NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

SEPT 2024 | VOLUME 3 | ISSUE 9

FASTEST

FVIIa for Acute hemorrhagic Stroke Administered at Earliest Time

Issue Contents:

Message from Dr. Broderick

Dear FASTEST colleagues,

We are getting close to a very a important step in the FASTEST Trial! In October, we will be completing the 180-day follow-ups for the first 430 participants in the *FASTEST* study. It is critical that we complete these follow-ups on time. These data will be used for the key interim analysis that the Data Safety Monitoring Committee will review and discuss with us at the beginning of December. This interim analysis will inform the decision to continue the trial as planned, add additional patients, continue trial but limit enrolment to patients 70 years or less, or stop recruitment for futility. We appreciate all of your great efforts but please make every effort to complete scheduled 180- and 90-day follow-ups to ensure the best possible data for this key decision point. In the meantime, help this fall be our best recruitment months thus far!

Joseph Broderick, MD
Fastest Principal Investigator
Director NIH StrokeNet
Director UC Gardner
Neuroscience Institute

Please join us for the *FASTEST* Monthly Webinar

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

- Dr Alejandro Bustamante from HU Germans Trias i Pujol, Badalona, Spain will be presenting a case.
- Dr. Broderick will be discussing use of VIZ and Rapid for *FASTEST*.
- NDMC will review site quality report cards.

Join Zoom Meeting

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

Meeting ID: 992 3691 0048

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 = **531**

- US Randomizations: **144**
- International randomizations: **384**
  - Japan = **241**
  - Canada = **66**
  - Spain =**36**
  - Germany = **29**
  - UK = **15**

Randomization last month = **20**

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, A September 18th @ 2:00-3:00 pm EST**

FASTEST study team office hours: **Monday, October 14th, @ 1:00-2:00 pm.**

IMPORTANT NOTES

Imaging Uploads:

Please ensure that baseline and 24-hour imaging are uploaded as soon as they become available. In particular, we urge all sites to upload images promptly in cases of Serious Adverse Events (SAEs) so that they are available for review by the Independent Medical Safety Monitor (IMSM) along with the SAE report.

Enrollment and Screening Update:

We are reaching out to sites that have not enrolled or screened a subject for 3-9 months after being released to enroll. Please remember to document all screen failures in the screen failure log, which are reimbursed at $40 per appropriate exclusion (arrival of spontaneous ICH patient within 3 hours of onset). Our latest webinar (August) on the FASTEST Stroke Trial (nihstrokenet.org, Password: faster) discussed recruitment strategies and featured valuable insights from some of our top enrollers. Our goal and expectation is for all participating sites to enroll at least two subjects per year. Please let us know how we can support you in achieving this target and staying on track with enrollment.

Upcoming Data Freeze:

There will be a data freeze at the end of October in preparation for an upcoming DSMB meeting. Please ensure that all overdue data is entered promptly. Do not hesitate to reach out to NDMC data managers if you have any questions or need further assistance.

Site Performance Report Cards:

We will soon be issuing site-specific report cards to evaluate the performance of sites participating in the FASTEST trial. Please note that StrokeNet will also be issuing trial-specific report cards to gauge the performance of its participating sites moving forward. NDMC will provide a presentation about the report cards in the upcoming FASTEST webinar on Wednesday, September 18th. We encourage all sites to join this session.

New Sites... Welcome Aboard!

Health Sciences Centre, Winnipeg, MB, Canada

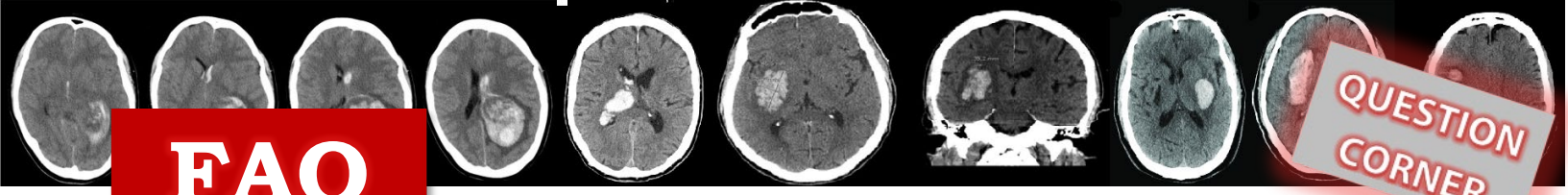
Site PI:
Nishita SINGH MD, DM, MSc

Jackson Memorial Hospital, Miami, FL

Site PI:
Erika MARULANDA-LONDONO MD

FASTEST MEDIA COVERAGE

We are excited to share that the story on the FASTEST trial, featuring Dr. Broderick's interview, which is gaining traction and being covered by local news stations across the country. Recently, MSN also picked up the story from a station in Louisiana. To check out the report and watch Dr. Broderick's interview: https://www.msn.com/en-gb/health/other/health-headlines-new-drug-could-help-in-crucial-time-during-stroke/ar-AA1q7h9c?ocid=BingNewsVerp#



FAQ

Q: We need some clarity regarding the protocol for documenting SAEs after day 4. Should all serious adverse events that are both unrelated to study intervention and are not known complications of ICH be documented on WebDCU. Also, are there any additional data collection resources or trainings outside of the Data Collection Guidelines or the Manual of Procedures?

