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ISRCTN97695350

TRANEXAMIC ACID FOR INTRACEREBRAL HAEMORRHAGE: TICH-3 TRIAL

INVESTIGATOR MEETING

Professor Nikola Sprigg

On behalf TICH-3 Trial Team

21ST March 2023

Agenda

1. UK Recruitment update
2. Delegation log
3. Self-referral for TICH-3 account
4. DOAC guidance and FAQs
5. Randomisation
6. Data correction guidance
7. Co-enrolment with TICH-3
8. Upcoming events
9. Thank you
10. Questions?

UK Recruitment Update

Site Status	Number
Sites open to recruitment Recruited *(171 participants in total)* Not recruited	51 40 11
In set up	14
Initial feasibility assessments	7
Declined for now (capacity issues)	10
Withdrawn	10

Delegation log

Enrolling investigators

The more enrolling investigators on the delegation decreases the risk of eligible participants not being enrolled. The emergency department doctors would be worth approaching to get on the delegation log. There is a streamlined version of the 'Enrolling Investigator Training' for team members whose only role will be to take enrolment consent. https://stroke.nottingham.ac.uk/docs/TICH-3/UK_site_training/TICH-3%20Enrolling%20Investigator%20Training%20Final%20v1.7%2028.07.2022.pdf

CONSENT MUST NOT BE TAKEN BY ANYONE IF THEY HAVEN'T BEEN APPROPRIATELY TRAINED IN TICH-3 AND ARE NOT AUTHORISED BY THE LOCAL PI ON THE TICH-3 ONLINE DELEGATION LOG

Recruitment accruals

If the participant is recruited through the emergency department the accrual can be attributed locally to the trauma and emergency portfolio and a per participant basis, your trust will be able to advise how to do this.

Deputy PI

Each site can nominate one deputy PI, which is advisable, this team member will have the role to approve the delegation log in the absence of the PI. The deputy PI can be a non-medic however they will not be able to adjudicate SAEs.

- Please inform the co-ordinating centre of who you would like to nominate as deputy PI

Self-referral for TICH-3 account

- We do now have a self-referral process which can be used once a team member has completed training (instead of sending us the training logs). This process reduces the time frame from someone completed training then completed the training log but also reduces any data entry errors from reading handwritten training logs.

- Please find the different training slides/video on the TICH-3 documents page https://stroke.nottingham.ac.uk/sif/docs/?sid=TICH-3

