NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

OCTOBER 2023 | VOLUME 2 | ISSUE 10

FASTEST

FVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Spokoyny

It is such an honor to be among the enrolling centers in the FASTEST trial! We have enrolled 4 patients, 3 of whom were identified on our Mobile Stroke Unit. MSUs have changed the pre-hospital landscape for stroke patients - both ischemic and hemorrhagic. We are now able to rapidly identify hemorrhages, start anti-hypertensive therapy, and enroll in a groundbreaking clinical research trial - all before reaching the hospital. Along with the MSU, EFIC has been the key to maximizing enrollment and offering more patients the opportunity to participate in clinical research. Patients enrolled through EFIC have all been grateful to not have been overlooked because of their inability to consent in the moment. Here's to hoping the enrollment momentum continues and FASTEST gives us a long-awaited disease modifying treatment for hemorrhagic stroke!

Ilana Spokoyny, MD
Vascular Neurology
Sutter West Bay Medical Group
Medical Director, Mobile Stroke Unit
FASTEST Site PI

Please join us for the *FASTEST* Monthly Webinar

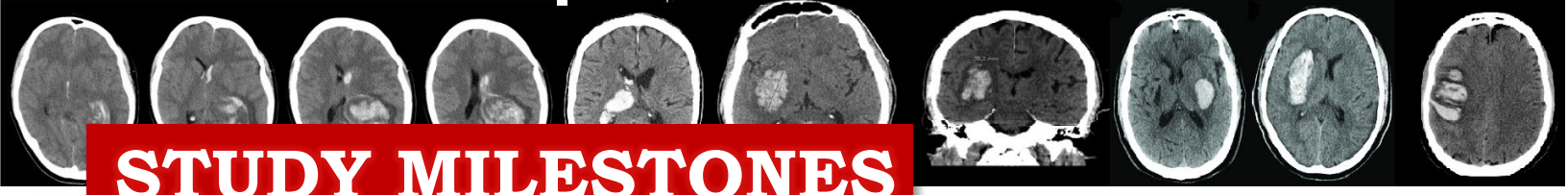
Wednesday October 18th, 2:00-3:00 pm EST

- Dr. Lowenkopf and his team from Providence Stroke Center will be discussing case at their site.
- Dr Gbinigie and his team from John Radcliffe Hospital, Oxford, United Kingdom will be discussing case at their site.
- Update about ICH trials from WSO and other ICH publications.

Join Zoom Meeting
https://nam11.safelinks.protection.outlook.com/?url=https%3A%2F%2Fucincinnati.zoom.us%2Fj%2F91270599326&data=05%7C01%7Cquadrisd%40ucmail.uc.edu%7C59de671893534b5f411808db91e5229c%7Cf5222e6c5fc648eb8f0373db18203b63%7C0%7C0%7C638264185548573076%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=E5dRFfb7oIW1z8MCqQ%2Bbz5zs%2Fb6N1KbkElfCvsgt6NQ%3D&reserved=0

Meeting ID: 912 7059 9326

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



STUDY MILESTONES

Total Sites Released to Enroll: **69** (**36** USA, **33** OUS: **5** Germany, **14** Japan, **4** Spain, **6** Canadian, **4** UK)

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

Total Randomization = **280**

- US Randomizations: **77**
- International randomizations: **203** (**133** Japan, **35** Canadian, **20** Spain, **11** Germany, **4** UK)

Randomization last month = **18**
Total Screen Failures = **850**
Subjects Randomized by MSU = **12**
Subjects Terminated Early = **1**
eConsent Used = **6**
Remote Consent Used = **7**

CALENDAR OF EVENTS

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

FASTEST study team office hours: **Monday, October 23rd, @ 2:00-3:00 pm**

TOP ENROLLING SITES

JAPAN UPDATE?

1. Kobe City Medical Center General Hospital, Kobe, Japan = 31
2. National Cerebral and Cardiovascular Center, Osaka, Japan =30
3. Iwate Prefectural Central Hospital, Morioka, Japan = 15

USA

1. Memorial Hermann Texas Medical Center, Houston, TX = 17
2. University of Cincinnati Medical Center, Cincinnati, OH = 7
3. Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA = 7

CANADA

1. University of Calgary - Foothills Medical Centre, Calgary, AB, Canada =20
2. Ottawa Hospital, Ottawa, ON, Canada = 6
3. Vancouver General Hospital, Vancouver, BC, Canada =5

SPAIN

1. Vall d'Hebron Hospital, Barcelona, BCN, Spain = 9
2. Girona University Hospital, Girona, GI, Spain =5
3. Santa Creu and Sant Pau Hospital, Barcelona, BCN, Spain = 4

