University of Nottingham
UK | CHINA | MALAYSIA

ISRCTN97695350

# TRANEXAMIC ACID FOR INTRACEREBRAL HAEMORRHAGE: TICH-3 TRIAL

# INVESTIGATOR MEETING

Brittany Hare and Nikola Sprigg

On behalf TICH-3 Trial Team

25th January 2024

# Agenda

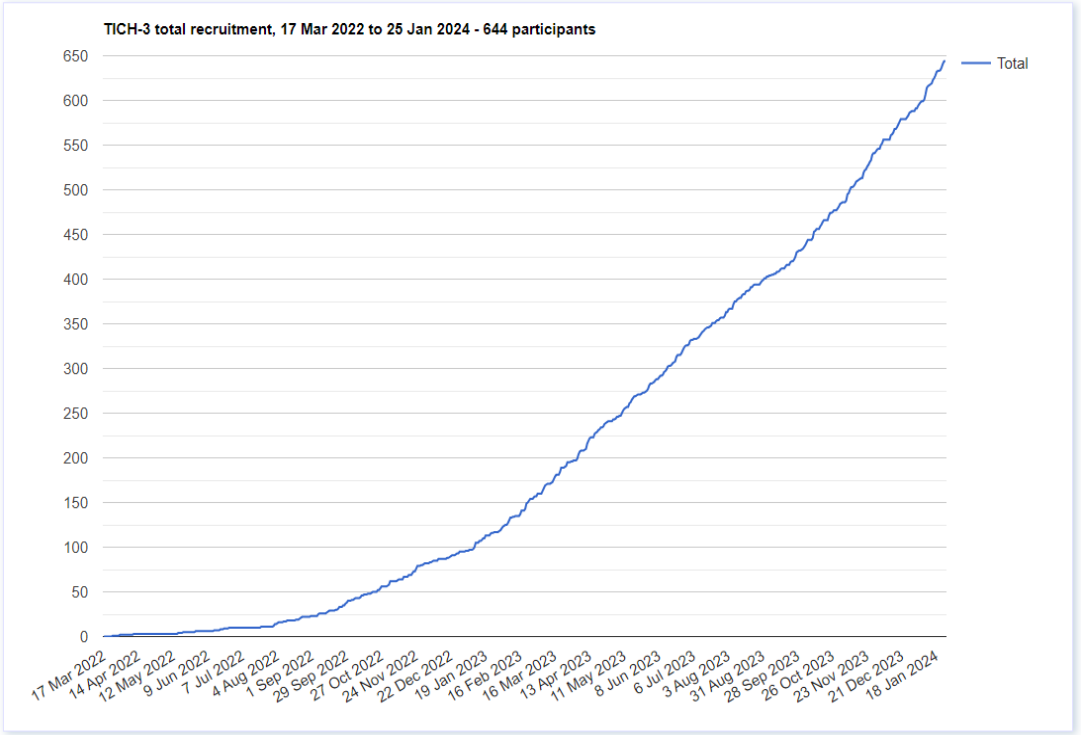
1. Recruitment update
2. Pilot progression review: updated targets
3. Reminding the team of TICH-3
4. Streamlined recruitment process
5. Eligibility checklist
6. Point of randomisation
7. Training slides update
8. Co-enrolment with TICH-3
9. SWAT QR code template
10. Upcoming events
11. What's new in ICH
12. Thank you
13. Questions?

# UK Recruitment Update

| Site Status *(updated 25/01/2024)* | No. |
|---|---|
| Sites open to recruitment | 66 |
| Recruited *(438 participants in total)* | 58 |
| Not recruited | 8 |
| In set up | 4 |
| Initial feasibility assessments | 7 |
| Declined for now (capacity issues) | 7 |
| Withdrawn | 10 |

# International Recruitment Update

| *(updated 25/01/2024)* | Sites open | Recruited |
|---|---|---|
| Malaysia | 13/14 | 143 |
| Finland | 1/1 | 28 |
| Georgia | 3/4 | 23 |
| Denmark | 1/4 | 10 |
| Italy | 1/25 | 3 |
| France | 3/16 | 1 |
| Ireland | 1/6 | 0 |
| Totals | 23/70 | 208 |





