University of Nottingham
UK | CHINA | MALAYSIA

ISRCTN97695350

TRANEXAMIC ACID FOR INTRACEREBRAL HAEMORRHAGE: TICH-3 TRIAL

INVESTIGATOR MEETING

Professor Nikola Sprigg

On behalf TICH-3 Trial Team

24th January 2023

Agenda

1. UK Recruitment update
2. Protocol amendment – IN REVIEW
3. Recruiting out of hours
4. Haematoma volume estimation
5. Eligibility: seizures
6. Consent forms flowchart
7. Safety events and SAE reporting
8. SWAT summary
9. Co-enrolment with TICH-3
10. Upcoming events
11. Thank you
12. Questions?

UK Recruitment Update

Site Status	Number
Sites open to recruitment Recruited *(113 participants in total)* Not – recruited	50 33 17
In set up	9
Initial feasibility assessments	9
Declined for now (capacity issues)	9
Withdrawn	9

Protocol amendment – IN REVIEW

- SA_04_22 **NOT yet approved**

Protocol amendment, the protocol that sites should adhere by is now TICH-3 Protocol Final v2.0 xx/xx/xxx

Summary of changes

1. Patients that are on DOACs at the time of ICH are now eligible to be enrolled into TICH-3
2. Trial background information literature review updated
3. Inclusion of adults clarified to (≥ 18 years)
4. Safety reporting – pregnancies occurring in trial participants or partners of trial participants will not be followed up as TXA has a short half life and TXA is very commonly used during pregnancy.
5. Appendix 1
   i. Table one wording has been amended to EXPECTED EVENTS NOT SUBJECT TO EXPEDITED SUSAR REPORTING. Note: Table one isn't whether the event is to be reported or not but states the events that are expected after tranexamic acid but not subject to expedited reported as they are expected so are not a SUSAR.
   ii. Table two been removed as they are common side effects after haemorrhagic stroke and are unnecessary to be reported. Table 1's text has been updated so that it is clear the events that should be reported isn't whether the event is to be reported or not but states the events that are expected after tranexamic acid but not subject to expedited reported as they are expected so are not a SUSAR.
6. Health economics outcomes have been moved from the Health economics chapter to secondary outcomes.
7. Layout corrections

Recruiting out of hours

- “Exciting to be involved. My feedback on the enrolment process is that it was very simple, even out of hours without a research nurse to support, and now I have done one, my next randomisation will be really easy and quick.” – Dr Peter Anderton, Doncaster Royal Infirmary

- Aberdeen Royal Infirmary have recruited 4 participants out of hours!

Principal Investigator Petrus Elofuke and Research Nurse Janice Irvine kindly offered to share their process of recruiting out of hours.

- Royal Derby Hospital has recruited 4 participant out of hours!

Research nurse Lisa Mayles kindly offered to share their process of recruiting out of hours.

Recruitment Experience

"Our ED Consultants and Research Nurses are switched on with research and hands on. The consent process is straightforward. Measuring the hematoma volume is straight forward enough."

Dr Petrus Elofuke, Aberdeen Royal Infirmary

"The consent process is simple, and measuring hematoma volume has not been a problem. We have a folder with instructions which also helps."

Lisa Mayles, Royal Derby Hospital

Haematoma volume estimation

TICH-3 trial
Tranexamic acid for
IntraCerebral Haemorrhage 3

Room S/D2123, Stroke Trials Unit
School of Medicine, University of Nottingham
Queen's Medical Centre, Derby Road
Nottingham NG7 2UH, United Kingdom
TICH-3 trial office <tich-3@nottingham.ac.uk>