GERMANY

1. Tubingen University Hospital, Tubingen, Germany = 5
2. University Hospital Augsburg, Augsburg, Germany =2
3. Clinic Frankfurt Hoechst, Frankfurt, Germany = 2
4. Charite University Medicine Berlin, Berlin, Germany =2

UK

1. Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom =2
2. John Radcliffe Hospital, Oxford, United Kingdom = 1
3. Queens Medical Centre, Nottingham, United Kingdom =1

Mobile Stroke Unit (MSU)

1. Grady Memorial Hospital, Atlanta, GA = 4
2. Mills Peninsula Medical Center, Burlingame, CA =3
3. Central DuPage Hospital, Winfield, IL =2
4. Charite University Medicine Berlin, Berlin, Germany =2

New Sites... Welcome Aboard!

The following new sites were **released to enroll** in the *FASTEST* study during the last month.

M Health Fairview Ridges Hospital, Burnsville, MN

Site PI:
Christopher Streib, MD

M Health Fairview St. John's Hospital, Maplewood, MN

Site PI:
Christopher Streib, MD

Mayo Clinic Saint Marys Campus, Rochester, MN

Site PI:
Eugene L. Scharf, M.D

Congratulations on 1st Enrollment!!!

Congratulations to Dr. Nina GENTILE and her team at the Temple University Hospital, Philadelphia, PA for enrolling their first subject in FASTEST.

FAQ

QUESTION CORNER

Q: When reporting adverse event outcome, when would I select 'Unknown'?
A: An adverse event should only be unknown when a subject is lost to follow up and the medical record does not confirm the outcome. If a subject completes the study through the Day 180 Visit, another outcome must be selected. Remember to check-in on all previously reported ongoing events at each study visit.

Q: The 180 day follow up of our FASTEST subject. The participant has a clinic visit planned this Wednesday and is unlikely we will be able to arrange a in person follow up in October. We would need to do the follow up remote. Would it be preferred to do a mRS and EQ-5D in person out of window (3 weeks early) in the clinic as well or do we just wait to do these remote?
A: The protocol encourages in-person follow up at 180 days. However, a remote follow up can also be done if in-person is not possible.

Q: I have recently concluded the 30-Day visit for the subject and learned that they sought medical attention at an urgent care facility due to hypertension and an elevated morning blood sugar. During the visit, the healthcare provider adjusted the dosage of medications for both blood pressure and diabetes management. I am seeking clarification regarding whether this should be documented as an Adverse Event (AE). It's worth noting that both hypertension and diabetes are pre-existing medical conditions within the subject's medical history, which leads us to assume that it may not qualify as an AE. Any guidance or clarification would be greatly appreciated.
A: As per study protocol and MOP any adverse events (AE) are to be reported only during the first 4 days. However, all serious adverse events (SAE) are to be reported throughout the study period (until 180 days). In your case at 30-day follow-up, depends on if the Site PI deems this to be an SAE or just an AE. If the Site PI considers this an SAE and reportable, please report it. Otherwise, AE are not required to be reported at 30 days.

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

SHOUT OUTS!!

Congratulations to all our US sites that have completed their EFIC reports and gained Advarra full study approval. UPDATE?

Thank you to the sites recently released to enroll for their hard work:

University Hospital Erlangen, Erlangen, GermanyM Health Fairview Ridges Hospital, Burnsville, MN

M Health Fairview St. John's Hospital, Maplewood, MN

1.

Thank you to the sites that have gotten CIRB/REB/EC approval and preparing for readiness:

1. **North Shore University Hospital, Manhasset, NY**
2. **Prisma Health Greenville Memorial Hospital, Greenville, SC**
3. **University of Colorado Hospital, Aurora, CO**

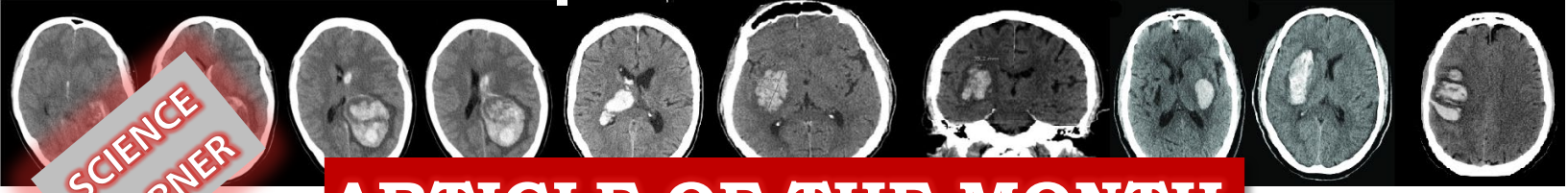
Top Enrolling Site

Congratulations to **Kobe City Medical Center General Hospital, Kobe, Japan** for being the highest enrolling site in the study.

