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ISRCTN97695350

TRANEXAMIC ACID FOR INTRACEREBRAL HAEMORRHAGE: TICH-3 TRIAL

INVESTIGATOR MEETING

Professor Nikola Sprigg

On behalf TICH-3 Trial Team

11th August 2022

Agenda

1. Recruitment update
2. Haematoma volume measurement
3. Recruiting out of hours
4. Recruiting experience – King’s College Hospital and Princess Royal Hospital
5. Associate PI scheme
6. SAE reporting
7. Research reset/stop go decision
8. Thank you
9. Questions?

Recruitment Update

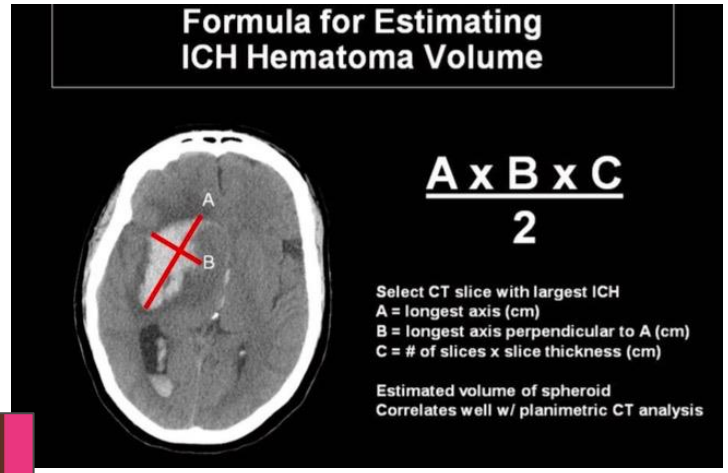
Site Status	Number
Sites open to recruitment Recruited Not – recruited	22 10 12
In set up	32
Initial feasibility assessments	11
Declined for now (capacity issues)	11
Withdrawn	6

Haematoma Volume Measurement

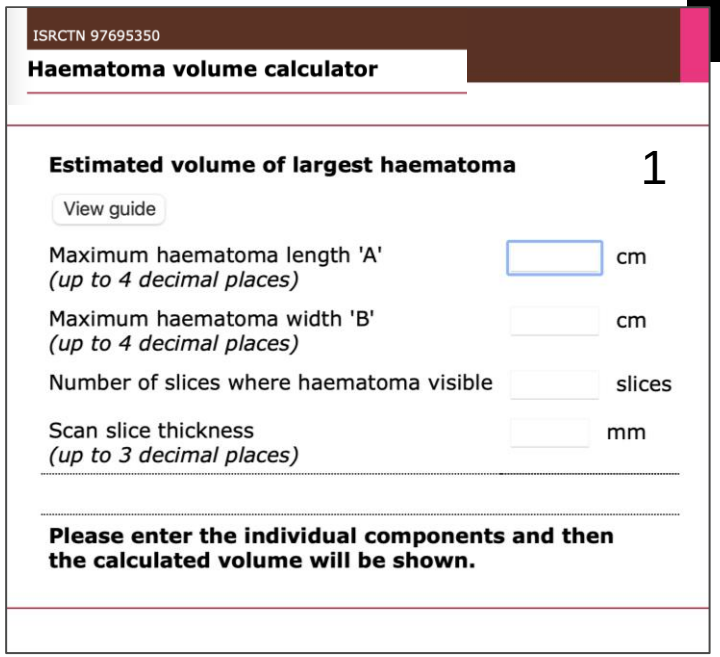
Exclude patients with massive haematoma (usually >60ml)

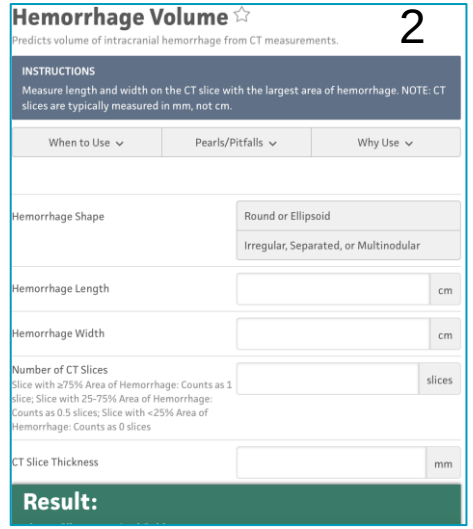
1. If CT scan uses automated haematoma volume software – patient can be enrolled if HV not greater than 60mls (60cm^3)
2. Calculate HV manually using TICH-3 HV=ABC/2 calculator on the website[1] or alternatives e.g. mdcalc app[2] Dimensions can be obtained from neuroradiology or measured directly. *Please note 1ml = 1cm3*
3. If ABC/2 not possible: measure the maximum length of the haematoma. If A < or = 5cm include Exclude - if max length A > 5cm