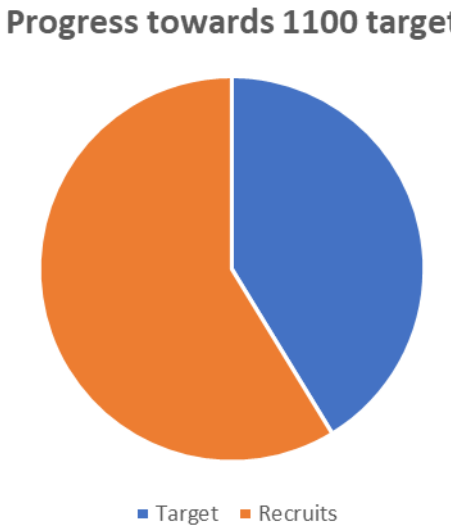
**Combined total recruitment: 646**

*We have reached over 600 participants!*

*Thank you for all your recruitment into the TICH-3 trial, we couldn't do it without you!*

# Pilot progression review: updated targets

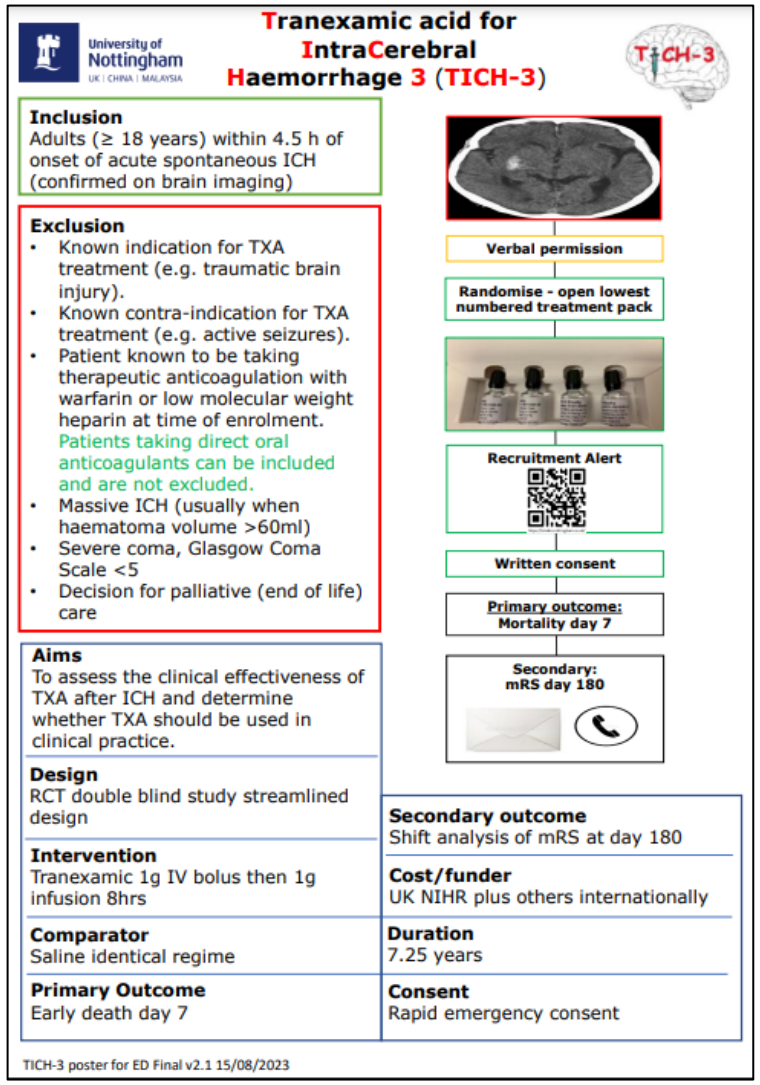
- Data to be reviewed again end of August 2024
- HTA 1,100 ppts 120 (75 UK) sites by 31/08/2024




We are 58.73% towards the target participant recruitment

| Project Month | Month | New Target | Actual No. sites |
|---|---|---|---|
| 29 | September-23 | 55 | 57 |
| 30 | October-23 | N/A | 57 |
| 31 | November 23 | 60 | 60 |
| 32 | December 23 | 62 | 63 |
| 33 | January 24 | 64 | 66 |
| 34 | February 24 | 65 | |
| 35 | March 24 | 66 | |
| 36 | April 24 | 67 | |
| 37 | May 24 | 68 | |
| 38 | June 24 | 70 | |
| 39 | July 24 | 73 | |
| 40 | August 24 | 75 | |

