NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

JANUARY 2024 | VOLUME 3 | ISSUE 1

FASTEST

FVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Naidech

As 2024 begins, we hope you all had a great holiday season with friends and family. We also hope you share our excitement for FASTEST, one of the "fastest" recruiting trials in the NIH StrokeNet. Management for ICH is rapidly evolving, and we are excited for this golden opportunity to show how medical management reduces hematoma expansion and improves functional outcomes.

Andrew M Naidech, MD MSPH
Professor Northwestern University
Feinberg School of Medicine
Department of Neurology
Northwestern Memorial Healthcare

Please join us for the *FASTEST* Monthly Webinar

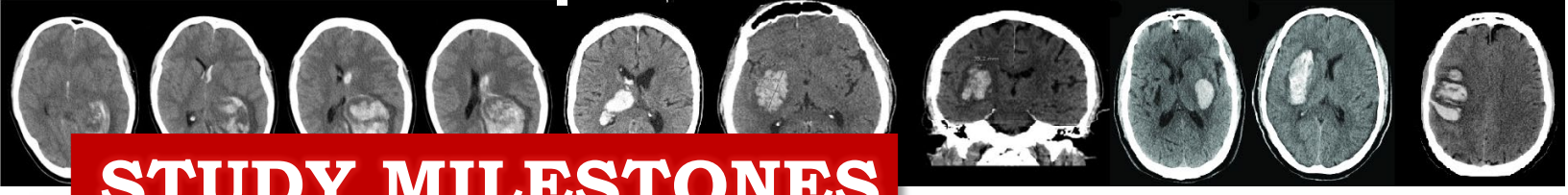
Wednesday January 17th, 2:00-3:00 pm EST

- Dr. Ilana Spokoyny and her team from Mills-Peninsula Medical Center, CA will be discussing case at their site.
- Year in Review: Statis and Updates from 2023
- Detailed review of consenting and enrollment process
- RFA and EQ-5D Reminders & Guidelines
- Managing IP Temperature Monitoring

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: **78** (**44** USA, **34** OUS: **6** Germany, **14** Japan, **4** Spain, **6** Canadian, **4** UK)

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

Total Randomization = **354**

- US Randomizations: **100**
- International randomizations: **254**
  - Japan = **167**
  - Canada = **45**
  - Spain =**20**
  - Germany = **14**
  - UK = 8

Randomization last month = **24**

Total Screen Failures = **1253**

Subjects Randomized by MSU = **13**

Subjects Terminated Early = **3**

eConsent Used = **15**

Remote Consent Used = **11**

Enrollment Stats from 2023

Country	Total Enrollments	Enrollments in 2023	Mean (average) Enrollment rate (enrollemnt per month)	Highest Enrollment in a month
JAPAN	167	127	10.58	20 (October)
USA	98	71	6	9 (April)
CANADA	44	30	2.5	5 (March & Dec)
United Kingdom	8	8	0.6	2
Germany	13	10	0.83	4 (Jan)
Spain	20	16	1.3	4 (March & Feb)
	350	**262**	**21.81**	

CALENDAR OF EVENTS

Upcoming *FASTEST* Monthly Webinars: **Wednesday, Jan 17th and Feb 21st, @ 2:00-3:00 pm EST**

FASTEST study team office hours: **Monday, January 29th, @ 2:00-3:00 pm.**

IMPORTANT NOTE

Obtaining RFA and EQ-5D

The Rankin Focused Assessment (RFA) is the designated tool for determining the mRS score in the FASTEST trial. All sites are mandated to employ the RFA for mRS assessments, as it has demonstrated exceptional inter-rater reliability. Failure to adhere to this protocol and utilize the RFA is deemed a protocol deviation.

All participating sites must utilize the EQ-5D for the assessment of health-related quality of life failure to do so is considered a protocol deviation.

Updated FASTEST MOP

The revised FASTEST MOP – Version 2.0 (Jan 2024) has been distributed to all sites and is also accessible on WebDCU. Please be informed that the MOP has been extensively updated and you will be able to find solutions to all your queries within the MOP.

New Sites... Welcome Aboard!

