, if they meet the other eligibility criteria.

Patient already enrolled into ENRICH-AF or OPTIMAS trials can they then go into TICH-3?

If the participant is enrolled into the ENRICH-AF trial or OPTIMAS trial, they experience a new ICH event then they are eligible to be enrolled into the TICH-3 trial (we do not exclude participants by already being enrolled into a trial). You would need to check with the ENRICH-AF/OPTIMAS team if they would allow the participant to go into the TICH-3 trial if they are an existing ENRICH-AF/OPTIMAS participant.

Question and answers (DOACS and UKSF)

Tranexamic acid as standard of care for DOACs?

We are aware that some sites use tranexamic acid as standard of care for certain patients presenting who are on DOACs. If your standard of care treatment is to use tranexamic acid for these participants, they then cannot be enrolled into TICH-3.

Would you like to share your experience of TICH-3 at UKSF 2023?

This year's UKSF is in Birmingham 4 – 6th December 2023. If you would like to share your experience of TICH-3 during the TICH-3 investigator meeting at UKSF please let us know.