NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

DEC 2024 | VOLUME 3 | ISSUE 12

FASTEST

FVIIa for Acute hemorrhagic Stroke Administered at Earliest Time

Issue Contents:

Message from Dr. Singh

Dear FASTEST family,

Greetings from San Francisco!

We successfully enrolled our first FASTEST patient! The key to achieving this milestone was seamless collaboration, flexibility, and quick decision-making, as we administered the study drug within 57 minutes of the patient's arrival at the ED. This impressive achievement has energized our research group at UCSF, and we are excited to share a few tips to help others achieve similar successes:

1. Instead of relying on an in-person interpreter, save the phone number of the interpreter in your contacts. That way, you'll have quick access whenever you need it!
2. Ensure the ICU nursing and pharmacy are trained and prepared for a rapid transfer from the ED. A dedicated ED pharmacist who went the extra mile to deliver the drug to the ICU nurse was crucial to our success.
3. It's essential to designate a timekeeper to keep everything on track!

It's been a pleasure being part of FASTEST. Happy Holidays, everyone!

Looking forward to a fantastic 2025.

Vineeta Singh, MD
Professor, Neurology
UCSF Weill Institute for Neurosciences

Please join us for the *FASTEST* Monthly Webinar

Wednesday December 18th, 2:00-3:00 pm EST

- Prof Jan Purrucker from University Hospital, Germany will be discussing a case.
- Dr. Laura C. Gioia from University of Montreal Hospital, Montreal, QC, Canada will be discussing a case.
- Dr. Broderick will be discussing an update.
- NDMC will review F206 Study Drug Administration Update.

Join Zoom Meeting

https://ucincinnati.zoom.us/j/99236910048

Meeting ID: 992 3691 0048

Recoding of the Webinar can be accessed here

https://www.nihstrokenet.org/trials/fastest/webinar
Password **Faster**

Prior presentations and slides are available at, https://www.nihstrokenet.org/fastest/webinars

STUDY MILESTONES

Total Sites Released to Enroll: **91** (**52** USA, **39** OUS: **6** Germany, **14** Japan, **6** Spain, **9** Canadian, **4** UK)

Total MSUs Released to Enroll: **12** (**10** US and **2** OUS)

Total Randomization = **611**

- US Randomizations: **170**
- International randomizations: **438**
  - Japan = **270**
  - Canada = **80**
  - Spain =**43**
  - Germany = **31**
  - UK = **17**

Randomization last month = **29**

Total Screen Failures = **2085**

Subjects Randomized by MSU = **17**

Subjects Terminated Early = **4**

eConsent Used = **27**

Remote Consent Used = **23**

CALENDAR OF EVENTS

Upcoming *FASTEST* Monthly Webinars: **Wednesday, December 18th @ 2:00-3:00 pm EST**

FASTEST study team office hours: **Monday, January 13th, @ 1:00-2:00 pm.**

IMPORTANT NOTES

Continuing Review: Please make sure that you have responded to any queries requested by the cIRB as part to the continuing review asap. Expiration date is fast approaching 01/8/2024. Please reach out to Emily Stinson if you have questions.

Protocol v8: Please make sure that you are updating your regulatory documents in WebDCU associated with the updated protocol v8, PSP and PI training attestations.

Updated 1572: Please make sure to update your 1572 with study team changes. Box 6 of the 1572 should have investigators listed that perform study procedures. Please reach out to Emily Stinson or Kim Lever if you have questions

Subject enrollment in another trial

Kindly note that subject enrollment in a non-interventional trial following enrollment in FASTEST should not present any issues. However, we kindly request that you notify us in advance if your team plans to enroll any subject in an additional trial.