# Reminding the team of TICH-3




## Please regularly remind the local team of TICH-3

- ED poster (please note there was a typo in the footer, stated version 3.0 15/08/2023 when should be v2.1 15/08/2023 which has now been corrected on TICH-3 documents page)
- Please add TICH-3 to your local research meeting agendas as a reminder
- Involve ED doctors to get on the delegation log to take initial enrolment consent
- Nominate deputy PI – please inform us of the named team member
- NIHR Associate PI Scheme Website great for your CV! Register: NIHR Associate PI Scheme Applicant Registration Form

# Streamlined Recruitment Process

- Patient suspected of suffering a stroke
- CT/MRI scan shows bleeding and is within 4.5 hours of symptom discovery
- Contact local Research Coordinating Team or TICH-3 trained Medic if out-of-hours
- **Confirm eligibility** can be completed by any clinician they do not need to be on the TICH-3 delegation log
- **Delegated investigator** obtains initial oral consent, consent process just needs to be documented in the medical record. We also allow remote recruitment over phone/telemedicine. If no relatives, then ask an independent doctor and use brief consent form to document.
- **Lowest numbered TICH-3 treatment pack** is prescribed and administered by appropriate staff (they do not need to be on the delegation log or GCP trained)
- **Alert coordinating centre** that patient has been enrolled into the trial using the randomisation alert on the prescribing and administration guide
- Research team will obtain follow on written consent when next on site

# Streamlined Recruitment Process Q & As

## Does the person taking oral consent need to be on the delegation log?

Yes, they need to be approved on the local electronic delegation log with code J delegated to take enrolment consent. Code J can be applied to research nurses/ACPs if they have had appropriate training/experience, and the local PI and trust are happy for this role to be delegated to them.

Note: Confirming eligibility is defined as a medical decision, so must be undertake by a medically qualified doctor under the clinical trials regulations.

## Can telephone consent be given by relatives?

- Oral consent can be taken remotely if the enrolling investigator is not on site either on the phone or via telemedicine.
- Oral consent can be given remotely by a relative, if the patient does not have capacity. It is good practice to witness the phone call e.g. a ward nurse could ask the relative to repeat to them that they are giving consent for their relative to be enrolled.

Method of assessing eligibility and obtaining consent must be documented in the patients' medical notes.

## GCP certificates for local team.

We do not mandate has to be refreshed every 2 years however do need to have a GCP certificate dated after 2017 as ICH-GCP guidelines changed in 2017.

# Eligibility checklist

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## TICH-3 ELIGIBILITY CHECKLIST

**(Final Version 1.0: 23/11/2023)**

**Title of Study:** TICH-3 **IRAS Project ID:** 297457 **CTA ref:** 03057/0074/001-0001

**Name of Participant:**

I confirm that I have been given a copy of the eligibility checklist (version 1.0 dated 23/11/2023) and I have assessed the participant as suitable using the below approved checklist.

| | **Inclusion Criteria (protocol Final v2.0 07/10/2022)**<br>**(all criteria must be yes for participant to be enrolled into TICH-3)** | **Yes** | **No** |
|---|---|---|---|
| 1 | Adult (18 years and over). | | |
| 2 | Clinical diagnosis of acute spontaneous ICH (confirmed on brain imaging). | | |
| 3 | Within 4.5 hours of symptom onset (When onset of symptoms are unknown patient must be within 4.5 hours of symptom discovery and have no other exclusion criteria). | | |

| | **Exclusion Criteria (protocol Final v2.0 07/10/2022)**<br>**(Patients cannot be enrolled if 'YES' is ticked for any exclusion criteria)** | **Yes** | **No** |
|---|---|---|---|
| 1 | Patient with a known indication for TXA treatment *(e.g. traumatic brain injury)*. | | |
| 2 | Patient with contraindication for TXA treatment *(e.g. seizures or known active venous thromboembolism)*. | | |
| 3 | 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. | | |
| 4 | Massive ICH for which haemostatic treatment seems futile (This would ordinarily be when haematoma volume is estimated as larger than 60ml).<br>*Any recognised method for estimating haematoma volume is accepted, automated software or ABC/2 calculation. If measurement is not possible in the time available a simple single measurement of the largest haematoma diameter provides an accurate estimate, if the length measurement is greater than 5cm the haematoma volume is likely to be greater than 60mls and the patient should be excluded.* | | |
| 5 | Severe coma (Glasgow Coma Scale <5). | | |
| 6 | Decision already taken for palliative (end of life) care with withdrawal of active treatment. | | |

