NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

AUGUST 2023 | VOLUME 2 | ISSUE 8

FASTEST

FVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Mathew

Some of the best parts of working in the field of vascular neurology is being able to deliver potentially lifesaving treatments and being able to witness the development of these treatments firsthand. Participation in the FASTEST trial is the perfect embodiment of both. Despite joining the FASTEST team less than a year ago, Stony Brook University, has become the 3rd highest enrolling site in the US. We attribute our success to the widespread engagement of all clinical staff (trainees, nursing, radiology techs), persistent clinical research coordinators who help incorporate study screening into clinical workflow, and passionate vascular neurologists dedicated to pushing the field forward. Additionally, at Stony Brook we are equipped with two mobile stroke units (MSUs) which has greatly facilitated rapid identification of study patients and timely drug administration. I knew our FASTEST study messaging campaign was a success, when MSU crew members started being the first ones verifying the candidacy of ICH patients! Thank you to the FASTEST leadership team for the invitation to be part of this meaningful work and thank you to all of the participating FASTEST sites tirelessly working to transform the way we treat intracerebral hemorrhage.

Jason Mathew, DO
Assistant Professor of Neurology
Fellowship Director, Vascular Neurology
Stony Brook University Hospital
FASTEST Site PI

Please join us for the *FASTEST* Monthly Webinar

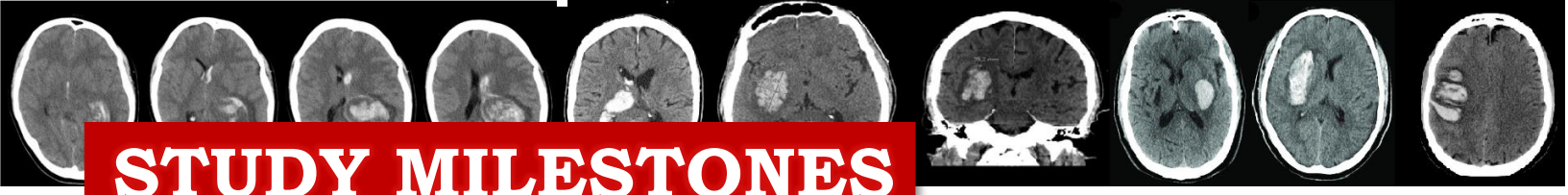
Wednesday Aug 23rd, 2:30-3:30 pm EST

- Dr. Mathew and his team from Stony Brook University Hospital, Stony Brook, NY will be discussing the MSU case at their site.
- Clarification on 120 min + 5 min deviation and how to fill out the CRF.
- Review of ICH volume calculation.
- NDMC will go over the documentation for APTT & PTT and enrollment >120 min.

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: **10** (**8** US and **2** OUS)

Total Randomization = **238**

- US Randomizations: **66**
- International randomizations: **172** (**108** Japan, **31** Canadian, **19** Spain, **11** Germany, **3** UK)

Randomization last month = **20**
Total Screen Failures = **685**
Subjects Randomized by MSU = **10**
Subjects Terminated Early = **0**
eConsent Used = **6**
Remote Consent Used = **5**

CALENDAR OF EVENTS

Upcoming *FASTEST* Monthly Webinar: **Wednesday, Aug 23rd @ 2:30-3:30 pm EDT**

FASTEST study team office hours: **Monday, Aug 14th and 28th @ 2:00-3:00 pm EDT**

IMPORTANT NOTE

Protocol Training Signatures

Please sign and upload these two documents to WebDCU

1. PI Protocol Traning Attestation attesting to study team training for the updates to the new Protocol v7
2. The new Protocol v7 Signature Page .

Please reach out to Emily Stinson stinsoey@ucmail.uc.edu if you have any questions.

Congratulations on 1st Enrollment!!!

Congratulations to Dr. Yusuke YAKUSHIJI and the team at the KMU University Hospital, Osaka, Japan for enrolling their first subject in FASTEST.

New Sites…Welcome Aboard!