A: All serious adverse events (SAEs), regardless of their relation to the study intervention or whether they are known complications of ICH, should be documented in WebDCU for IMSM review. Please refer to the study Manual of Procedures (MOP), **pages 48-54**, for a detailed description of the reporting requirements.

Additionally, you can review past webinars on the StrokeNet website (link, Password: faster), which provide valuable insights and information. Please also check the FAQ section in previous FASTEST newsletters, a great resource for familiarizing yourself with study-related issues. This section includes a variety of queries related to different aspects of the trial, submitted by sites as they encountered challenges while actively enrolling subjects. You will find all these FAQs very helpful.

We also encourage all PSC you to join our monthly office hours with any questions or concerns. These sessions offer a great opportunity to have your queries addressed and to learn from others about how they handle similar challenges at their sites.

Q: Can a patient on novel oral anticoagulants (NOAC), such as apixaban be enrolled in the trial?

A: Anticoagulants (NOAC), such as apixaban, dabigatran, rivaroxaban and edoxaban within the past seven days are an exclusion criterion.

Q: If site fail to utilize the lowest kit number during the randomization, will that cause any queries when the research staff completes the enrolment form in WebDCU?

A: No, you will not get queries in WebDCU for not using the lowest kit number.

Q: Can we use estimated weight to calculate the IP dose?

A: Actual weight is preferred, but estimated weight **is acceptable.** Estimated body weight is appropriate to use for dosage determination, especially since we can't always wait for a stroke patient to be weighed. However, to ensure that there is no overdose and to calculate the dose check **we do need the sites to report the subject's actual weight** in the WebDCU. This can be done at any time during their hospitalization.

Q: Can the baseline troponin be a "point of care" troponin? This is what is ordered and resulted for most of our stroke alert patients.

A: Yes, the baseline troponin is usually the "point of care" troponin done for stroke patients and is reported in F105-Laboratory Tests.

Q: How do we enter SAE which happened between 24h and day 30 when we still in between? And I am not sure if the patient is going to survive to day 30?

A: Please enter the SAE according to the date closest to the relevant time point. For example, an SAE occurring on day 6 (while still in the hospital) it should be reported within the 24-hour timeline. If the SAE occurs on day 20, it should be reported with the 30-day follow-up. Typically, sites follow up with patients after discharge at 30, 90, and 180 days. If it is discovered during these follow-ups that the patient visited the ER or a doctor for a serious issue, it should be reported at the corresponding follow-up.

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 that have completed EFIC and will be submitted to the CIRB for review/approval for emergency consent.

1. **Medical University of South Carolina University Hospital, Charleston, SC Parneet**
2. **Prisma Health Greenville Memorial Hospital, Greenville SC**
3. **San Francisco General Hospital, San Francisco, CA**

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 = 60!!

Congratulations to Enrolling Sites last Month!

Kyushu Medical Center, Fukuoka, Japan	1 Subject
National Cerebral and Cardiovascular Center, Osaka, Japan	2 Subject
Japanese Red Cross Kyoto Daini Hospital, Kyoto, Japan	1 Subject
Jichi Medical University Hospital, Shimotsuke, Japan	1 Subject
NHO Osaka National Hospital, Osaka, Japan	1 Subject
Kagoshima City Hospital, Kagoshima, Japan	1 Subject
Kobe City Medical Center General Hospital, Kobe, Japan	1 Subject
Gifu University Hospital, Gifu, Japan	1 Subject
Vancouver General Hospital, Vancouver, BC, Canada	2 Subject
Clinic Frankfurt Hoechst, Frankfurt, Germany	1 Subject
Memorial Hermann Memorial City Medical Center, Houston, TX	2 Subject
Providence St. Vincent Medical Center, Portland, OR	1 Subject
Kaiser Permanente Fontana Medical Center, Fontana, CA	1 Subject
Kaiser Permanente South Bay Medical Center, Harbor City, CA	1 Subject
Grady Memorial Hospital, Atlanta, GA	1 Subject
Temple University Hospital, Philadelphia, PA	1 Subject
Bellvitge University Hospital, Barcelona, B, Spain Barcelona, B, Spain	1 Subject
Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom	1 Subject