***Eligibility must be confirmed by a Medic***

*(The medic does **not** have to be on the TICH-3 delegation log or GCP trained)*

_____ _____

***(Name of Doctor confirming eligibility)*** ***(Date)***

Please document eligibility confirmation in the participant's medical notes (this form can be stored in their medical notes).

Eligibility checklist TICH-3 - Final v1.0 23.11.2023

Eligibility can be confirmed by a medic that is not on the TICH-3 delegation log. An appropriate research team member on the delegation will then take oral enrolment consent, this can be completed remotely.

There is an eligibility checklist on the TICH-3 documents page that can be used to document participants eligibility confirmation whether this was completed remotely or on site.

This is an optional document that is not required to be completed but is available if you wish to use this.

All processes off eligibility assessment and consent must be documented in the participants medical notes.

# Point of randomisation

- Point of randomisation of is selecting and OPENING the next lowest numbered treatment pack *(we are making this clearer in the protocol in the upcoming protocol amendment)*
- Some participants may become ineligible AFTER they have been randomised but BEFORE treatment administration
  - They remain as a recruit in the trial due to intention to treat analysis
  - Explain to the participant/relative that even though they haven't had treatment we they are still part of the trial and continue to gain follow on written consent as normal
  - Please continue with eCRF data collection – you will report on the eCRF that treatment was not administered
  - Report any safety events as applicable – you will state 'before' treatment and in comments can say IMP was not administered
  - Every time speak to participant, they are reconsented e.g. day 180 f/w asked if happy to complete over phone and returning questionnaire is implied consent

# Participants repatriated prior to day 7 Q & As

## Site to site transfer

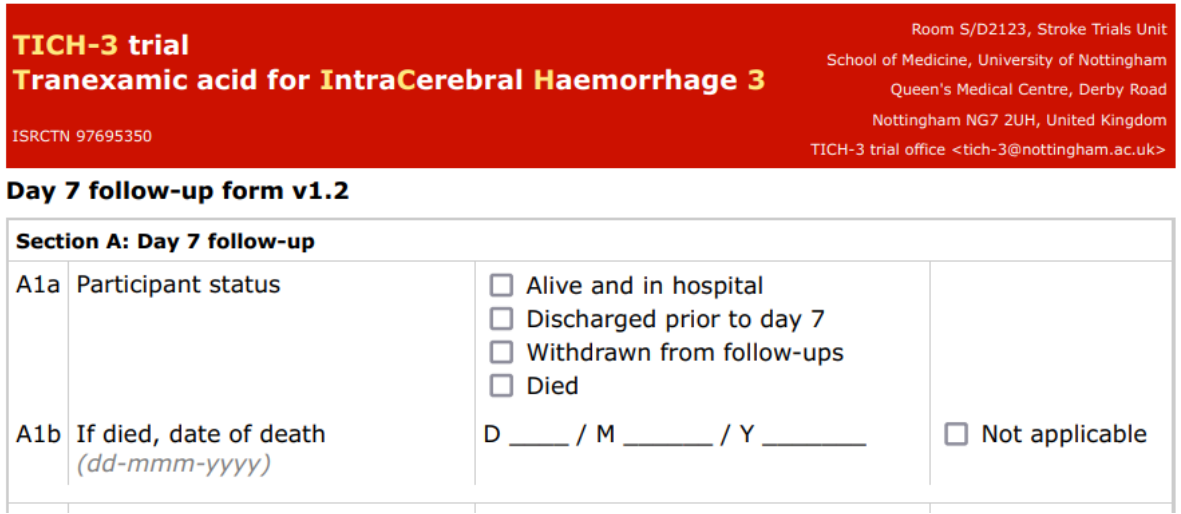
If participant is transferred to another TICH-3 centre prior to day 7 please complete site to site transfer, this appears as a button on the death/discharge eCRF. Both sites can then complete the day 7 eCRF and discharge/death or submit a data correction to the eCRFs, there will only ever be one death/discharge form per participant.

