NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

NOV 2024 | VOLUME 3 | ISSUE 11

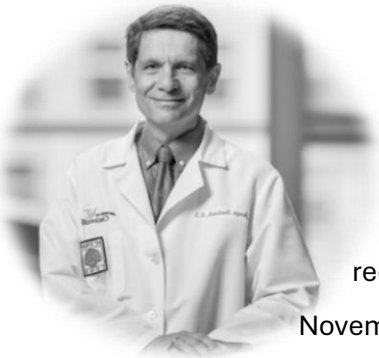
FASTEST

FVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Broderick



As the Game of Thrones series of books says, "Winter is coming," and traditionally that is the season when recruitment increases in ICH trials. November has gotten off to a great start so let's push hard to make this winter an excellent time for recruitment. We also have an important interim analysis on December 6th that will determine next steps for FASTEST. We will update all once we are given direction by the DSMB. But as of November 17th, recruiting 582 ICH participants worldwide within 2 hours of onset makes us by far the largest ultra-early treatment trial of ICH ever done. I am extremely proud of our investigator team throughout the world for the progress we have made thus far. Keep it up!

Joseph Broderick, MD
Director NIH StrokeNet
FASTEST Principal Investigator

Please join us for the *FASTEST* Monthly Webinar

Wednesday November 20th, 2:00-3:00 pm EST

- Dr. Ezzeddine from Wake Forest Baptist Medical Center, Winston-Salem, NC will be discussing a case.
- Dr. Broderick will be discussing IVH calculations
- Review reconsent and e-consent process.
- NDMC will review F212/F244 and F245 updates.

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**

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 = **582**

- US Randomizations: **164**
- International randomizations: **418**
  - Japan = **258**
  - Canada = **77**
  - Spain =**38**
  - Germany = **29**
  - UK = **16**

Randomization last month = **22**

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, November 20th @ 2:00-3:00 pm EST**

FASTEST study team office hours: **Monday, December 9th, @ 1:00-2:00 pm.**

IMPORTANT NOTES

Emerald temp logger replacement:

Recalibrated Emerald loggers were sent to the sites a few weeks ago for their MSUs and EDs. However, it appears that some sites have not yet replaced their existing Emerald logger with the newly calibrated ones. The logger should have been replaced the week it was sent.

All sites are required to record and send a 48-hour temperature log using the newly calibrated Emerald logger provided. Once we review and confirm that the new logger is functioning correctly, you may proceed with replacing the old one.

If you are experiencing any issues with syncing or setting up the recently sent Emerald loggers, please don't hesitate to reach out to us for assistance.

After switching on to the new logger kindly send us the old Emerald loggers at your site using the FedEx Account # **1043-7706-8** for returns. The old Emerald temperature monitor should be sent to the following address:

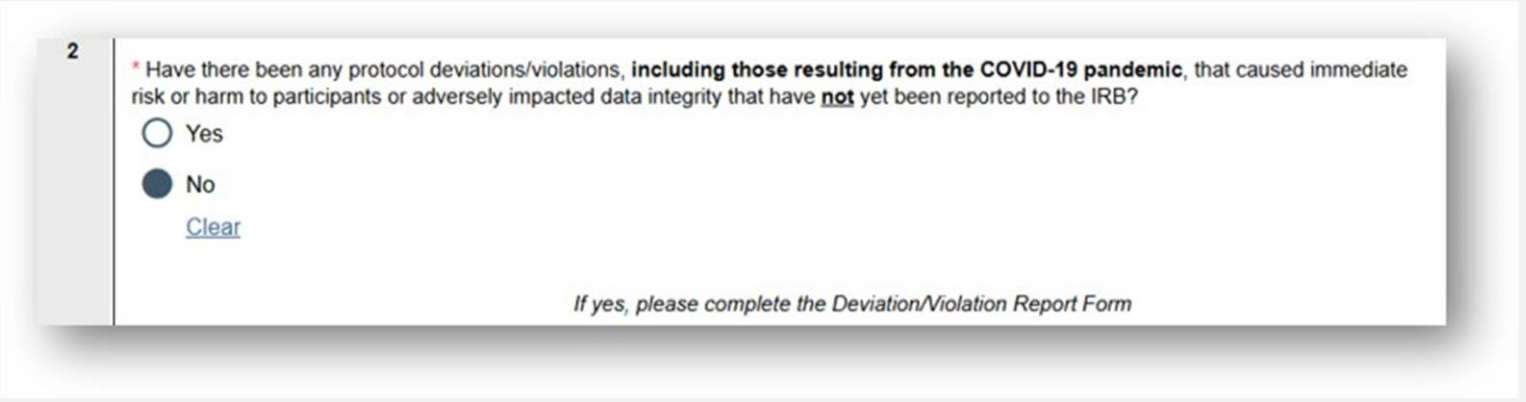
Syed Quadri
The NIH StrokeNet National Coordinating Center
University of Cincinnati Academic Health Center
260 Stetson St., Suite 5221 ML 0525
Cincinnati, Ohio 45219