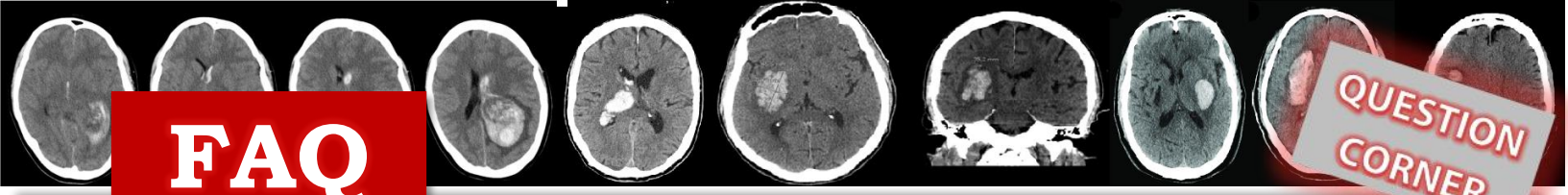
MOP version 3.1

The new version of the study MOP, version 3.1 is now available in the toolbox in WebDCU.

Documentation Update: Mobile Stroke Unit (MSU) Cases

To enhance documentation, we request that all cases involving subjects transported to the Emergency Department via a Mobile Stroke Unit (MSU) be recorded, regardless of the treatment location. As part of this effort, a new field, **Q23: "Mobile Stroke Unit arrived on scene,"** has been added to the CRF.

For further details, please refer to the **F206 Study Drug Administration Update** under the "Helpful Reminders and Tips" section below.



Q: Could you please confirm if it is permissible to continue co-enrolling patients in a trial if they qualify for both? We are referring to a non-interventional trial that involves MRI imaging to assess whether early brain structural deterioration occurs within the first hours of acute ICH.
A: It is OK to enroll in both since there's no intervention but just additional imaging. As long as a 24-hour imaging for CT is completed in Fastest and the clinical follow ups are completed, there should be no problem.

Q: We have a question regarding our recent FASTEST enrollment. The issue is that the 24-hour study CT was obtained outside of the visit window. However, the patient was co-enrolled in another trial (non-interventional), which necessitated follow-up MRIs at 24 hrs. Can you please advise what is the correct procedure to report this event in WebDCU?
A: As per the study protocol (Version 8, Page 19), MRI is acceptable if performed routinely at the site, as highlighted below. Please ensure to add a note or description when uploading the MRI imaging for 24 hours. Additionally, the protocol requires the site to upload all additional scheduled and unscheduled images (CT and MRI) if performed. Kindly upload all additional images for this subject, as "unscheduled images."

Q: if transfer patients arrive in our study window, could we consider them for enrollment? We have read in the MOP about direct admits being considered for enrollment, so I wanted to check.
A: Yes, transfer subjects can be enrolled if eligible and within time window.

Q: Currently only the PI can formally sign off on eligibility. The fellows are trained and will help. Since the fellows are trained and will assist, is it necessary for them to complete the imaging training to be authorized to sign off on eligibility as well?
A: Yes, trained sub-I's can determine eligibility as long as they are delegated with that task on the DoA. However, they must also complete the imaging training to be authorized to sign off on eligibility.

Q: In the Advarra Chinese Short Form, the LAR failed to print her name, but correctly filled out the other fields (e.g., signature, date, relationship).
A: This constitutes a minor protocol deviation and a non-compliance issue. As such, it must be reported to the cIRB. Kindly upload the response or acknowledgment letter from the cIRB once available.

Q: The study consent form we used is not the most up to date one. The ICD signed was version 2023, instead of 2024, which removed the Medical Center address due to that site closure. Other than this administrative change, the ICD language is identical.
A: Using an old version of consent form is a major protocol violation. All non-compliance issues with ICF and major protocol violations need to be reported to the cIRB within two weeks (preferably as soon as the site becomes aware of the incident). Please refer to the FASTEST MOP v3.1, pages 52–57, for detailed guidelines.