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

Medical University of South Carolina University Hospital, Charleston, SC

Site PI:
Christine Holmstedt, MD

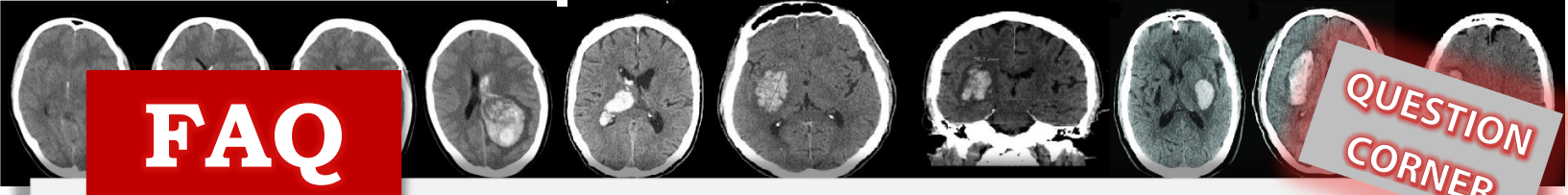
Wishing Ruth Reinsel a Joyful Retirement

As Ruth Reinsel the PSC at Stony Brook University Hospital embarks on a well-deserved retirement, we want to take a moment to express our heartfelt appreciation for the dedication, commitment, and invaluable contributions to the FASTEST trial.

Throughout the years, Ruth has been an esteemed and invaluable member of the clinical research team within the Department of Neurology at Stony Brook University Hospital. Her contributions have extended far and wide, playing a pivotal role in numerous significant clinical trials.

Please join us in celebrating Ruth's achievements and sending her our warmest wishes for a joyful retirement.

Ruth, we wish you all the best as you embrace the next phase of your journey!



FAQ

QUESTION CORNER

Q: The exclusion criterion 17 indicates that individuals who are unable or suspected to be unable to adhere to the trial protocol, for reasons such as alcoholism, drug dependency, or mental health disorders, are to be excluded. Based on this, would a participant with a history of dementia or Alzheimer's disease be considered ineligible? I

A: Patients with mild dementia or Alzheimer's disease living at home with their family, who can be easily followed up for the study, should be considered for enrollment in the trial. However, patients with severe dementia or Alzheimer's disease living at a nursing facility, who would present challenges in being adequately followed up, should be deemed ineligible for enrollment in the trial. Such patients would eventually end up lost to follow-up. Ensuring appropriate follow-up is essential for the integrity of the study. Therefore, carefully assess each patient's living situation and cognitive status to make informed and responsible enrollment decisions.

Q: How do living arrangements, such as nursing homes or group homes, impact the evaluation of a participant's modified Rankin Scale (mRS). If a participant resides in such a setting, would their mRS score be automatically assessed as more than 2, leading to their exclusion from the study?

A: Nursing home residents may have a range of mRS scores, from 0 (no symptoms) and above. It is essential to remember that nursing home residents have diverse medical histories and conditions and reasons for being in assisted living or nursing facility (sometimes even temporary as they may be recovering from recent surgery). Rather than automatically assessing/assuming the mRS for such patients as more than 2 it should be based on the mRS score you get from a patient or family member at the time of enrollment.

Q: Should a patient have persistent chronic neurological impairments resulting from a stroke that occurred over 90 days ago, would they still be considered for study participation, provided their modified Rankin Scale (mRS) score is 2 or less?

A: According to the *exclusion criteria #6* -Symptomatic thrombo-embolic or vaso-occlusive disease in past 90 days (e.g., cerebral infarction, myocardial infarction, pulmonary embolus, deep vein thrombosis, or unstable angina). Therefore, such patients can be enrolled in the trial if they had a stroke more than 90 days ago. If they have a neurological impairment due to the previous stroke leading to a mRS score 2 or less, they should qualify for the trial. However, if the neurological impairment from the previous stroke is severe enough to yield an mRS score of greater than 2, then the patient does not meet the criteria for enrollment in the FASTEST trial.