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Haematoma volume calculator

Investigator: **Chaamanti Sivakumar** Log out

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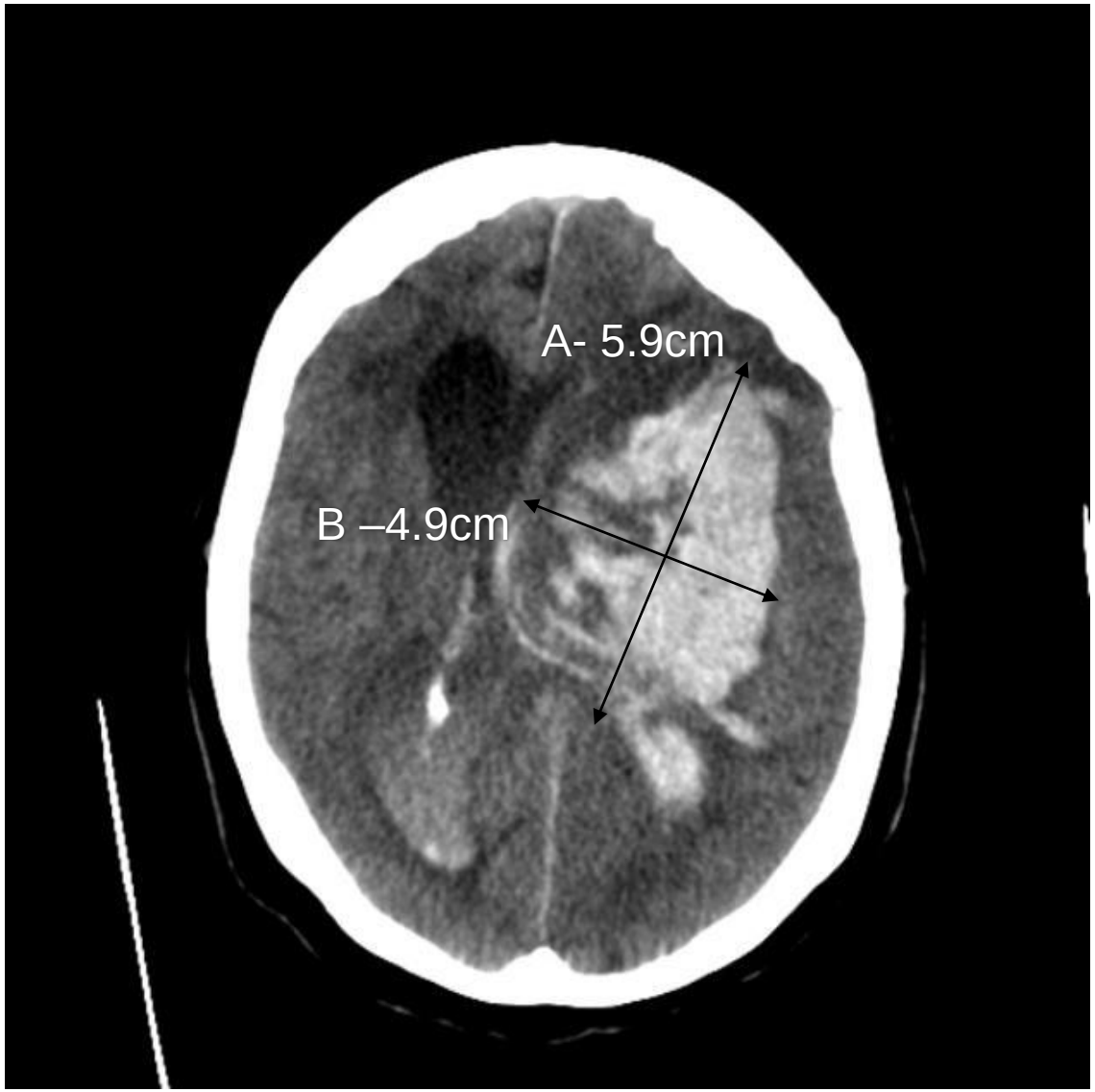
Estimated volume of largest haematoma

View guide

Maximum haematoma length 'A' *(up to 4 decimal places)*	5.9	cm
Maximum haematoma width 'B' *(up to 4 decimal places)*	4.8	cm
Number of slices where haematoma visible	25	slices
Scan slice thickness *(up to 3 decimal places)*	5	mm

Calculated volume (ABC/2) = 177 cm³

Please enter the individual components and then the calculated volume will be shown.