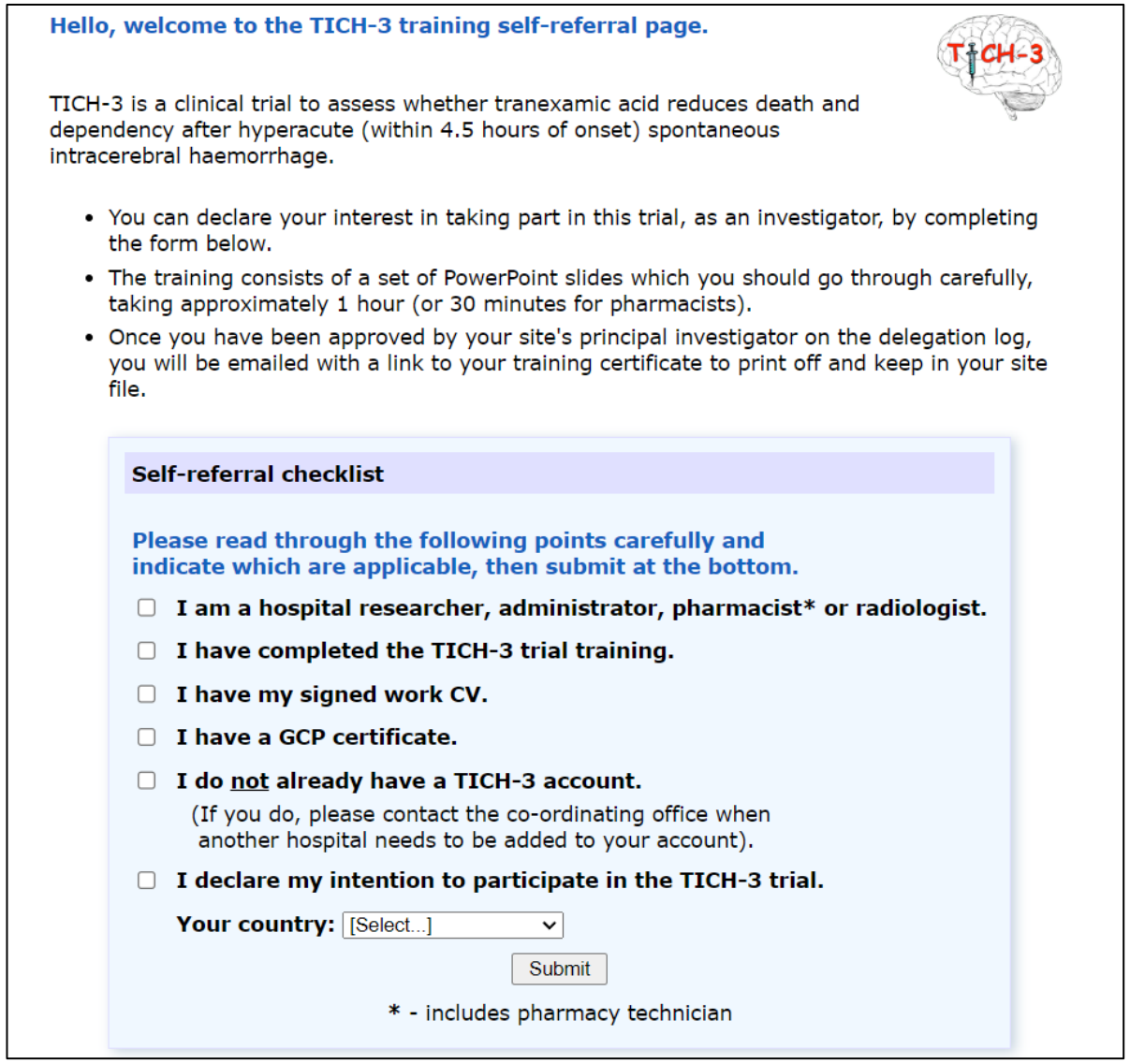
There are 3 versions of the training slides

1. Investigator training which gives a detailed description of the whole trial process, intended for the PI and research nurses/coordinators. There is also a video of this training.
2. Enrolling investigator training this streamlined training is intended for team members who will only be taking enrolment consent i.e. consultants
3. Pharmacy training this streamlined training is intended for members of pharmacy team

Self-referral for TICH-3 account (2)

- Once training has been completed please use the self-referral link http://tich-3.ac.uk/?ZSelfRef to create the account for the TICH-3 website, the PI will then be notified by email to authorise the team member onto the delegation log.

- The self-referral link can be completed by the individual themselves or a member of the administrative team/research team at the site.



Updated Eligibility Criteria

Inclusion criteria

- Spontaneous ICH (confirmed on brain imaging) < 4.5 h of onset

CT (or MRI) is conducted pre-recruitment in line with standard care, the haematoma volume measurement will help assess whether the participant is eligible.

Note - ICH secondary to ruptured aneurysm or vascular malformation or brain tumor or ischaemic stroke (haemorrhagic transformation of infarct, HTI) or thrombolysis or venous infarct is NOT spontaneous ICH

Exclusion criteria

- Known indication for TXA treatment (e.g. traumatic brain injury) *in view of treating physician*
- Known contra-indication for TXA treatment (e.g. active seizures) *in view of treating physician*
- Patient known to be taking therapeutic anticoagulation with warfarin or low molecular weight heparin at time of enrolment. Patients taking direct oral anticoagulants can be included and are not excluded.
- Massive ICH (usually when haematoma volume > 60ml)
- Severe coma, Glasgow Coma Scale <5
- Decision for palliative (end of life) care

DOAC Guidance

- These are the only DOACs being used at the moment in the UK
- **Direct thrombin inhibitor** – Dabigatran
- **Factor 10a inhibitor** – Apixaban, rivaroxaban, edoxaban
- If they have only recently started taking a DOAC, for as long as they have regularly taken it for the last 48 hours, we would enrol them as patients taking regular DOAC