Tracking info:
Kindly remember to provide following email or phone for tracking purpose.
quadrisd@ucamai.uc.edu
Phone: 617 999 2541

FAQ

QUESTION CORNER

Q: We had a subject who could not be followed up at 90 days (not able to complete mRS and EQ5D). We are currently working on submitting the continuing review. The CR form's question asks: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* Have there been any protocol deviations/violations, **including those resulting from the COVID-19 pandemic**, that caused immediate risk or harm to participants or adversely impacted data integrity that have **not** yet been reported to the IRB?

○ Yes

● No

Clear

If yes, please complete the Deviation/Violation Report Form

A: This message concerns major violations that have not been reported to the CIRB. For this major protocol violation, the NCC usually leaves a comment in the issues table:

"Failure to perform Day 90 Follow-up (not able to complete mRS and EQ5D) constitutes a major protocol deviation. Please ensure that this major protocol violation is reported in the annual Continuous Review (CR) process, as per the instructions outlined in the study MOP."

While this major violation (not collecting mRS and EQ5D) does not impact patient safety, it does affect data integrity and therefore must be reported in the CR. Please select "Yes" for this question. For further guidance on reporting, kindly refer to the table provided on **pages 55–56** of the MOP V3.1.

mRS (with RFA) or EQ-5D not collected at Day 30 or 90 visit	Major violation	Report aggregately	Report aggregately with the annual CR	According to CIRB/CRB/Ethics boards procedures and country regulations
mRS (with RFA) or EQ-5D not collected at Day 180 visit*	Major violation	Report aggregately	Report aggregately with the annual CR	According to CIRB/CRB/Ethics boards procedures and country regulations
Day 30, 90 or 180 mRS (with RFA) or				According to CIRB/CRB/Ethics

Q: I was hoping someone could please clarify the below notification regarding continuing review. Is this continuing review solely for our site approval for the study? Our site has not opened to enrollment yet as we are still pending Institutional Approval, and so I do not believe that we have any updates/ site-specific study activity to report. Or is this for the overall continuing review for this study?

A: All sites that are cIRB approved will have to go through the continuing review process. There is an application that you will fill out. You will have very little to report since you have not opened for enrollment yet so it should only take you a few minutes to fill out and submit.

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 = 66!!

Congratulations to Enrolling Sites last Month!

National Cerebral and Cardiovascular Center, Osaka, Japan	3 Subject
Iwate Prefectural Central Hospital, Morioka, Japan	1 Subject
Kyushu Medical Center, Fukuoka, Japan	1 Subject
Toranomon Hospital, Tokyo, Japan	1 Subject
Gifu University Hospital, Gifu, Japan	1 Subject
Ottawa Hospital, Ottawa, ON, 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
Vall d'Hebron Hospital, Barcelona, B, Spain	1 Subject
Memorial Hermann Memorial City Medical Center, Houston, TX	4 Subject
The Queen's Medical Center, Honolulu, HI	2 Subject
Wake Forest Baptist Medical Center, Winston-Salem, NC	1 Subject
Providence St. Vincent Medical Center, Portland, OR	1 Subject
Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA	1 Subject

SCIENCE CORNER

ARTICLE OF THE MONTH

Predictors of severe intracerebral hemorrhage expansion

Andrea Morotti 1 2, Qi Li 3, Jawed Nawabi 4, Giorgio Busto 5, Federico Mazzacane 6, Anna Cavallini 6, Ashkan Shoamanesh 7, Mauro Morassi 8, Frieder Schlunk 9, Laura Piccolo 10, Giacomo Urbinati 11, Debora Pezzini 1, Maurizio Paciaroni 12, Enrico Fainardi 5, Ilaria Casetta 13, Alessandro Padovani 1 2, Andrea Zini 10

Eur Stroke J. 2024 Sep;9(3):623-629. doi: 10.1177/23969873241247436

Background

Severe hematoma expansion (sHE) has the strongest impact on intracerebral hemorrhage (ICH) outcome. We investigated the predictors of sHE.