Consented using the wrong protocol version	Major PV	Yes	Yes	According to CIRB/CRB/Ethics boards procedures and country regulations
Consent dated or patients name by someone other than the person signing it	Major Compliance Issue	Yes	Yes	According to CIRB/CRB/Ethics boards procedures and country regulations
Consent Related Issues (e.g., wrong date, HIPAA not signed, witness page signed by error, impartial witness not available, etc.)	Non-compliance	Yes	Yes	According to CIRB/CRB/Ethics boards procedures and country regulations

Please send in your questions and we will address them accordingly and share with others in the next Newsletter.

SHOUT OUTS!!

Congratulations to US sites submitted to the cIRB for review and approval under prospective consent.

1. **Staten Island University Hospital - North Campus, Staten Island, NY**

Great job on sites recently released to begin enrolling.

1. **Health Sciences Centre, Winnipeg, MB, Canada**

The Top Enrolling Site

Congratulations to **National Cerebral and Cardiovascular Center, Osaka, Japan** for being the highest enrolling site in the study.

Subjects enrolled = 69!!

Congratulations to Enrolling Sites last Month!

National Cerebral and Cardiovascular Center, Osaka, Japan	3 Subject
Kobe City Medical Center General Hospital, Kobe, Japan	3 Subject
Iwate Prefectural Central Hospital, Morioka, Japan	1 Subject
Niigata City General Hospital, Niigata, Japan	1 Subject
NHO Osaka National Hospital, Osaka, Japan	1 Subject
Toranomon Hospital, Tokyo, Japan	1 Subject
Gifu University Hospital, Gifu, Japan	2 Subject
Vancouver General Hospital, Vancouver, BC, Canada	2 Subject
University of Alberta Hospital, Edmonton, AB, Canada	1 Subject
University of Montreal Hospital, Montreal, QC, Canada	1 Subject
Bellvitge University Hospital, Barcelona, B, Spain	1 Subject
Girona University Hospital, Girona, GI, Spain	1 Subject
Santa Creu and Sant Pau Hospital, Barcelona, B, Spain	1 Subject
St. Joseph's Hospital and Medical Center, Phoenix, AZ	1 Subject
The Queen's Medical Center, Honolulu, HI	2 Subject
M Health Fairview Southdale Hospital, Edina, MN	1 Subject
Jackson Memorial Hospital, Miami, FL	1 Subject
University of Cincinnati Medical Center, Cincinnati, OH	1 Subject
San Francisco General Hospital, San Francisco, CA	1 Subject
Mills Peninsula Medical Center, Burlingame, CA	1 Subject
Tubingen University Hospital, Tubingen, Germany	1 Subject
Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom	1 Subject

SCIENCE CORNER

ARTICLE OF THE MONTH

Tranexamic Acid Within 4.5 Hours of Intracerebral Hemorrhage With the CTA Spot Sign

Nawaf Yassi, Vignan Yogendrakumar, Leonid Churilov, Atte Meretoja, Teddy Wu, Bruce C V Campbell, Daniel Strbian, Jiann-Shing Jeng, Lisa J Woodhouse, Christian Ovesen, Zhe Kang Law, Hong-Qiu Gu, Ximing Nie, Jingyi Liu, Henry H Ma, Henry Zhao, Philip M Bath, Liping Liu, Nikola Sprigg, Geoffrey Alan Donnan, Stephen M Davis Giacomo Urbinati, Debora Pezzini, Maurizio Paciaroni, Enrico Fainardi, Ilaria Casetta, Alessandro Padovani, Andrea Zini

Neurology. 2024 Dec 24;103(12):e210104. DOI: 10.1212/WNL.0000000000210104

Background

The antifibrinolytic agent tranexamic acid has been tested in intracerebral hemorrhage trials with overall neutral results. Ongoing contrast extravasation on CT angiography (spot sign) can identify individuals with ongoing bleeding who may benefit from anti-fibrinolytic therapy. We aimed to investigate the effect of tranexamic acid on hematoma growth in patients with spot signs treated within 4.5 hours of onset.