Subjects enrolled = 32!!

Congratulations to Enrolling Sites last Month!

Kobe City Medical Center General Hospital, Kobe, Japan	**3 Subjects**
National Cerebral and Cardiovascular Center, Osaka, Japan	**3 Subject**
Kagoshima City Hospital, Kagoshima, Japan	**2 Subjects**
KMU University Hospital, Osaka, Japan	**1 Subject**
Gifu University Hospital, Gifu, Japan	**1 Subject**
Kyorin University Hospital, Tokyo, Japan	**1 Subject**
University of Calgary - Foothills Medical Centre, Calgary, AB, Canada	**1 Subjects**
Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom	**1 Subject**
Grady Memorial Hospital, Atlanta, GA	**1 Subjects**
Temple University Hospital, Philadelphia, PA	**1 Subject**
Memorial Hermann Texas Medical Center, Houston, TX	**2 Subjects**
Mills Peninsula Medical Center, Burlingame, CA	**1 Subject**



SCIENCE CORNER

ARTICLE OF THE MONTH

Association Between Hematoma Expansion Severity and Outcome and Its Interaction With Baseline Intracerebral Hemorrhage Volume

Andrea Morotti, Gregoire Boulouis, Jawed Nawabi, Qi Li, Andreas Charidimou, Marco Pasi, Frieder Schlunk, Ashkan Shoamanesh, Aristeidis H Katsanos, Federico Mazzacane, Giorgio Busto, Francesco Arba, Laura Brancaleoni, Sebastiano Giacomozzi, Luigi Simonetti, Andrew D Warren, Michele Laudisi, Anna Cavallini, Edip Gurol, Anand Viswanathan, Andrea Zini, Ilaria Casetta, Enrico Fainardi, Steven M Greenberg, Alessandro Padovani , Jonathan Rosand, Joshua Goldstein

Neurology. 2023 Aug 21:10.1212/WNL.0000000000207728. doi: 10.1212/WNL.0000000000207728.

Background:

Hematoma expansion (HE) is a major determinant of neurological deterioration and poor outcome in intracerebral hemorrhage (ICH) and represents an appealing therapeutic target. We analyzed the prognostic effect of different degrees of HE.

Methods:

Retrospective analysis of ICH patients admitted at eight academic institutions in Italy, Germany, Canada, China and United States. All patients underwent baseline and follow-up imaging for HE assessment. Relative HE (rHE) was classified as follows: (none < 0%), mild (0-33%), moderate (33.1-66%) and severe (> 66%). Absolute HE (aHE) was classified as none (< 0 mL), mild (0-6.0 mL), moderate (6.1-12.5 mL) and severe (> 12.5 mL). Predictors of poor functional outcome (90 days modified Rankin Scale 4-6) were explored with logistic regression.

Results:

We included 2163 subjects, of whom 1211 (56.7%) had poor outcome. The occurrence of severe aHE or rHE was more common in patients with unfavorable outcome (13.9% vs 6.5%, p<0.001 and 18.3% vs 7.2 %, p<0.001 respectively). This association was confirmed in logistic regression (rHE OR 1.98, 95% CI 1.38-2.82, p<0.001; aHE odds ratio (OR)1.73,95% confidence interval (CI) 1.23-2.45, p=0.002) while there was no association between mild or moderate HE and poor outcome. The association between severe HE and poor outcome was significant only in patients with baseline ICH volume below 30 mL.

Conclusions:

The strongest association between HE and outcome was observed in patients with smaller initial volume experiencing severe HE. These findings may inform clinical trial design and guide clinicians in selecting patients for anti-expansion therapies.