- HV can be estimated by anyone trained to do so



The ABC/2 calculator can be used to calculate haematoma volumes during eligibility checks, without needing to be logged in.





https://www.mdcalc.com/abc2-formula-intracerebral-hemorrhage-volume

Decision to confirm eligibility rests with treating physician

Haematoma Volume Measurement FAQs

- **Is the 60ml estimation an absolute cut off?**

There could be a 10% leeway to HV of 60ml however if patient appears unwell and low GCS then the participant shouldn't be enrolled. Ultimately it is clinical judgement. Balance of GCS and NIHSS, IVH and haematoma location. Will preventing haematoma expansion affect the outcome?

- **The HV calculation is showing in cm**

1ml = 1cm3

- **Should we measure volume of IVH?**

No, patients with isolated IVH shouldn't be included

- **Are the patients eligible if they have a lesion on the brain?**

Haematoma into mass lesion isn't spontaneous and shouldn't be included

Any questions?

Recruiting Out of Hours

- The person taking verbal consent must be appropriately trained and delegated by the PI to take consent on the delegation log

- If patient lacks capacity - relatives (or close friends) can provide oral consent if they can be contacted rapidly in time frame required. Oral consent can be given over the telephone, bearing in mind emergency nature of the clinical situation.

- Where the doctor assesses the patient via telephone/telemedicine, verbal consent will be obtained and witnessed by someone present in the hospital and this will be recorded in the medical notes.

- Written consent should be obtained as soon as possible but doesn't have to be within 24 hours i.e. if enrolled Friday evening, written consent can be taken on Monday morning

Recruiting Out of Hours FAQs

- **Reporting SAEs out of hours**

The local trial team report the SAE within 24 hours of them becoming aware of it and the participant would be treated clinically i.e. stop the infusion. The TICH-3 emergency helpline numbers could be left with the ward staff so that if they have any concerns, they can call these out of hours.

- **Who can prescribe and administer the IMP?**

Anyone who is appropriately training to do so, they do not need to be on the delegation log.

We are currently investigating feasibility of investigators being added to other sites delegation logs therefore if they were on call at other sites they would be able to take consent.

Any questions?

Recruiting Out of Hours – Q&A during the meeting

Does oral consent and written consent have to be taken by the same person?

No, a doctor could take the enrolment consent and then a research nurse could complete the follow on written consent.

If consent is being witnessed, does the witness have to be on the delegation log?

No the witness can be anyone. Having a witness is not a legal requirement however it is advisable for audit reasons for documenting the process that occurred for enrolment of the participant into the TICH-3 trial to be witnessed.

Does the witness have to be an independent person?

No, it is only the independent Dr consent that needs to be independent. A witness that is independent (i.e. not on the delegation log) might be more reliable.

Recruiting Experience

Colleagues from King's College Hospital and Princess Royal Hospital are going to share their experience of recruiting into the TICH-3 trial

Is there anyone else on the call who would like to share?

Recruiting Experience Shared During Meeting

Con from Kings College Hospital, London

- Recruited 2 participants so far
- Pragmatic
- Challenge with telephone consent as thought witness had to be on the delegation on but informed this is not the case
- Have used independent doctor for enrolment consent
- Easy
- Enjoyed recruiting into TICH-3

Beatrix from Princess Royal Hospital, London

- Recruited 1 participant so far
- Smooth process to recruit
- Had problem that the bolus leaked during infusion, rang emergency phone number for TICH-3 at the time and was informed not to open a new treatment pack as couldn't be sure if any treatment has been administered so followed the advise of the coordinating centre to administer the remaining 2 vials as a bolus and then did not administer the infusion. It was then reported on eCRF that not all the trial treatment was given.