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

Hospital Universitari Germans Trias i Pujol, Barcelona, B, Spain

Site PI:
Alejandro BUSTAMANTE RANGEL, MD

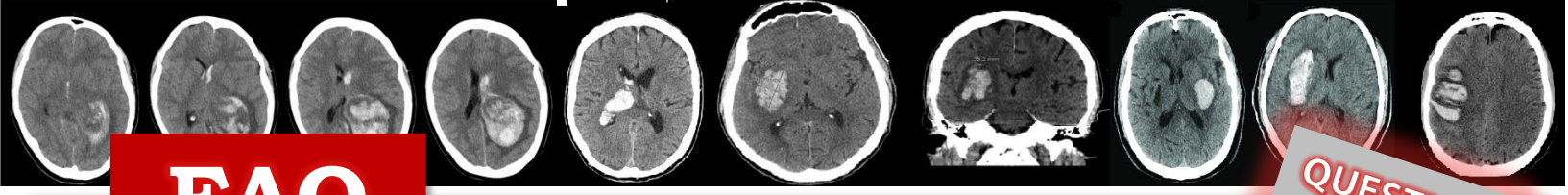
North Shore University Hospital, Manhasset, NY

Site PI:
Richard Elias Temes, MD

Congratulations on 1st Enrollment!!!

Congratulations to Dr. Yasushi OKADA and his team at the Kyushu Medical Center, Fukuoka, Japan for enrolling their first subject in FASTEST.

Congratulations to Dr. Atif ZAFAR and his team at the St. Michaels Hospital, Toronto, ON, Canada for enrolling their first subject in FASTEST.



FAQ

QUESTION CORNER

Q: An aneurysm was identified after enrollment. Is this a n eligibility violation?
A: The identification of an incidental aneurysm post-enrollment is not considered an eligibility violation.

Q1: Are sites allowed to "waste" IP if we feel there is a good candidate but want to start prep early to be ready to treat?
A: Certainly, sites are allowed to "waste" Investigational Product (IP) if they identify a suitable candidate and wish to initiate preparation early to ensure readiness for treatment but don't end up enrolling the patient.

Q: How many times can we preemptively begin to mix IP before it's considered a "waste" and advised we fix our workflow?
A: We will assess this on a case by case or site by site basis. Drug wastage has not been a big issue to date, and we have not had a site that seems to be wasting too much IP yet. We would prefer sites prepare the IP asap so this would not be a barrier to randomization. We have planned for IP wastage. But sites should confirm age, volume of ICH, IVH eligibility and time from onset prior to mixing medication. OK not have consented or identified family member.

Q: In WebDCU, will we be able to register a subject and release a dispensation before conferring ALL eligibility criteria since EFIC is now a factor?
A: Due to the hyper acute nature of the trial, we expect randomization to happen prior to enrollment of the subject into WebDCU. Sites are expected to enroll the subject into WebDCU within 12 hours of IP infusion. EFIC enrollments will require extra documentation in the EFIC log until written consent is obtained. Filling out the EFIC log should happen as soon as possible along with filling out the enrollment CRF's in WebDCU.

Q: Can an NIHSS done per standard of care be used during the Screening/Baseline period if an investigator is not available?
A: Yes, as long as the physician, if not part of the study team, has an NIHSS certification and are being overseen by the PI.

Q: can the investigators collectively select few individuals to act as evaluators for the sake of an NIHSS for research purposes?
A: Yes, as long as they are NIHSS certified and being overseen by the PI.

Q: As NIHSS, mRS, and GCS are done as SOC, do these measurements taken at baseline need to be done by a physician documented on the DOA?
A: We would prefer that these basslines and/or eligibility assessments be done by the trained study team listed on the DoA. The mRS and GCS as not typically being SOC. The NIHSS could be done by other physicians not on the study team if they are certified but again, it is prefer that the trained study team perform the baseline/eligibility assessments if possible.

Q: Is protocol training required to be completed by the sub-I's before they are added to the 1572?
A: It is fine to add your sub-I's that plan to participate in the trial to the 1572. Please also add them to the DoA and have them do the protocol training as soon as possible. However, they should not perform study procedures until they complete all required study training.

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.