Q: What if the patient had a previous hemorrhagic stroke and now returns to the hospital within more than 90 days from their initial stroke and with worsening of their symptoms or new hemorrhagic stroke in the other parts of their brain, will they be eligible to participate in FASTEST?

A: Yes, such patients can be enrolled. However, it is important to consider the exclusion criteria #8, which states that patients with brainstem location of hemorrhage should be excluded from enrollment. It's worth noting that patients with cerebellar hemorrhage are eligible for enrollment in the trial.

Q: Criterion 6 indicates that patients with Symptomatic thrombotic or vaso-occlusive disease in past 90 days (e.g., cerebral infarction, myocardial infarction, pulmonary embolus, deep vein thrombosis, or unstable angina will be excluded from the study? Is the term 'cerebral infarction' synonymous with an ischemic stroke? Additionally, what would be the implications for a patient who has experienced a hemorrhagic stroke less than 90 days prior to their emergency department admission and subsequent screening for eligibility in the FASTEST study? Would this patient be eligible for FASTEST study?

A: Yes, 'cerebral infarction' is indeed synonymous with an ischemic stroke. It is important to note that both hemorrhagic and ischemic strokes occurring within the last 90 days are considered exclusion criteria for enrollment in the trial. As a result, any patient presenting to the emergency room with a history of stroke, regardless of its type, within the last 90 days should be excluded from participating in the trial.

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.

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

1. **Mt. Sinai Hospital, NY**
2. **WellStar Hosp. GA**
3. **Royal Stoke University Hospital, United Kingdom**
4. **John Radcliffe Hospital, Oxford, United Kingdom**
5. **University of Alberta Hospital, Edmonton, AB, Canada**

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

1. **Ronald Reagan, CA**
2. **Henry Ford, MI**

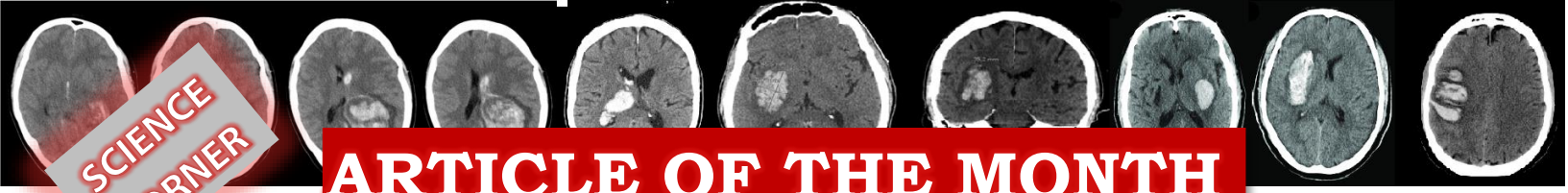
Top Enrolling Site

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

Subjects enrolled = 25!!

Congratulations to Enrolling Sites last Month!

Kobe City Medical Center General Hospital, Kobe, Japan	**2 Subjects**
National Cerebral and Cardiovascular Center, Osaka, Japan	**1 Subject**
Iwate Prefectural Central Hospital, Morioka, Japan	**1 Subject**
Niigata City General Hospital, Niigata, Japan	**3 Subjects**
Kagoshima City Hospital, Kagoshima, Japan	**1 Subject**
KMU University Hospital, Osaka, Japan	**1 Subject**
Nakamura Memorial Hospital, Sapporo, Japan	**2 Subjects**
Kyorin University Hospital, Tokyo, Japan	**1 Subject**
Vancouver General Hospital, Vancouver, BC, Canada	**1 Subject**
University of Calgary - Foothills Medical Centre, Calgary, AB, Canada	**1 Subjects**
Vall d'Hebron Hospital, Barcelona, Spain	**2 Subjects**
Memorial Hermann Texas Medical Center, Houston, TX	**2 Subjects**
Stony Brook University Hospital, Stony Brook, NY	**1 Subject**
Toledo Hospital, Toledo, OH	**1 Subject**