Case courtesy of Dr David Cuete, Radiopaedia.org, rID: 27193

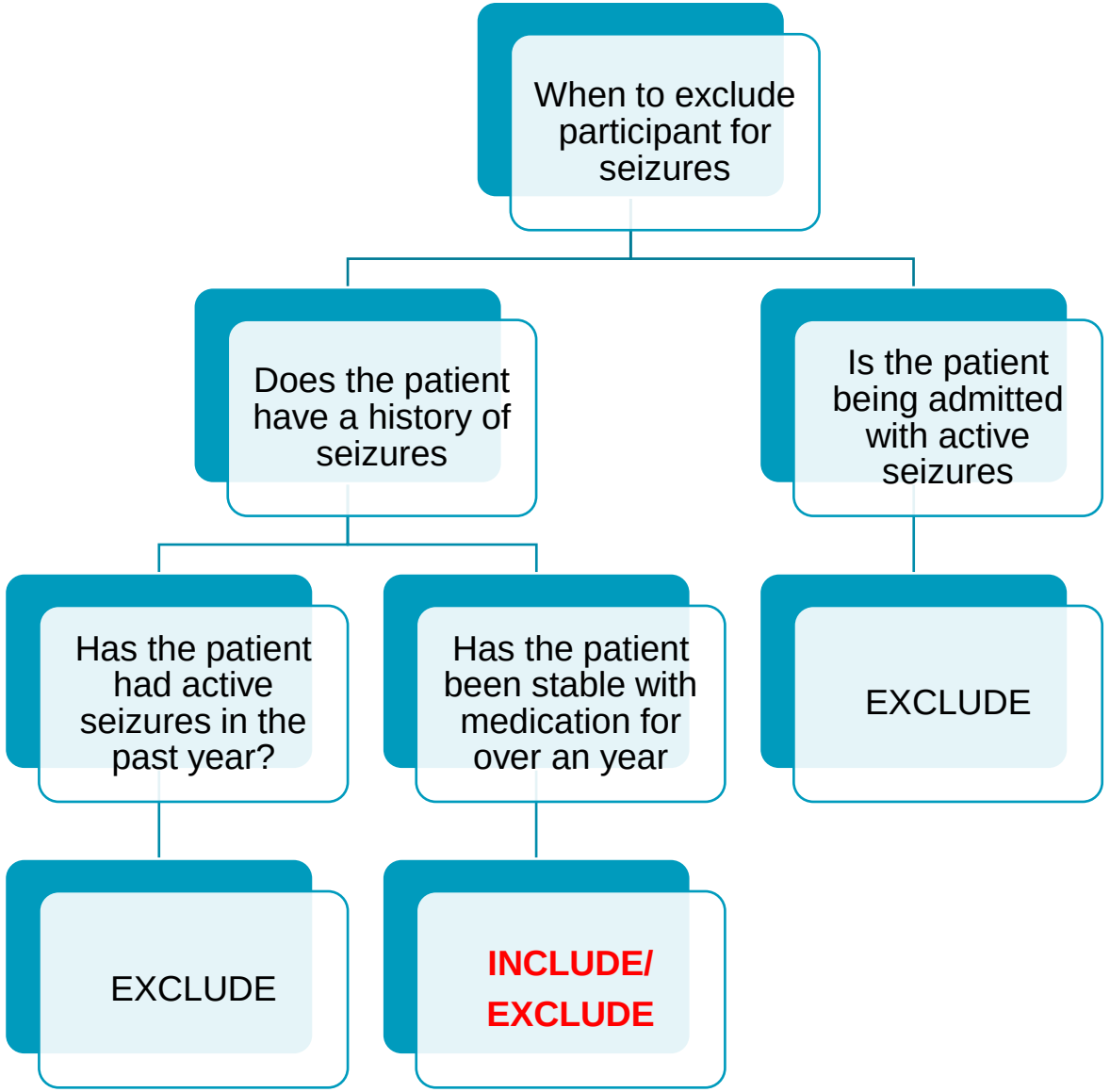
Eligibility: seizures

- Eligibility for TICH 3 in patients with a history of seizures is at the discretion of the treating physician