1. Henry Ford Hospital, Detroit, MI
2. UC Davis Medical Center, Sacramento, CA

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

1. **Hospital Universitari Germans Trias i Pujol, Barcelona, Spain**
2. **North Shore University Hospital, Manhasset, NY**

The Top Enrolling Site

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

Subjects enrolled = 39!!

Congratulations to Enrolling Sites last Month!

Kobe City Medical Center General Hospital, Kobe, Japan	1 Subject
National Cerebral and Cardiovascular Center, Osaka, Japan	1 Subject
Toranomon Hospital, Tokyo, Japan	1 Subject
Kyorin University Hospital, Tokyo, Japan	2 Subject
Niigata City General Hospital, Niigata, Japan	1 Subject
KMU University Hospital, Osaka, Japan	1 Subject
NHO Osaka National Hospital, Osaka, Japan	1 Subject
Nakamura Memorial Hospital, Sapporo, Japan	1 Subject
University of Alberta Hospital, Edmonton, AB, Canada	2 Subject
Hamilton General Hospital, Hamilton, ON, Canada	1 Subject
University of Calgary - Foothills Medical Centre, Calgary, AB, Canada	1 Subject
St. Michaels Hospital, Toronto, ON, Canada	1 Subject
Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom	2 Subject
University of Cincinnati Medical Center, Cincinnati, OH	1 Subject
Memorial Hermann Texas Medical Center, Houston, TX	1 Subject
M Health Fairview Southdale Hospital, Edina, MN	1 Subject
University of Alabama Hospital, Birmingham, AL	1 Subject
St. Joseph's Hospital and Medical Center, Phoenix, AZ	1 Subject
Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA	1 Subject
Charite University Medicine Berlin, Berlin, Germany	1 Subject
Clinic Frankfurt Hoechst, Frankfurt, Germany	1 Subject

SCIENCE CORNER

ARTICLE OF THE MONTH

Effects of blood pressure and tranexamic acid in spontaneous intracerebral haemorrhage: a secondary analysis of a large randomised controlled trial

Jason Philip Appleton, Zhe Kang Law, Lisa Jane Woodhouse, Rustam Al-Shahi Salman, Maia Beridze, Hanne Christensen, Robert A Dineen, Juan José Egea Guerrero, Timothy J England, Michal Karlinski, Kailash Krishnan, Ann Charlotte Laska, Philippe Lyrer, Serefnur Ozturk, Christine Roffe, Ian Roberts, Thompson G Robinson, Polly Scutt[2], David J Werring, Philip M Bath, Nikola Sprigg

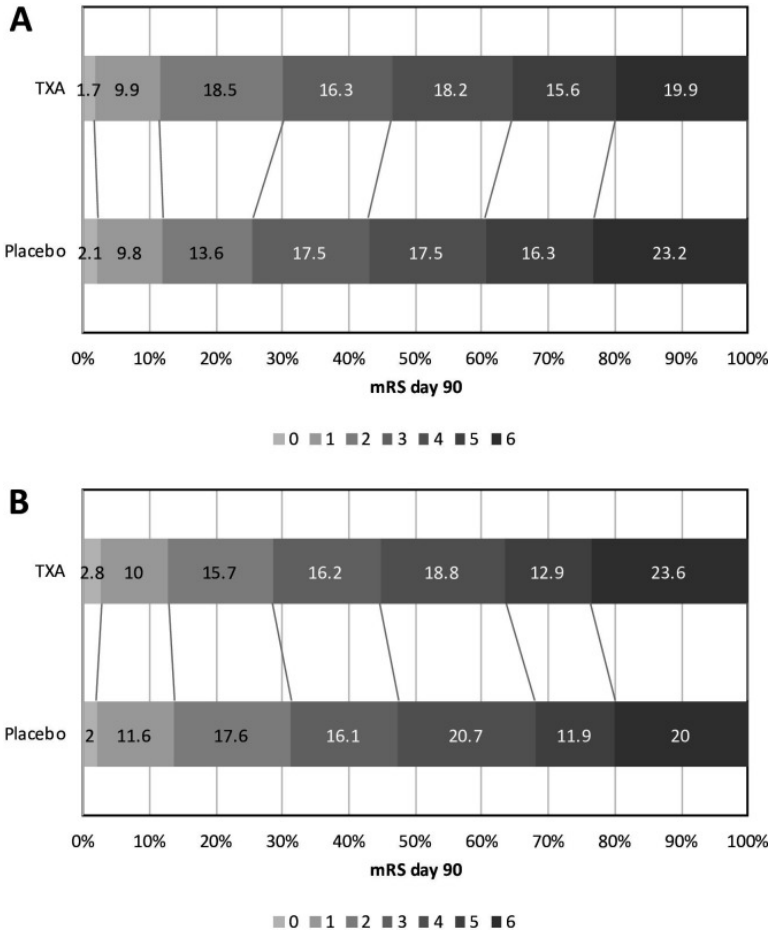
BMJ Neurol Open. 2023 Jun 12;5(1):e000423. doi: 10.1136/bmjno-2023-000423. eCollection 2023.