## Repatriated to another site within the same trust but not a TICH-3 site

If the rehab centre is not an active TICH-3 site but is within the same trust do not complete discharge form until the participant is discharged from the trust and do not complete day 7 early. Not technically classed as discharge as within same trust. C&C approvals would be in place for the trust. We ask that the staff at the recruiting site could contact the sister site in the same trust to ask for the data and record it themselves on the eCRFs.

## Repatriated to non TICH-3 site and outside trust

If the rehab centre is not an active TICH-3 site and is outsides of the trust, then death/discharge would be completed on the day of repatriation and complete day 7 eCRF early. We just ask that if possible if you could try and find out alive and well status on day 7 by contacting the hospital and if they have died enter this data on the day 7 eCRF by completing a data correction.



**TICH-3 trial**
**Tranexamic acid for IntraCerebral Haemorrhage 3**
ISRCTN 97695350

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>

**Day 7 follow-up form v1.2**

| **Section A: Day 7 follow-up** | | | |
|---|---|---|---|
| A1a | Participant status | ☐ Alive and in hospital<br>☐ Discharged prior to day 7<br>☐ Withdrawn from follow-ups<br>☐ Died | |
| A1b | If died, date of death *(dd-mmm-yyyy)* | D ____ / M _____ / Y _____ | ☐ Not applicable |

# Training slides updated

We have recently updated the training slides highlighting out of hours recruitment process. You can find the training slides on the TICH-3 documents page as a refresher of the trial processes https://stroke.nottingham.ac.uk/sif/docs/?sid=TICH-3

There are different versions of the training slides

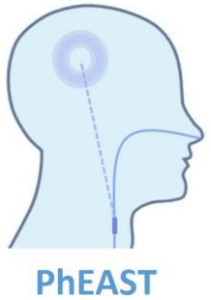
1. Investigator training which gives a detailed description of the whole trial process, intended for the PI and research nurses/coordinators. There is also a video of this training.
2. Enrolling investigator training, this streamlined training is intended for team members who will only be taking enrolment consent i.e. consultants, ED doctors, registrars
3. Pharmacy training, this streamlined training is intended for members of pharmacy team
4. NEW Ward Training, this training is to inform the ward staff of the trial so that they can assist with out of hours recruitment. Ward staff do not need to go onto the delegation log.

If you are a new team member, 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.

# 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-enrol 48 hours post recruitment to TICH-3)


**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)
- MARCH



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.