- If you have an eligibility query please call the emergency phone number

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

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



Consent forms flowchart

TICH-3 investigator receiving consent

Over the phone

Personal legal representative (Relative)

Verbal Consent over the phone
Witnessed by second member of staff and documented in source notes. Relative legal rep short information sheet and SWAT video (if relevant) provided by email.

Written Consent over the phone
Relative legal rep full consent form to be used. Relative information sheet and SWAT video (if relevant) provided by email. Professional legal rep. full consent form if no one available.

Professional legal representative (Independent Dr)

Written Consent over the phone
Received by enrolling investigator and witnessed by second member of staff. Document in source notes and use Professional Legal Rep. Short Info sheet and Consent form.

Written Consent over the phone
Relative, if available. Relative legal rep full consent form to be used. Relative information sheet and SWAT video (if relevant) provided by email.

In person

Participant/personal legal representative (Relative)

Verbal Consent
Documented in source notes and use participant/personal legal rep. short information sheet and SWAT video (if relevant).

Written Consent
Full consent form participant/relative and participant/relative information sheet and SWAT video (if relevant). Telemedicine to be used if required. Professional legal rep. full consent form if no one available.

Professional legal representative (Independent Dr)

Written Consent
Received by enrolling investigator. Document in source notes and use Professional Legal Rep. Short Info sheet and Consent form.

Written Consent
Participant/personal legal representative (relative) if available, including telemedicine if required. Full consent form participant/relative and participant/relative information sheet and SWAT video (if relevant).

Enrolment Consent

Follow On Consent

Consent FAQs

How do I complete the consent form for relative giving consent over the phone?

Tick the boxes on the relative full consent form, please write relatives name but leave signature section for relative blank. Person receiving consent prints name, signs and dates and witness should write on the bottom of form that they are witnessing relative giving consent over the phone, sign, date and state their job title. Then if the relatives does come on site they should sign the consent form.

Does written consent need to be obtained if independent doctor was used for enrolment consent?