Methods

Retrospective analysis of ICH patients admitted at nine sites in Italy, Germany, China, and Canada. The following imaging features were analyzed: non-contrast CT (NCCT) hypodensities, heterogeneous density, blend sign, irregular shape, and CT angiography (CTA) spot sign. The outcome of interest was sHE, defined as volume increase >66% and/or >12.5 from baseline to follow-up NCCT. Predictors of sHE were explored with logistic regression.

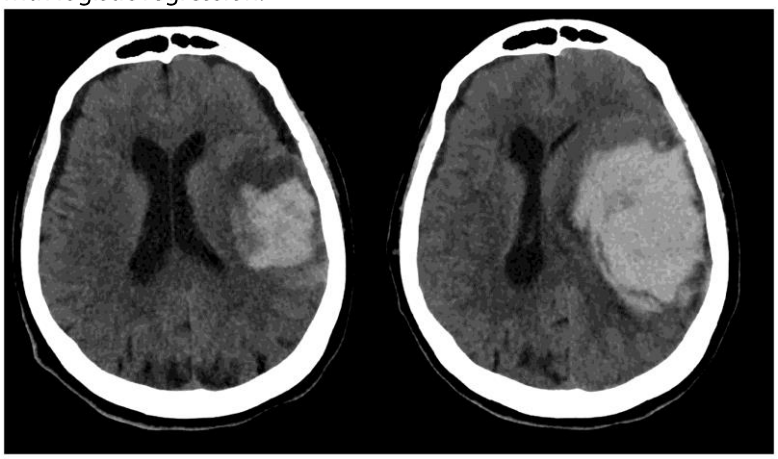


Figure 1. Severe hematoma expansion. Baseline volume 38 mL (a), follow-up volume 119 mL (b).

Results

A total of 1472 patients were included (median age 73, 56.6% males) of whom 223 (15.2%) had sHE. Age (odds ratio (OR) per year, 95% confidence interval (CI), 1.02 (1.01-1.04)), Anticoagulant treatment (OR 3.00, 95% CI 2.09-4.31), Glasgow Coma Scale (OR 0.93, 95% CI 0.89-0.98), time from onset/last known well to imaging, (OR per h 0.96, 95% CI 0.93-0.99), and baseline ICH volume, (OR per mL 1.02, 95% CI 1.02-1.03) were independently associated with sHE. Ultra-early hematoma growth (baseline volume/baseline imaging time) was also a predictor of sHE (OR per mL/h 1.01, 95% CI 1.00-1.02). All NCCT and CTA imaging markers were also predictors of sHE. Amongst imaging features NCCT hypodensities had the highest sensitivity (0.79) whereas the CTA spot sign had the highest positive predictive value (0.51).