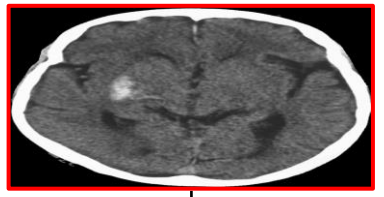
1. If they are taking Dabigatran they can be recruited to the trial whether or not they have been given idacarizumab
2. If they are on Edoxaban they can be recruited to the trial
3. If they are on Apixaban or Rivaroxaban they can be recruited to the trial however they cannot be co-enrolled with ANNEXA-4 Trial
4. All patient on DOAC should be treated according to their local protocol and can be given octaplex/PCC alongside recruitment to TICH-3
5. If local protocol is to treat DOAC related ICH with TXA (please note this is not standard of care), then they cannot be recruited to TICH 3

DOAC FAQs

- **Can a reversal agent/PCC be administered at the same time as TICH-3 treatment?**
- Do not delay starting the TICH-3 trial treatment, reversal agent/PCC can be administered at the same time as the TICH-3 trial treatment as long as through separate IV cannula.
- **If the patient is on a DOAC is the haematoma volume of 60ml still the cut off?**
- Yes, the cut off remains at around 60ml

Randomisation

- Randomisation into the TICH-3 trial is defined as when the lowest numbered treatment pack is opened
- If the participant consents, is randomised and then the trial treatment is not administered they are still a recruit in the trial
- The participant will still be followed up with CRF data completion and SAE completed if required (e.g. seizure occurred prior to administration of trial treatment)
- Please contact the coordinating centre TICH-3@nottingham.ac.uk to inform us of the non-administration of treatment



Verbal permission

Randomise - open lowest numbered treatment pack

Recruitment Alert

Written consent

Primary outcome:
Mortality day 7

Secondary:
mRS day 180

Data corrections example

Example of how to complete data correction request form

A5: Question ID and label is the number and title of question and the data originally entered

A6: Enter question ID of where the new data is to be entered, and the values that should appear once the CRF record has been amended

A7: Please enter the reason for the change

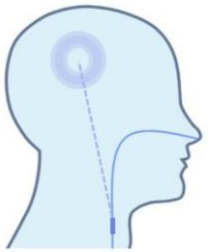
A5	Existing data Please list each: *Question ID* *Question label* *Data shown on report*	A2c: Explanation if treatment not received or data missing - "Test". Explanation for missing data: "Transferred before day 7".
A6	New data Please list each: *Question ID* *New value(s)*	A2c: "Participant transferred for surgery before full dose given." Explanation for missing data: "Transferred on first day for surgery".
A7	Reason for change	Required full explanation had not been given.

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

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

- ESOC Munich, 23 to 26 May 2023
  Stand in exhibition hall and TICH-3 Investigators meeting Weds lunchtime