SCIENCE CORNER

ARTICLE OF THE MONTH

Desmopressin for patients with spontaneous intracerebral haemorrhage taking antiplatelet drugs (DASH): a UK-based, phase 2, randomised, placebo-controlled, multicentre feasibility trial

Michael J R Desborough, Rustam Al-Shahi Salman, Simon J Stanworth, Diane Havard, Lisa J Woodhouse, Jennifer Craig, Kailash Krishnan,Paul M Brennan, Robert A Dineen, Tim J Coats, Trish Hepburn, Philip M Bath, Nikola Sprigg, for the DASH trial investigators

Lancet. 2023 Jul 1;402(10395):27-40. https://doi.org/10.1016/S0140-6736(23)00806-1

Background:

The risk of death from spontaneous intracerebral haemorrhage is increased for people taking antiplatelet drugs. We aimed to assess the feasibility of randomising patients on antiplatelet drug therapy with spontaneous intracerebral haemorrhage to desmopressin or placebo to reduce the antiplatelet drug effect.

Methods:

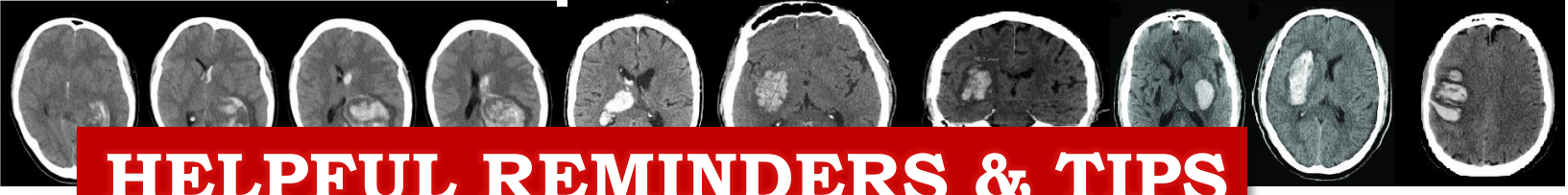
DASH was a phase 2, randomised, placebo-controlled, multicentre feasibility trial. Patients were recruited from ten acute stroke centres in the UK and were eligible if they had an intracerebral haemorrhage with stroke symptom onset within 24 h of randomisation, were aged 18 years or older, and were taking an antiplatelet drug. Participants were randomly assigned (1:1) to a single dose of intravenous desmopressin 20 μg or matching placebo. Treatment allocation was concealed from all staff and patients involved in the trial. The primary outcome was feasibility, which was measured as the number of eligible patients randomised and the proportion of eligible patients approached, and analysis was by intention to treat. The trial was prospectively registered with ISRCTN (reference ISRCTN67038373), and it is closed to recruitment.

Findings:

Findings Between April 1, 2019, and March 31, 2022, 1380 potential participants were screened for eligibility. 176 (13%) participants were potentially eligible, of whom 57 (32%) were approached, and 54 (31%) consented and were subsequently recruited and randomly assigned to receive desmopressin (n=27) or placebo (n=27). The main reason for eligible patients not being recruited was the patient arriving out of hours (74 [61%] of 122 participants). The recruitment rate increased after the enrolment period was extended from 12 h to 24 h, but it was then impaired due to the COVID-19 pandemic. Of the 54 participants included in the analysis (mean age 76·4 years [SD11·3]), most were male (36 [67%]) and White (50 [93%]). 53 (98%) of 54 participants received all of their allocated treatment (one participant assigned desmopressin only received part of the infusion). No participants were lost to follow-up or withdrew from the trial. Death or dependency on others for daily activities at day 90 (modified Rankin Scale score >4) occurred in six (22%) of 27 participants in the desmopressin group and ten (37%) of 27 participants in the placebo group. Serious adverse events occurred in 12 (44%) participants in the desmopressin group and 13 (48%) participants in the placebo group. The most common adverse events were expansion of the haemorrhagic stroke (four [15%] of 27 participants in the desmopressin group and six [22%] of 27 participants in the placebo group) and pneumonia (one [4%] of 27 participants in the desmopressin group and six [22%] of 27 participants in the placebo group).