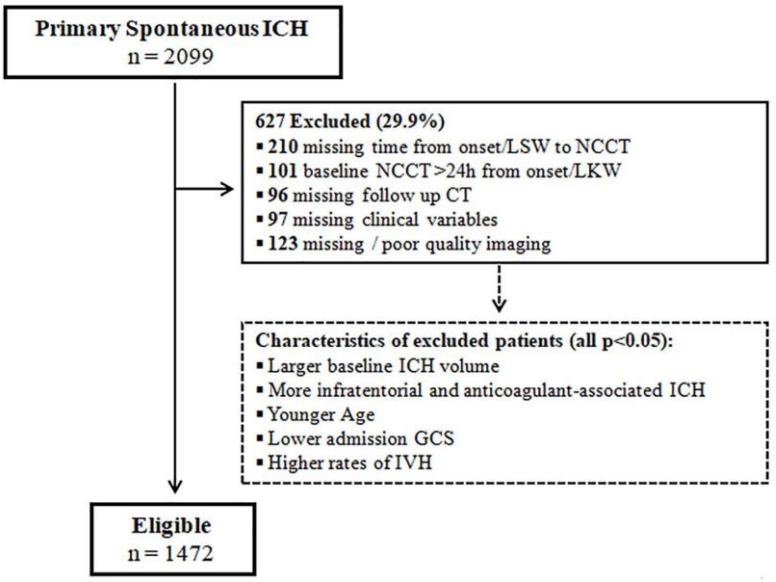
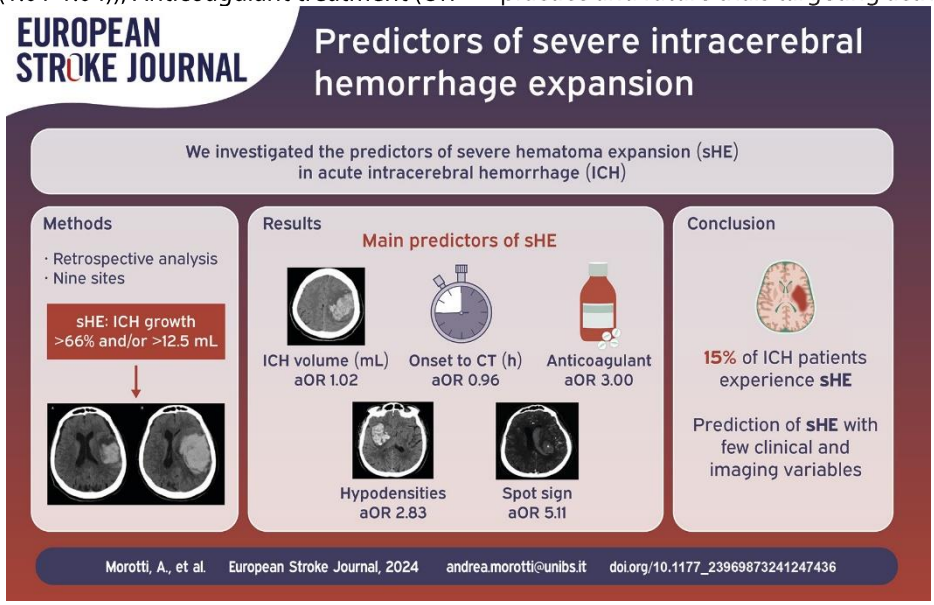


Figure 2. Selection flowchart.

Conclusion

sHE is common in the natural history of ICH and can be predicted with few clinical and imaging variables. These findings might inform clinical practice and future trials targeting active bleeding in ICH.



HELPFUL REMINDERS & TIPS

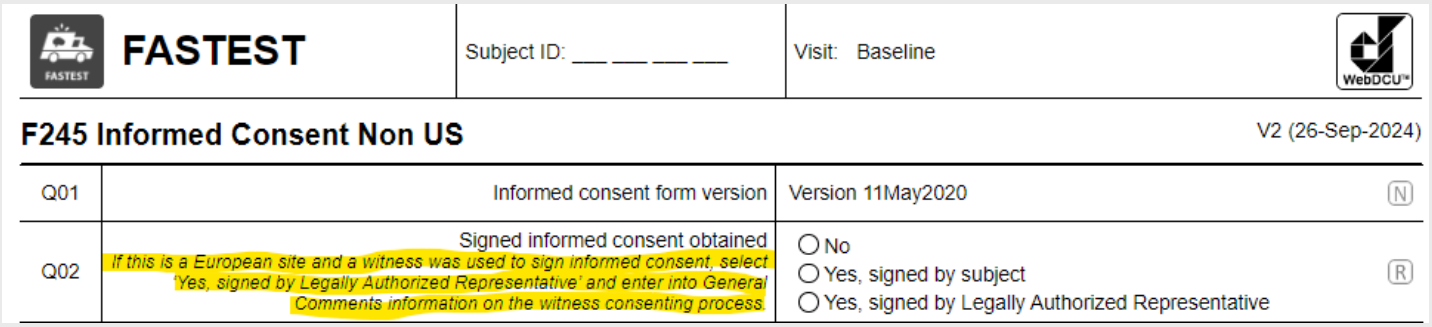
For Project Managers, Study Coordinators & Study Teams

- **For Upcoming DSMB meeting:** Thank you for entering all overdue data in preparation for the upcoming DSMB meeting in a timely manner!

- **Note from Pharmacy:** High- enrolling sites have been selected to receive additional kits with their upcoming shipment to increase their site's par level.

- **F212/F244 and F245 updates:**
  - If a subject is enrolled via EFIC and consent has not yet been obtained by the subject or LAR, please complete F245 indicating (Q02) = 'No'.
  - Once consent has been obtained, you can then update F245 to document this.

- ***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/