Etiology of Primary Cerebellar Intracerebral Hemorrhage Based on Topographic Localization

Diego Incontri, MD; Sarah Marchina, PhD; Alexander Andreev, MD; Mitchell Wilson, MD; Jia-Yi Wang, MD; David Lin, BA; Elizabeth C. Heistand, BA; Filipa Carvalho, BA; Magdy Selim, MD, PhD; Vasileios-Arsenios Lioutas, MD

Stroke. 2023 Dec;54(12):3074-3080. DOI: https://doi.org/10.1161/STROKEAHA.123.044271

Background

Cerebellar intracerebral hemorrhage (cICH) is often attributed to hypertension or cerebral amyloid angiopathy (CAA). However, deciphering the exact etiology can be challenging. A recent study reported a topographical etiologic relationship with superficial cICH secondary to CAA. We aimed to reexamine this relationship between topography and etiology in a separate cohort of patients and using the most recent Boston criteria version 2.0.

Methods

We performed a retrospective analysis of consecutive patients with primary cICH admitted to a tertiary academic center between 2000 and 2022. cICH location on brain computed tomography/magnetic resonance imaging scan(s) was divided into strictly superficial (cortex, surrounding white matter, vermis) versus deep (cerebellar nuclei, deep white matter, peduncular region) or mixed (both regions). Magnetic resonance imaging was rated for markers of cerebral small vessel disease. We assigned possible/probable versus absent CAA using Boston criteria 2.0.

Results

We included 197 patients; 106 (53.8%) were females, median age was 74 (63-82) years. Fifty-six (28%) patients had superficial cICH and 141 (72%) deep/mixed cICH. Magnetic resonance imaging was available for 112 (57%) patients (30 [26.8%] with superficial and 82 [73.2%] with deep/mixed cICH). Patients with superficial cICH were more likely to have possible/probable CAA (48.3% versus 8.6%; odds ratio [OR], 11.43 [95% CI, 3.26-40.05]; P<0.001), strictly lobar cerebral microbleeds (51.7% versus 6.2%; OR, 14.18 [95% CI, 3.98-50.50]; P<0.001), and cortical superficial siderosis (13.8% versus 1.2%; OR, 7.70 [95% CI, 0.73-80.49]; P=0.08). Patients with deep/mixed cICH were more likely to have deep/mixed cerebral microbleeds (59.2% versus 3.4%; OR, 41.39 [95% CI, 5.01-341.68]; P=0.001), lacunes (54.9% versus 17.2%; OR, 6.14 [95% CI, 1.89-19.91]; P=0.002), severe basal ganglia enlarged perivascular spaces (36.6% versus 7.1%; OR, 7.63 [95% CI, 1.58-36.73]; P=0.01), hypertension (84.4% versus 62.5%; OR, 3.43 [95% CI, 1.61 to -7.30]; P=0.001), and higher admission systolic blood pressure (172 [146-200] versus 146 [124-158] mm Hg, P<0.001).

Conclusion

Our results suggest that superficial cICH is strongly associated with CAA whereas deep/mixed cICH is strongly associated with hypertensive arteriopathy.

Table 1. Differences in Baseline Characteristics Between Patients With Deep/Mixed Cerebellar ICH and Superficial Cerebellar ICH

Variable	Deep/mixed cerebellar ICH (n=141)	Superficial cerebellar ICH (n=56)	*P* value
Age, y, median (IQR)	75 (64–82)	74 (62–83)	0.71
Females, n (%)	77 (54.6)	29 (51.8)	0.72
Comorbidities on admission			
Active smoking, n (%)	14 (10.4)*	7 (12.7)†	0.63
Active alcohol use, n (%)	17 (12.6)*	10 (18.2)†	0.31
Atrial fibrillation, n (%)	43 (30.5)	15 (26.8)	0.60
Hypertension, n (%)	119 (84.4)	35 (62.5)	0.001
DM type 2, n (%)	29 (20.6)	15 (26.8)	0.34
Hyperlipidemia, n (%)	58 (41.1)	23 (41.1)	0.99
CAD, n (%)	19 (13.5)	17 (30.4)	0.006
Prior ICH, n (%)	5 (3.5)	3 (5.4)	0.56
Prior ischemic stroke, n (%)	31 (22)	5 (8.9)	0.03
Cognitive impairment, n (%)	15 (10.6)	9 (16.1)	0.29
Coagulopathy (INR>1.4 or platelets<100 000), n (%)	33 (23.4)	20 (35.7)	0.07
Medications on admission			
Anticoagulation, n (%)	46 (32.9)†	22 (40)†	0.34
Antiplatelet, n (%)	48 (34.8)‡	21 (38.2)†	0.65
Statin, n (%)	58 (42)‡	22 (40)†	0.79
Clinical characteristics on admission			
SBP, median (IQR)	172 mm Hg (146–200)§	146 mm Hg (124–158)*	<0.001
DBP, median (IQR)	85.5 mm Hg (74–98)‖	78 mm Hg (67–92)§	0.02
MAP, median (IQR)	113.3 mm Hg (99.3–130.7)‖	97 mm Hg (86–114)§	<0.001
NIHSS, median (IQR)	4 (2–16.5)¶	2 (1–11)*	0.06
ICH score, median (IQR)	2 (1–3)	2 (1–3)	0.08
Presence of IVH, n (%)	56 (39.7)	10 (17.9)	0.003
Glucose, median (IQR)	152 mg/dL (127–179)#	144 mg/dL (117–166)#	0.12