Background: Tranexamic acid reduced haematoma expansion and early death but did not improve functional outcome in the tranexamic acid for hyperacute spontaneous intracerebral haemorrhage-2 (TICH-2) trial. In a predefined subgroup, there was a statistically significant interaction between prerandomisation baseline systolic blood pressure (SBP) and the effect of tranexamic acid on functional outcome (p=0.019).

Methods: TICH-2 was an international prospective double-blind placebo-controlled randomised trial evaluating intravenous tranexamic acid in patients with acute spontaneous intracerebral haemorrhage (ICH). Prerandomisation baseline SBP was split into predefined ≤170 and >170 mm Hg groups. The primary outcome at day 90 was the modified Rankin Scale (mRS), a measure of dependency, analysed using ordinal logistic regression. Haematoma expansion was defined as an increase in haematoma volume of >33% or >6 mL from baseline to 24 hours. Data are OR or common OR (cOR) with 95% CIs, with significance at p<0.05.

Results: Of 2325 participants in TICH-2, 1152 had baseline SBP≤170 mm Hg and were older, had larger lobar haematomas and were randomised later than 1173 with baseline SBP>170 mm Hg. Tranexamic acid was associated with a favourable shift in mRS at day 90 in those with baseline SBP≤170 mm Hg (cOR 0.73, 95% CI 0.59 to 0.91, p=0.005), but not in those with baseline SBP>170. mm Hg (cOR 1.05, 95% CI 0.85 to 1.30, p=0.63). In those with baseline SBP≤170 mm Hg, tranexamic acid reduced haematoma expansion (OR 0.62, 95% CI 0.47 to 0.82, p=0.001), but not in those with baseline SBP>170 mm Hg (OR 1.02, 95% CI 0.77 to 1.35, p=0.90).

Conclusions: Tranexamic acid was associated with improved clinical and radiological outcomes in ICH patients with baseline SBP≤170 mm Hg. Further research is needed to establish whether certain subgroups may benefit from tranexamic acid in acute ICH.



HELPFUL REMINDERS & TIPS

For Project Managers, Study Coordinators & Study Teams

- **Imaging Reminders:** Submit all head imaging performed as SOC within 30 hours from stroke onset to IMC (i.e., NCCT, CTA, MRI if performed)
  - Baseline/first scan obtained either in ED or MSU to determine trial eligibility AND prior to study product administration.
  - 24 (+/6) hours from stroke onset follow-up scan
  - "Unscheduled" scan obtained for clinical deterioration or immediately prior to any surgical intervention (i.e., surgical removal of ICH or IVC placement) if planned prior to 24-hour scan.
    ***Failure to obtain a pre-op scan results in missing imaging endpoint (i.e., ability to calculate ICH growth between baseline scan and unscheduled pre-op scan)