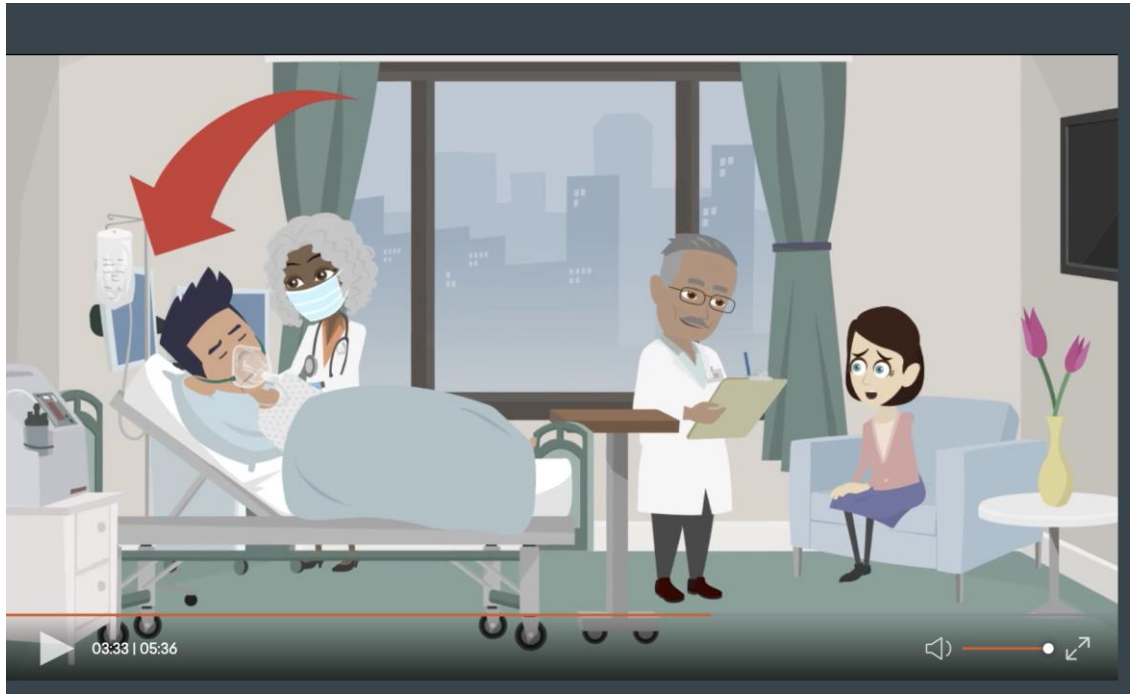
- UKSF ICC Birmingham, 4 to 6 December 2023

- Enrolling Investigator Webinars

> We are considering conducting webinars for enrolling investigator training to help get more team members on the delegation log if you think this would be beneficial?

SWAT Meeting

- Thank you to the SWAT active sites that attended the recent meeting



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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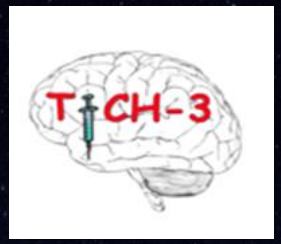

Any questions?

Q & A during session (1)

- Q: Is there any limitation on time with the Associate PI scheme?
- A: There is no time limitation, we are listed on the Associate PI scheme and we welcome more APIs.

- Q: Does TICH-3 co-enrol with interventional trial such as GECKO?
- A: Yes we can co-enrol with GECKO as this is a rehab study. If the study was regarding a drug we would require an explicit co-enrolement agreement in place.

- Q: Does TICH-3 co-enrol with ENRICH-AF?
- A: Yes, there is a 14 day wash out period after enrolment into TICH-3. Please let us know if you are taking part in ENRICH-AF and will send you the template contract for localising.

- Q: There are some concerns over reversal agent with TXA on top, is there further guidance on this
- A: As far as we are aware there are no safety concerns as shown in the TICH-NOAC trial.

Q & A during session (2)

- Q: Does TICH-3 co-enrol with OPTIMAS?
  A: OPTIMAS is an Ischaemic Stroke trial so does not share the same pool of participants as TICH-3

- Q: If a patient develops seizure – do we continue or pause the infusion?
  A: Must stop the infusion straightaway and report a safety event.

- Q: Does TICH-3 co-enrol with PRESTIGE?
  A: We were approached by PRESITGE for co-enrolment which we were interested in however as details were finalised, PRESTIGE were looking to close soon which did not fit into the timeline with TICH-3. We were also recently approached by the MARCH trial which we are keen on but contracts currently not signed.

- Q: Is a recording of the meeting available?
- A: The presentation slides with Q&As will be available on the TICH-3 website

Interest in DASH sub study and Enrolling Investigator Webinars

- TICH-3 team offered to deliver webinars if there was interest, the following sites replied expressing interest: Royal Cornwall Hospital, Dartford and Gravesham, Milton Keynes University Hospital, Royal Derby Hospital.

- Update by Royal United Hospital Bath that they have an ED Consultant as PI.

- Professor Niki Sprigg introduced DASH as an amendment to TICH-3. Would require extra consent form and would also count as extra accrual. The team will send EOI out, interest shown from the following sites: Aberdeen Royal Infirmary, St George's Hospital, Leeds General Infirmary, University Hospital of North Durham and Royal Cornwall Hospital.

- Regarding MOSAIC, Kelly Hubbard will send details and the protocol to the TICH-3 team