Methods

We conducted a systematic review and individual patient meta-analysis, which we report according to the Preferred Reporting Items for Systematic Review and Meta-analyses of Individual Participant Data guidelines. PubMed and Embase were searched from inception to May 29, 2023, using the terms ((stroke) AND (randomised OR randomized) AND (tranexamic acid) AND (haemorrhage OR hemorrhage)). We included randomized trials comparing tranexamic acid with placebo in participants with primary intracerebral hemorrhage who had a spot sign and who had follow-up imaging within the required timeframe. Individual patient data were provided by each study and were integrated by the coordinating center. Data were pooled using a random-effects model. The primary endpoint was hematoma growth within 24 hours, defined as ≥33% relative or ≥6 mL absolute hematoma expansion compared with baseline, analyzed using mixed-effects-modified Poisson regression with robust standard errors, adjusted for baseline hematoma volume. Safety outcomes were mortality and major thromboembolic events within 90 days.

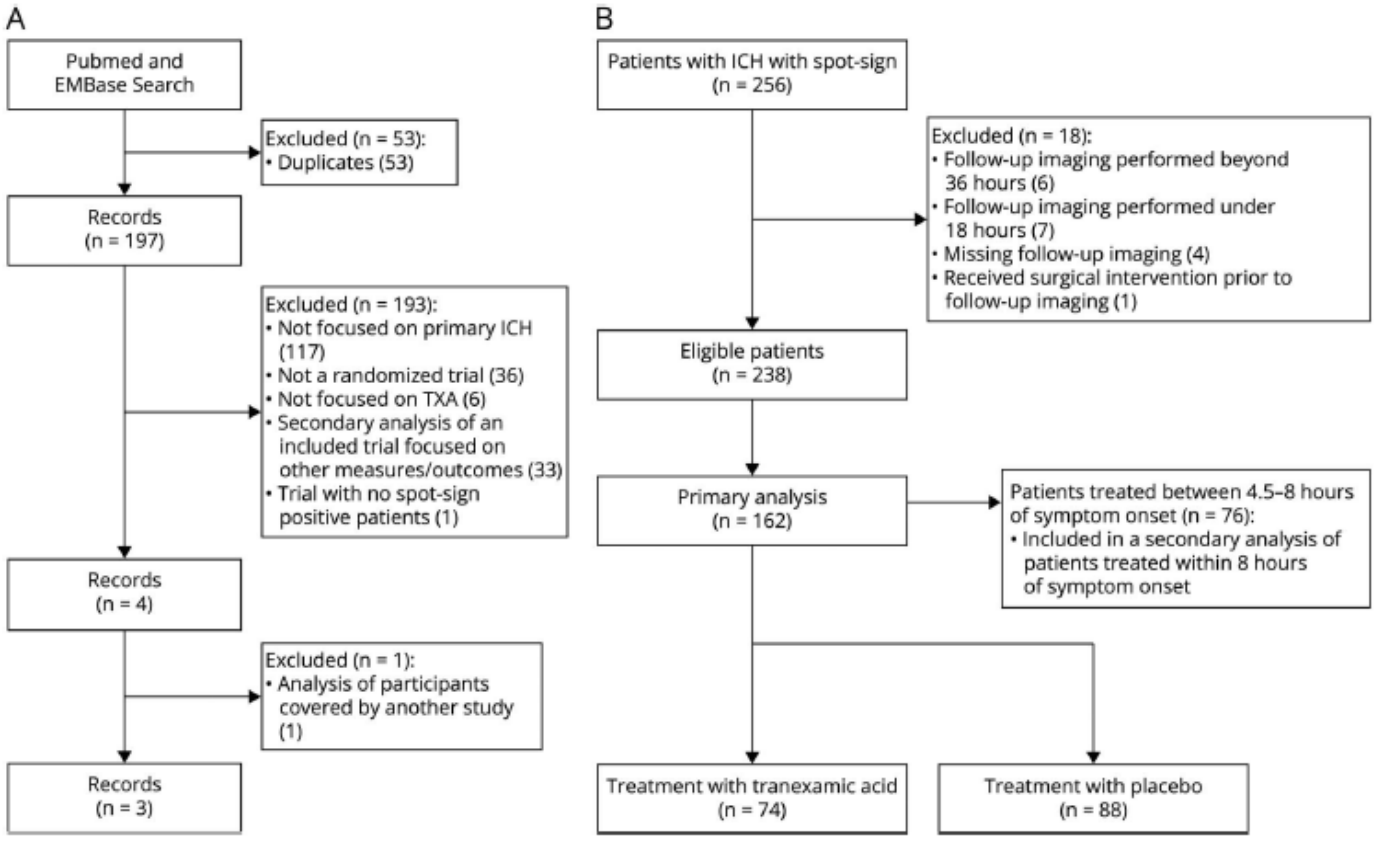
Results

Of 197 studies identified, 3 were eligible, contributing 162 participants for the primary analysis (60 female and 102 male). Hematoma growth occurred in 36 of 74 (49%) participants treated with tranexamic acid, compared with 48 of 88 (55%) participants treated with placebo (adjusted risk ratio 0.86, 95% CI 0.84-0.89, $p < 0.001$). Adjusted median absolute hematoma growth was 1.60 mL (95% CI 0.77-2.43) lower with tranexamic acid vs placebo. No differences in functional outcome or safety were observed.