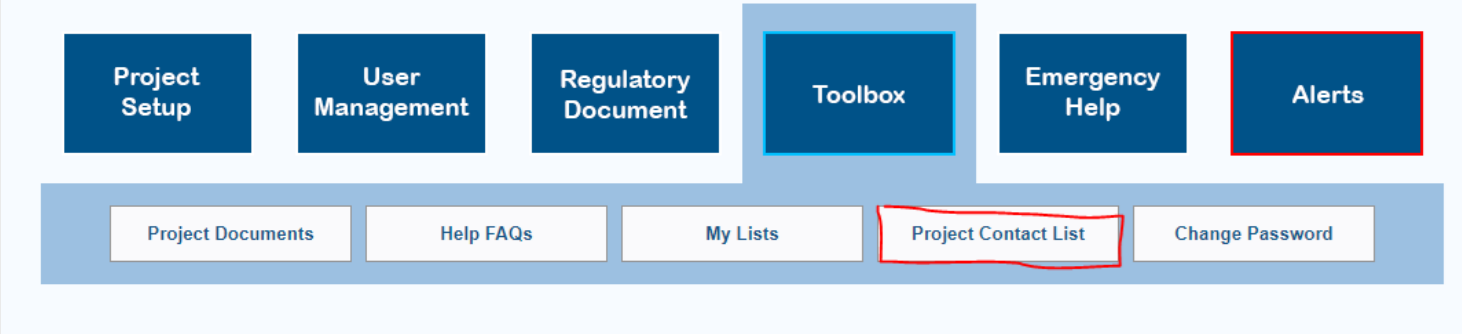
  Imaging must be submitted within 5-7 business days of subject randomization via the Ambra Health® platform.

  - Also includes submission of WebDCU F502 which is needed to process scans.

  ***Confirmation of receipt of ALL imaging is one of the requirements in triggering "Baseline through 24 hr. Payment" to your site.

- 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).

- 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

- **Recent temperature excursions in IDS Pharmacy:** There have been recent reports of temperature excursions at certain sites related to the storage of the study drug within the pharmacy. We strongly encourage all site PSCs to proactively engage with their trial pharmacist. Regular communication and periodic checks with the pharmacist will help ensure the consistent monitoring of temperature conditions and mitigate the risk of excursions.
  - The TERF needs to be submitted to the NCC project manager and Strokenet central pharmacy as soon as possible.
  - The site pharmacists should remove the effected study drug by filling out the WebDCU form in a timely manner in order to trigger a resupply. The sites are advised to add more people to the DOA in order to expedite the process of documenting things in WebDCU if necessary.

- 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.

INTERNATIONAL SITE OF THE MONTH

St. Michaels Hospital, Toronto, ON

St. Michael's Hospital, located in the vibrant city of Toronto, Ontario, is a renowned healthcare institution that has been a pillar of medical excellence since its establishment in 1892. Situated in the heart of the city's downtown, the hospital has played a crucial role in providing compassionate and high-quality care to the community for well over a century. As a teaching hospital affiliated with the University of Toronto, St. Michael's has not only been at the forefront of medical innovation but has also been a hub for educating the next generation of healthcare professionals.

This institution nestled in the heart of Toronto, Ontario, boasts a rich history that dates back to its founding in 1892 by the Sisters of St. Joseph. The hospital's inception was driven by a deep sense of compassion and a mission to provide care to the city's vulnerable populations. Over the years, St. Michael's has evolved into a world-class healthcare facility, blending its historic roots with a commitment to cutting-edge medical practices. Throughout its storied history, St. Michael's Hospital has been a cornerstone of medical education, serving as a teaching hospital affiliated with the University of Toronto. The hospital's legacy is interwoven with the tapestry of Toronto's diverse communities, reflecting a commitment to addressing the unique healthcare needs of a multicultural population.

What sets St. Michael's apart is its commitment to addressing the diverse healthcare needs of the community, reflecting the multicultural fabric of Toronto. The hospital is known for its cutting-edge research initiatives, innovative medical practices, and a comprehensive range of specialized services, including trauma care, cardiovascular services, and infectious diseases. With a mission deeply rooted in social justice and a vision for a healthier future, St. Michael's Hospital continues to be a beacon of hope and healing, fostering a legacy of excellence in patient care, education, and research.

Site PI: Atif Zafar, MD

Dr. Atif Zafar is a Stroke Neurologist at St. Michael's Hospital in Toronto, Ontario, where he brings expertise to the forefront of stroke care. He is the Medical Director of the Stroke Program at the St. Michael's Hospital.

Dr. Zafar focuses his research on critical aspects of stroke care, spanning prevention, treatment modalities, outcomes, and rehabilitation. His work delves into the intricate landscape of stroke research, exploring innovative therapies, advanced diagnostic tools, and strategic approaches aimed at enhancing overall patient care.

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/