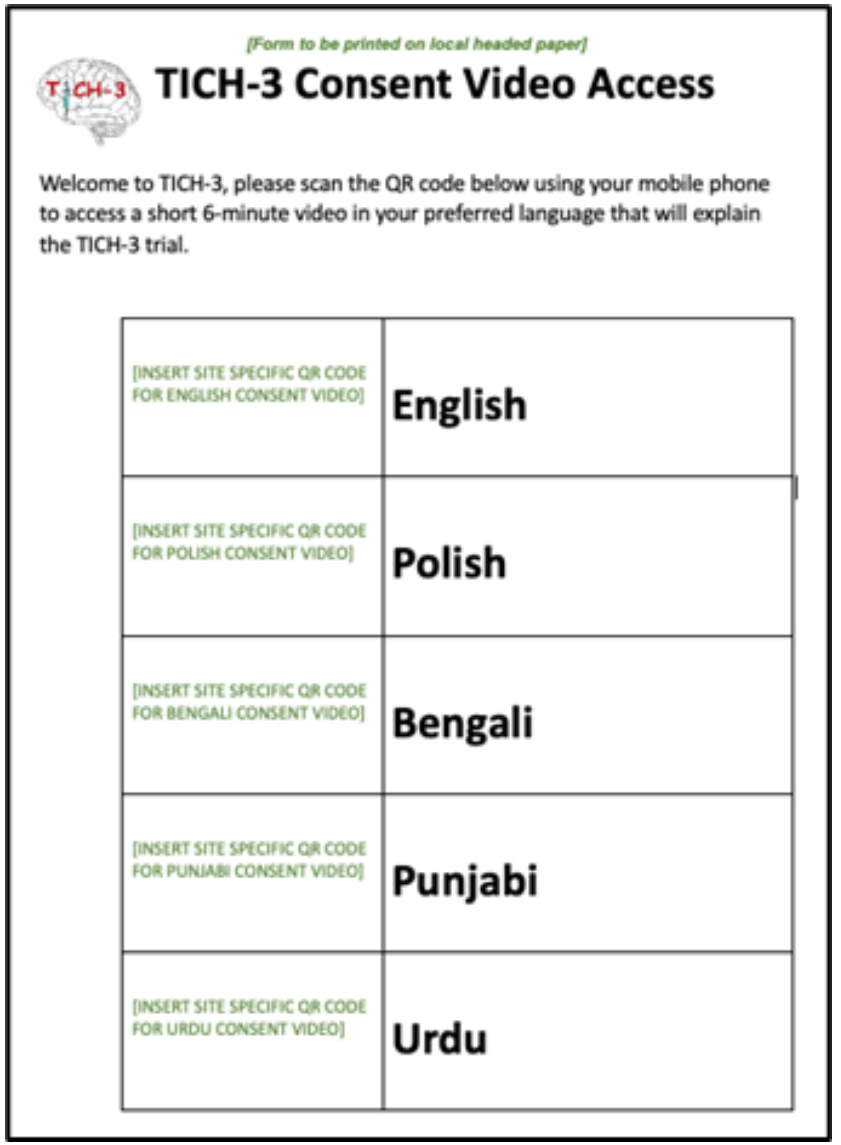
There is a co-enrolment log on the TICH-3 documents page https://stroke.nottingham.ac.uk/sif/docs/?sid=TICH-3

# SWAT QR codes template

## ONLY SITES RANDOMISED INTO ENHANCED CONSENT – ANIMATED VIDEO

We have created a document that can be used to give to participants/relatives to access the animated consent videos from their own devices by scanning the QR code.

This template is available on the TICH-3 documents page.



*[Form to be printed on local headed paper]*

**TICH-3 Consent Video Access**

Welcome to TICH-3, please scan the QR code below using your mobile phone to access a short 6-minute video in your preferred language that will explain the TICH-3 trial.

| | |
|---|---|
| [INSERT SITE SPECIFIC QR CODE FOR ENGLISH CONSENT VIDEO] | **English** |
| [INSERT SITE SPECIFIC QR CODE FOR POLISH CONSENT VIDEO] | **Polish** |
| [INSERT SITE SPECIFIC QR CODE FOR BENGALI CONSENT VIDEO] | **Bengali** |
| [INSERT SITE SPECIFIC QR CODE FOR PUNJABI CONSENT VIDEO] | **Punjabi** |
| [INSERT SITE SPECIFIC QR CODE FOR URDU CONSENT VIDEO] | **Urdu** |

# Upcoming events

- International Stroke Conference (ISC), Arizona USA, February 2024
- European Stoke Organisation Conference (ESOC) 15-17 May 2024, Switzerland
- International Clinical Trials Methodology Conference (ICTMC), Edinburgh, September 2024
- World Stroke Congress (WSC) – 26 Oct 2024, Abu Dabi
- UK Stroke Forum (UKSF) December 2024, Liverpool

# What's new in ICH ?

## Clinical Guidelines

- BP lowering, imaging, stroke unit care

## Andexanet alfa

- Results of ANNEX A-I study for reversal of DOAC FXa ICH

## Bundles of care

- Results of INTERACT-3 study
- ABC ICH care bundle

## Neurosurgery

- Result of ENRICH study

## National Audit Data

- Plans to increase ICH metrics

## Stroke Service Development

- Artificial Intelligence for detection of ICH – may help rapid access for treatments and trials


# 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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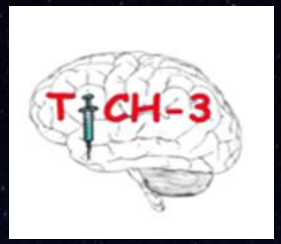


# Any questions?