Alan from Royal Infirmary of Edinburgh, Scotland

- Recruited 1 participant so far
- Straight forward
- Had a patient that was on a NOAC the day before but currently these patients are not eligible, the TICH-3 team are planning to submit a protocol amendment to allow patients on NOAC/DOAC to be included
- FASTEST – sites can take part in this trial, if participant is eligible they would be enrolled in FASTEST and not TICH and FASTEST is inclusion of within 2 hours

Associate PI Scheme

Are you a new researcher looking for training in research studies?

TICH-3 is registered for the Associate PI scheme, this is a great opportunity for doctors, nurses and other healthcare professionals to gain knowledge of what it means to deliver an NIHR portfolio trial.

Key points

- A 6 month in-work training opportunity providing practical experience for healthcare professionals starting their research career.
- Receive a certificate endorsed by NIHR and Royal Colleges
- Ideally you will apply to form the scheme 1 month before the site is ready to open and begin recruitment
- Engage with the TICH-3 coordinating centre during the 6 month scheme (we will sign off part of your checklist

You can find more information here: NIHR Associate PI Scheme Website.

You can register here: NIHR Associate PI Scheme Applicant Registration Form.

We recommend sites consider appointing an associate PI – please discuss if any questions.

Current TICH-3 sites with a registered Associate PI: Lincoln County Hospital, James Cook University Hospital, Craigavon Area Hospital, Salford Royal and York Hospital.

We are planning to arrange a non-PI support group if anyone would be interested?

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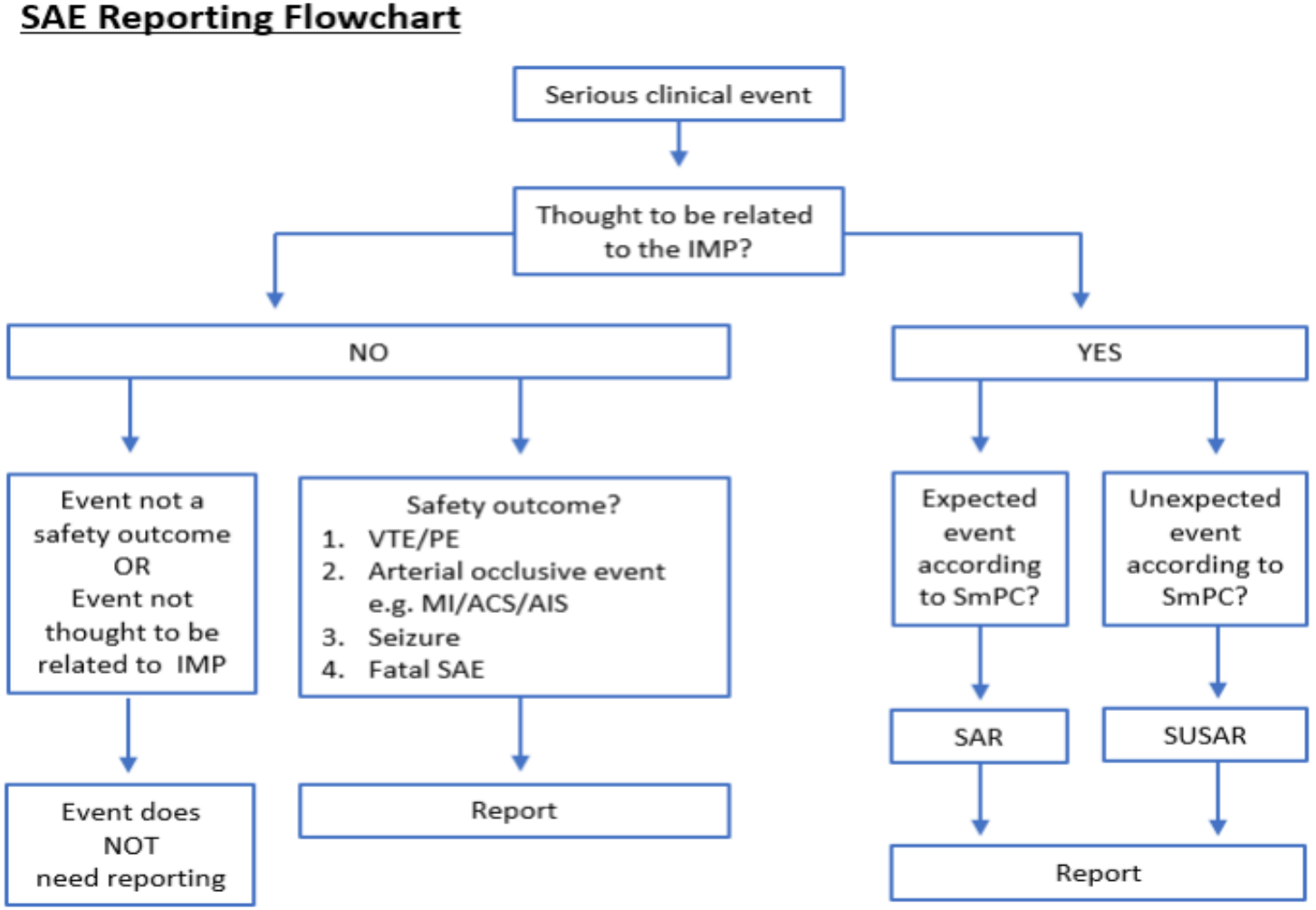
SAE Reporting Flowchart