Discussion

Tranexamic acid modestly reduced hematoma growth in patients with CT angiography spot signs treated within 4.5 hours of onset. Given the trials in the meta-analysis were individually neutral, these results require further validation before clinical application.

Figure 1 CONSORT Diagram (A) and Patient Selection Flow Diagram (B)

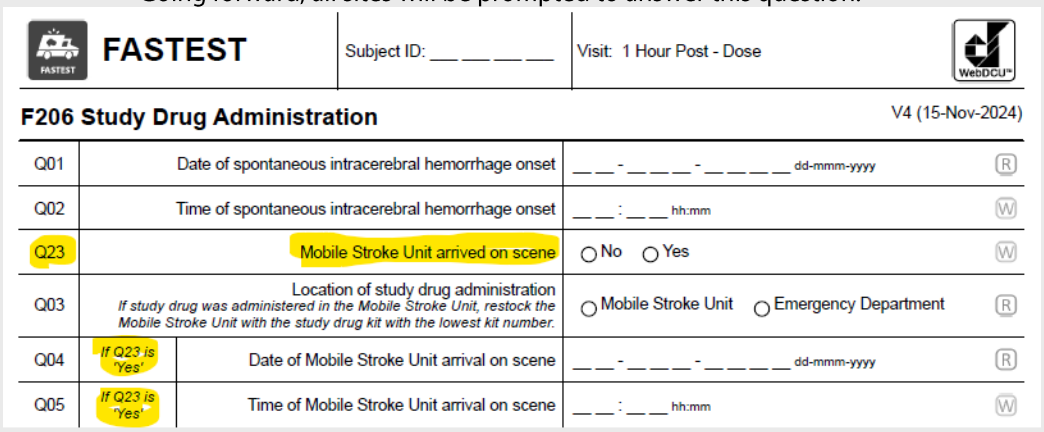


ICH = intracerebral hemorrhage; TXA = tranexamic acid.

HELPFUL REMINDERS & TIPS

For Project Managers, Study Coordinators & Study Teams

- **Site report cards:** the site report cards will be going out again in January.
- **F206 Study Drug Administration Database Update:** We would like to document cases of subjects transported to the Emergency Department in a Mobile Stroke Unit, regardless of treatment location, so (Q23) 'Mobile Stroke Unit arrived on scene' has been added to the CRF.
  - **i.** A few things to note:
    1. If your site has an MSU, (Q23) will be appearing as an open rule violation for all previously submitted F206 forms.
       - If this is the case, please update (Q23) for each subject.
    - Sites who do not have an MSU will not be required to answer this on previously submitted F206 forms.
    - Going forward, all sites will be prompted to answer this question.