HELPFUL REMINDERS & TIPS

For Project Managers, Study Coordinators & Study Teams

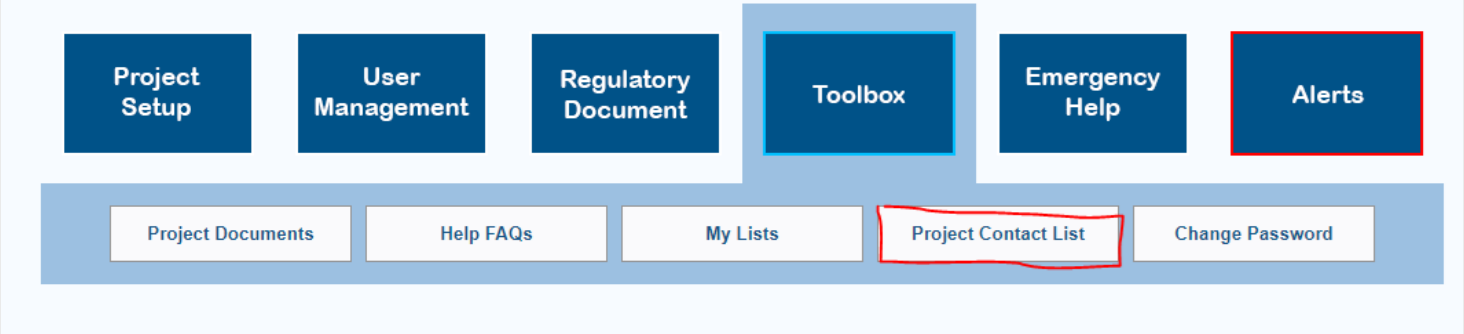
- **Updating 1572:** Compliance with regulatory requirements mandates that every modification to a 1572 form necessitates the PI signature to acknowledge the alteration. It is essential to understand that updates to an existing 1572 are not permissible; instead, a new 1572 form must be created for each update. Consequently, the PI is required to sign a new 1572 form with every update made.

- **Temperature excursion and monitoring: Please be very vigilant about temperature excursion and temperature monitoring documentation.** FASTEST sites using the ***Emerald temperature loggers*** provided by us for their MSU or ED we will be sending out weekly reminder email every Friday to the PSC. Checking once a week should ensure careful monitoring of temperature excursion and documentation, as well as avoiding the use of affected study drug.

- If kit that was affected was used for randomization it is advised to communicate with the subject to ensure that they are fully informed about the situation regarding the affected study drug. An update regarding this communication should be provided to the CIRB for their records (while reporting this deviation).

- **FASTEST is now operating under Version 7 of the Protocol.** Please sign and upload **PI Protocol v7 Training Attestation** and **new Protocol v7 Signature Page** to WebDCU.
  - It is mandatory for all PIs to sign a new **Training Attestation** for Protocol v7. By signing this attestation, the PI confirms that all individuals listed on the current DoA have received training on the updated protocol. Therefore, it is not necessary to collect a new training attestation from each investigator/study team member individually.
  - We kindly request all sites to maintain an internal training log as evidence that every individual has undergone training on the updated Protocol v7. This log will serve as documentation, which may be required during an FDA audit, to verify that the study team members have been sufficiently trained on the protocol updates.

- WebDCU have now included a "project contact list" feature, which contains all the important contact information that the site might require during the course of the trial. Sites can access it by navigating to FASTEST > ToolBox > Project Contact List.



From the *FASTEST* Central Pharmacy Team

- Instructions to fill out TERF from are in the toolbox in WebDCU.

- Kit #, DUN# and the Lot number could all be found in the 'Site Drug Kit Removing' section in the WebDCU.

- Please make sure to disseminate this newsletter to you site pharmacist/s too as it may contain helpful information regarding drug compounding, storage, accountability, etc.

INTERNATIONAL SITE OF THE MONTH

John Radcliffe Hospital, Oxford, United Kingdom

John Radcliffe Hospital (informally known as the JR) is a large tertiary teaching hospital in Oxford, England. It forms part of Oxford University Hospitals NHS Foundation Trust and is named after John Radcliffe, an 18th-century physician and Oxford University graduate, who endowed the Radcliffe Infirmary, the main hospital for Oxford from 1770 until 2007.

As one of the largest teaching hospitals in Oxfordshire, it is closely affiliated with the University of Oxford's medical school and plays a pivotal role in training the next generation of healthcare professionals. It is the main teaching hospital for Oxford University and Oxford Brookes University and incorporates the Oxford University Medical School.

The hospital boasts state-of-the-art facilities and a wide range of specialized departments, including cardiology, neurology, oncology, and more, allowing it to provide comprehensive healthcare services to its diverse patient population. It is a leading center for medical research, conducting groundbreaking studies that contribute to advancements in healthcare on a global scale.

With a commitment to patient-centered care, John Radcliffe Hospital places a strong emphasis on ensuring that patients receive the highest quality of treatment and support. Its dedicated and skilled medical staff work tirelessly to improve the health and well-being of the communities they serve, making it a vital healthcare institution in the region.

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/