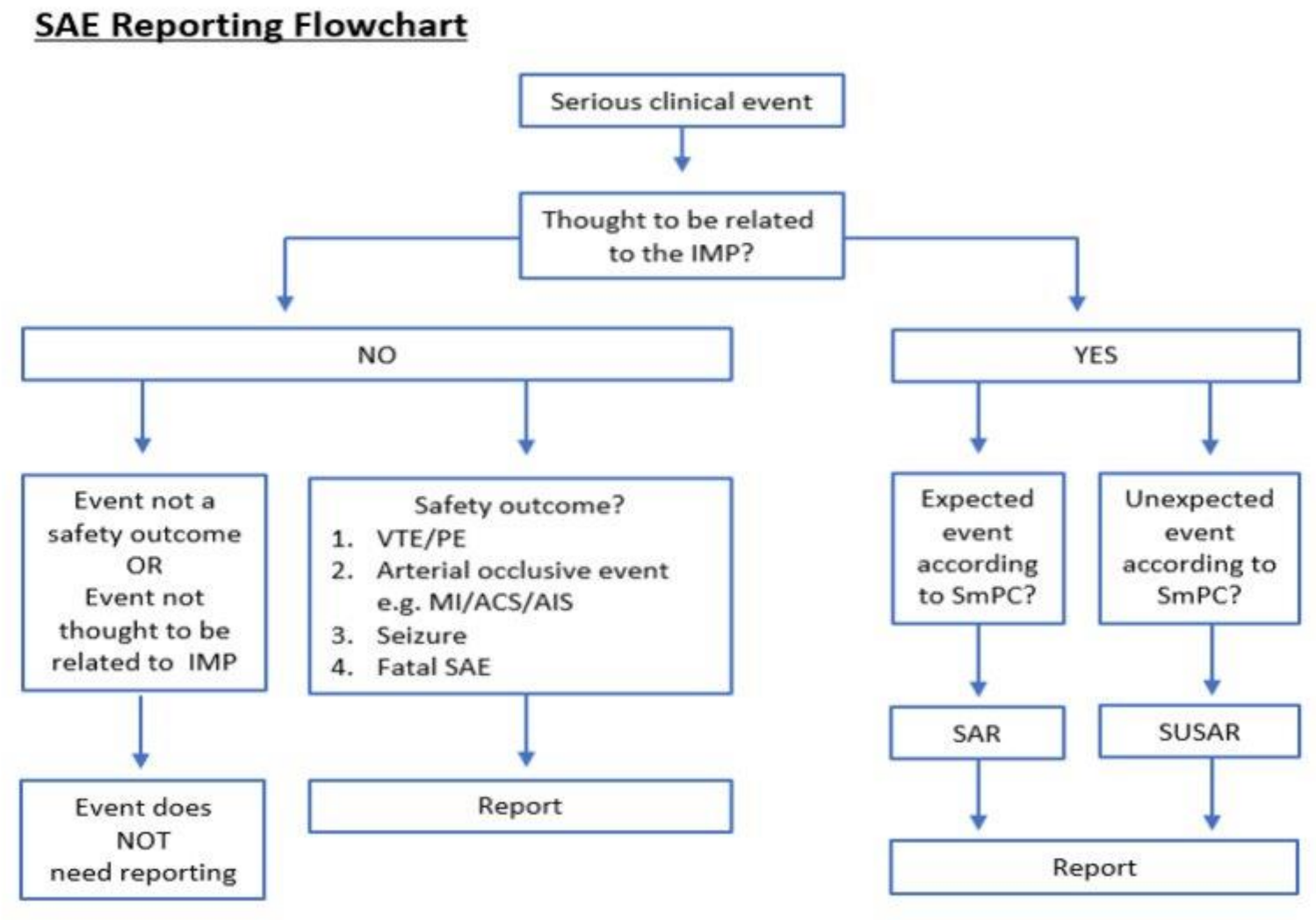
The professional legal representative short information and consent form used by independent doctor giving enrolment consent does give permission for contact details to be collected, the GP to be informed and the participant to be followed up at 6 months and therefore the independent doctor does then not need to complete the professional legal representative full consent form. If a relative becomes available or participant regains capacity, follow on written consent should be obtained.

Consent over the phone

Consent can be obtained over the phone for the person giving consent i.e. relative or person taking consent i.e. investigator. Consent over the phone should always be witnessed and documented in the source notes and on any consent form, stating what they are witnessing, sign, date and put their job title.

Note: witness can be anyone, they do not have to be on the delegation log and do not have to be independent from the trial i.e. ward nurse