Table 2. Differences in MRI Markers of cSVD Between Patients With Deep/Mixed Cerebellar ICH and Superficial Cerebellar ICH

Variable	Deep/mixed cerebellar ICH (n=82)	Superficial cerebellar ICH (n=30)	Unadjusted analysis		Multivariable adjusted analysis*	
			OR (95% CI)	*P* value	OR (95% CI)	*P* value
Possible or probable CAA, n (%)†	7 (8.6)‡	14 (48.3)‡	9.86 (3.40–28.59)	<0.001	11.43 (3.26–40.05)	<0.001
Lobar CMBs, n (%)	5 (6.2)‡	15 (51.7)‡	16.29 (5.09–52.03)	<0.001	14.18 (3.98–50.50)	<0.001
Deep/mixed CMBs, n (%)	48 (59.2)‡	1 (3.4)‡	40.72 (5.27–314.25)	<0.001	41.39 (5.01–341.68)	0.001
cSS, n (%)	1 (1.2)‡	4 (13.8)‡	12.8 (1.36–119.85)	0.02	7.70 (0.73–80.49)	0.08
Presence of lacunes, n (%)	45 (54.9)	5 (17.2)‡	5.83 (2.02–16.80)	0.001	6.14 (1.89–19.91)	0.002
Severe EPVS in BG, n (%)	26 (36.6)¶	2 (7.1)§	8.71 (1.93–39.29)	0.005	7.63 (1.58–36.73)	0.01
Severe EPVS in CSO, n (%)	19 (26.8)¶	11 (39.3)§	1.77 (0.70–4.45)	0.22	1.79 (0.63–4.97)	0.26
PV WMH Fazekas 2–3, n (%)	65 (80.2)‡	20 (66.7)	2.03 (0.79–5.17)	0.13	1.77 (0.59–5.39)	0.31
Deep WMH Fazekas 2–3, n (%)	45 (55.6)‡	13 (43.33)	1.63 (0.70–3.80)	0.25	1.50 (0.57–3.98)	0.40
Multispot WMH pattern, n (%)	10 (12.4)‡	9 (30)	3.04 (1.09–8.46)	0.03	2.19 (0.71–6.71)	0.17

HELPFUL REMINDERS & TIPS

For Project Managers, Study Coordinators & Study Teams

- **Data Collection Guidelines:**
  Data Collection Guidelines V5 can be found in the Toolbox in WebDCU.
  Fastest MOP V3 has been added to the Toolbox in WebDCU.

- **Adverse Events reporting reminders:**
  - Non-serious AEs should be reported from the time of study drug infusion through Day 4.
  - Serious AEs and AEs of special interest should be reported from the time of study drug infusion through Day 90.
  - Any fatality should be reported as an AE through Day 180. If death occurs, the AE name should be the event leading to death.
  - All SAEs should be submitted on F104 within 24 hours from time of knowledge.

- ***F246 – Informed Consent – Regained Capacity***
  - If the subject does regain capacity at some point during the trial or at end of study, but signed informed consent was not obtained, please enter the reasoning for why consent was not obtained into (Q09) 'Reason signed informed consent not obtained'.
  - If the subject does not regain capacity during the trial or at end of study, please enter the reason why into the General Comments section.
  - We will query for further information if needed.

- ***F104 Adverse Events***
  We have had a recent database change impacting **F104 Adverse Events**. This update includes the additional question (Q31) shown below. If (Q12) *Type of event = 'Acute cerebral infarction'*, you will be prompted to answer (Q31).

  The attached PDF is Version 7 of the form and can be used as the printable form. This can also be found in the CRF Collection Schedule in WebDCU.

  Any already submitted Adverse Event forms will have warning violations triggered on forms where (Q12) = Acute Cerebral Infarction. Please update your CRFs to answer (Q31) if needed.

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/