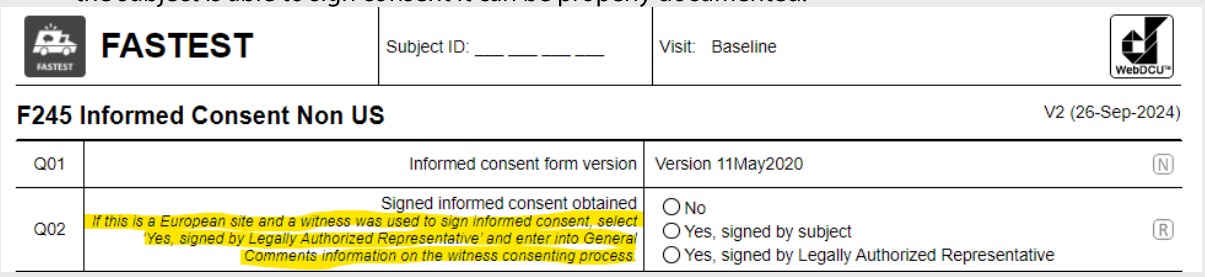


FASTEST | Subject ID: ___ ___ ___ ___ | Visit: 1 Hour Post - Dose | WebDCU

F206 Study Drug Administration V4 (15-Nov-2024)

Q01		Date of spontaneous intracerebral hemorrhage onset	__ __ - __ __ __ - __ __ __ __ dd-mmm-yyyy (R)
Q02		Time of spontaneous intracerebral hemorrhage onset	__ __ : __ __ hh:mm (W)
Q23		Mobile Stroke Unit arrived on scene	○ No ○ Yes (W)
Q03		Location of study drug administration *If study drug was administered in the Mobile Stroke Unit, restock the Mobile Stroke Unit with the study drug kit with the lowest kit number.*	○ Mobile Stroke Unit ○ Emergency Department (R)
Q04	*If Q23 is 'Yes'*	Date of Mobile Stroke Unit arrival on scene	__ __ - __ __ __ - __ __ __ __ dd-mmm-yyyy (R)
Q05	*If Q23 is 'Yes'*	Time of Mobile Stroke Unit arrival on scene	__ __ : __ __ hh:mm (W)

- ***F245 Updates – Impacts European Sites***
  - For European sites only:
    - If a witness is used for informed consent, but the witness is not considered an LAR, please select:
      - (Q02) = Yes, signed by Legally Authorized Representative
      - Please enter into General Comments on F245 details regarding the witnessed consent process.
      - This will cause F246 Informed Consent – Regained Capacity to populate in the Subject CRF Binder so that once the subject is able to-sign consent it can be properly documented.



FASTEST | Subject ID: ___ ___ ___ ___ | Visit: Baseline | WebDCU

F245 Informed Consent Non US V2 (26-Sep-2024)

Q01	Informed consent form version	Version 11May2020 (N)
Q02	Signed informed consent obtained *If this is a European site and a witness was used to sign informed consent, select 'Yes, signed by Legally Authorized Representative' and enter into General Comments information on the witness consenting process.*	○ No ○ Yes, signed by subject ○ Yes, signed by Legally Authorized Representative (R)

STUDY CONTACTS & USEFUL INFO

For any study related queries or help please reach out to ***FASTEST*** Project managers

International Sites: **Syed Quadri** (quadrisd@ucmail.uc.edu)

United States Sites: **Emily Stinson** (stinsoey@ucmail.uc.edu)

FASTEST Clinical Hotline: 1-855-429-7050

For more information regarding the ***FASTEST*** study please visit : https://www.nihstrokenet.org/fastest/home

For prior ***FASTEST*** Presentations and Webinars slides and recordings visit: https://www.nihstrokenet.org/fastest/webinars

For more information regarding the StrokeNet Trials please visit: https://www.nihstrokenet.org/