Safety events and SAE reporting



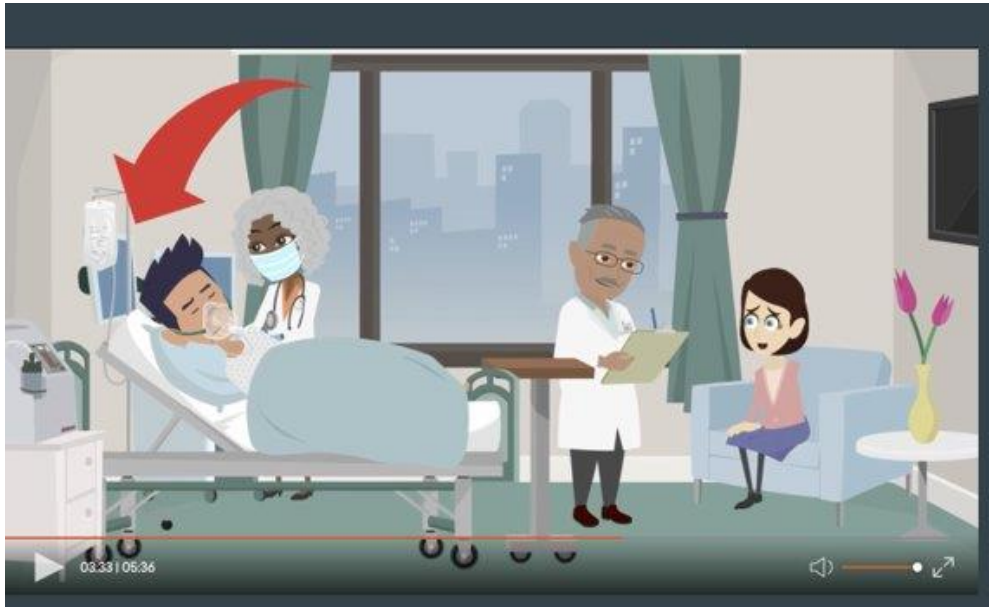
Serious adverse reactions (SAR) or Suspected Unexpected Serious Adverse Reactions (SUSAR):

- 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

If you are unsure if where and event should be reported or not please contact the coordinating centre TICH-3@nottingham.ac.uk

SWAT Summary

- Aim: To reduce inequalities in enrolling participants from minority communities.
- Population: All individuals recruited to the TICH-3 trial in the UK.
- Intervention: Animated participant video
- Control: Standard information sheets



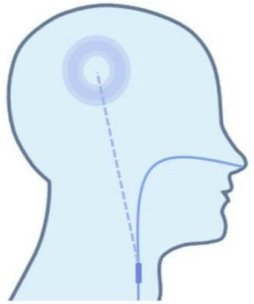
- Sites are informed on the greenlight email whether they have been randomised to animated participant video or standard information sheets
- We will soon be organising a meeting for the open sites that have been randomised to animated video

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
- PhEAST
- ENOS-2

MAPS-2



PhEAST

ENOS–2
Efficacy of Nitric Oxide in Stroke-2

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

- TRIDENT

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

- ENRICH-AF (contract pending)

TRIDENT
Triple therapy prevention of Recurrent Intracerebral Disease EveNts Trial

ENRICH-AF

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.

Upcoming events

- ISC 2023 (8-10 February)
- ESOC 2023 (24-26 May)

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!

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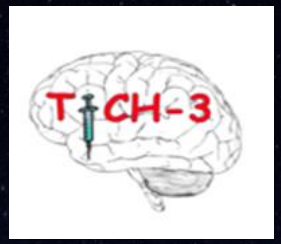

Any questions?

Q & A during session (1)

Q: Is 60ml the cut off for inclusion?

A: HV calculation is an estimate only, some recruits with HV>60 have been enrolled whereas as some patients with HV <60 have not been recruited, it depends on various factors including location of bleed, GCS, NIHSS etc. Should seek Physician advice if unsure.

Q: Can we recruit if someone has a history of seizure?

A: Yes, the exception being active seizures. The decision to enroll lies with the treating clinician.

Q & A during session (2)

Q: How to measure Haematoma volume?

A: One of the commonest and easiest formulas to use is the ABC/2 formula

- A – the largest length of the haematoma
- B – multiplied by B – the maximum width perpendicular to A
- C- multiplied by C – which is the height of the heamatoma – this is worked out by multiplying the number of slices that have the haematoma in by the slice thickness
- Thickness of the slice is usually on the bottom left of the screen – commonly 1mm or 5 mm