Serious adverse reactions (SAR) or Suspected Unexpected Serious Adverse Reactions (SUSAR):

- All events suspected to be related to the IMP will be assessed for seriousness, expectedness and causality by local investigator. Section 4.8 of the SmPC, date of last revision 02 February 2021, will act as the **Reference Safety Information:** Tranexamic Acid https://Tranexamic Acid_SmPC_20210202_REVISION.pdf

Safety Events, SARS and SUSARS FAQs

- **Should patient deterioration be reported?**

Neurological deterioration, haematoma expansion such as IVH and PHE are common after a stroke, these are not safety events and do not need reporting unless think it is related to the drug or patent dies.

Examples of SAEs reported so far

- Recurrent seizures

If the patient dies or is discharged please update SAE by completing a data correction so that it is no longer ongoing.

- Resolved
- Recovered with sequelae
- Death

Any questions?

Research Reset

Following the pandemic, the NIHR is taking urgent action to address the current clinical research delivery challenges in the NHS, termed the 'Research Reset' (more information can be found here). We believe TICH-3 satisfies the questions asked by NIHR.

- ✓ Research question is still of importance - ICH is devastating
- ✓ Care pathway for ICH is unchanged – there is currently no evidence for haemostatic therapies in standard care guidelines
- ✓ Able to recruit the target population – please help us to reach our recruitment target ahead of the stop-go decision in October 2023

Any questions?

Thank You

The TICH-3 trial would not be possible without the support of our investigators, thank you very much to everyone that has joined us thus far!

Q&A After the Presentation

NIHSS measure on Day 7 eCRF, should this be completed if not completed clinically?

Day 7 NIHSS is listed in the protocol as routine clinical procedure. If the NIHSS has been performed the result can be entered. If it is possible for the NIHSS to be performed then the data can be entered. If the NIHSS is not possible (patient too unwell, no staff available, patient discharged) then it can be entered as not done.

Can Advanced Care Practitioners (ACPs) or non consultant doctors be PI's?

Yes, the local PI does not have to be a consultant it could be an advanced care practitioner or trust grade doctor so long as they have the necessary time, experience and training to act as PI. We are going to try and arrange some non-consultant PI peer support groups.

Are screening logs to be collected?

No, we wanted to reduce the burden on sites which was greed by the TICH-3's Trial Steering Committee and the sponsor.

Q&A After the Presentation

When do we complete the Day 7 eCRF if patient is discharged early?

If the patient is discharged to another TICH-3 site you can complete site to site transfer and the sister site would complete follow up. It patient is discharged to non-TICH-3 site on day 4 you would complete day 7 form early and then complete death/discharge form. We would then ask that on day 7 if you could try and find out alive status and update the death/discharge eCRF by completing a data correction.

What exactly is meant by within 4.5 hours of ‘symptom discovery’?

In a patient with wake up stroke i.e. patient went to bed 10pm, woke up at 7am with symptoms - then came into ED at 10am this would be 3 hours from when they woke up (=symptom discovery) and could be enrolled. In patients without wake up stroke who are ‘found’ and time last know well is unknown – the time they are ‘found’ can be taken as symptom discovery. CT scan would confirm if eligible e.g. Still need to meet other inclusion criteria (haematoma volume not massive)

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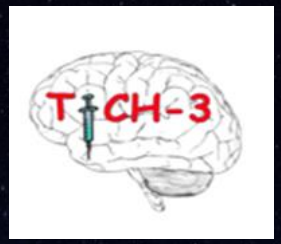

Any questions?