Interpretation:

Our results show it is feasible to randomise patients with spontaneous intracerebral haemorrhage who are taking antiplatelet drugs to desmopressin or placebo. Our findings support the need for a definitive trial to determine if desmopressin improves outcomes in patients with intracerebral haemorrhage on antiplatelet drug therapy.



HELPFUL REMINDERS & TIPS

For Project Managers, Study Coordinators & Study Teams

- **Adverse event reporting timeframes:** Kindly note that as per protocol and instructions in the study MOP all AEs are to be reported **only within the first 4 days** of enrollment while SAEs are to be reported **up to day 180**.

- **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.

- Please respond to all the pending open DCRs for our site. We also will be reaching out to sites with pending protocol deviation and violations to help them file these in the Issue table accordingly with a NTF.

- **Things to make sure with DOA changes**: We have noticed that there is an increase in DoA changes, and we understand that many sites are adding or removing investigators from the DoA. Considering this, we would like to emphasize the following points. We kindly request your attention to ensure the following:

  1. Update **box 6** of the **FDA 1572** to make sure it aligns with investigators listed on your current DoA
  2. Make sure if you are adding investigators to the DoA that you are also uploading their required documents in a timely manner.
  3. Investigators must do all trainings and have all documents uploaded and approved in WebDCU before performing study procedures.
  4. Please make sure that your study team has been updated on the recent changes to the protocol. Promptly upload the **PI attestation** form and the new **Protocol v7 Signature Page** if you have not done so already.

- **Screen failure logs: Please update the screen failure logs in WebDCU screen failure data is very important to the study. As you are aware we will be reimbursing the sites for their screen failures.**

From the ***FASTEST*** Central Pharmacy Team

- While the IP has a wide temperature range and could be stored either refrigerated OR room temperature, we highly encourage sites to **choose one range** and **keep this range for the duration of the trial**.

- **Temperature excursion and monitoring: Please be very vigilant about temperature excursion and temperature monitoring documentation.**

- 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

Kobe City Medical Center General Hospital, Kobe, Japan

Kobe City Medical Center General Hospital, located in Kobe, Japan, stands as a prominent and well-respected medical institution known for its commitment to providing comprehensive and advanced healthcare services. Established in 1953, the hospital has since grown to become one of the leading medical centers in the Hyogo prefecture, serving the local community and beyond.

The hospital boasts a wide range of medical specialties and cutting-edge facilities, ensuring that patients receive top-notch care across various disciplines. From general medicine and surgery to specialized fields like cardiology, oncology, and neurology, Kobe City Medical Center General Hospital is equipped to handle diverse healthcare needs. It houses state-of-the-art diagnostic and treatment technologies, allowing for accurate and timely medical assessments and interventions.

In addition to its clinical excellence, the hospital also actively engages in medical research and education. Collaborating with academic institutions and research organizations, it remains at the forefront of medical advancements and fosters a culture of continuous learning among its medical staff. The hospital's dedication to research and education contributes to the development of innovative medical practices and ultimately benefits patient care. With its unwavering commitment to delivering exceptional medical services, Kobe City Medical Center General Hospital plays a vital role in advancing healthcare in Japan and beyond, ensuring the well-being of its patients and the community it serves.

Site PI:
Dr. Nobuyuki SAKAI

Dr. Sakai is Director of Neurosurgery at the Kobe City Medical Center General Hospital and Director of Neuroendovascular Therapy at the Institute of Biomedical Research and Innovation. He served as professor at the Kyoto University Faculty of Medicine and head physician at the National Cerebral and Cardiovascular Center before joining the Kobe City Medical Center General Hospital in 2001.

Dr. Sakai also serves on the board or as a counselor or specialist at 15 medical societies including the Japan Neurosurgical Society, the Japanese Congress of Neurological Surgeons, the Japanese Stroke Society, the Japanese Society of Endovascular intervention, the Japanese Society of Cerebral Blood Flow, and Metabolism, the Japanese Society for Neuroendovascular Therapy.

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/