NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

DECEMBER 2022 | VOLUME 1 | ISSUE 9

FASTEST

FVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Bath

Investigator meetings are a great way to promote trials, remind attendees about the protocol and answer questions. We were delighted to hold a short face-to-face investigator meeting involving FASTEST at last week's 1600-participant UK Stroke Forum. We were pleased to welcome 28 colleagues from 25 different hospitals to the meeting, which was shared with two other ICH trials: TICH-3 (tranexamic acid for acute ICH) and MACE-ICH (mannitol for ICH-related cerebral oedema). Most attendees came from sites not intending to take part in FASTEST so hopefully we have sparked their interest! Two questions came up for FASTEST, first about sites taking part in more than one ICH trial (yes!) and the second on consent in patients lacking capacity. Please consider holding your own investigator meetings, perhaps at your own national stroke conference.

Philip M Bath FRCP DSc FMedSci
Nottingham City Hospital
Head, Division of Clinical Neuroscience
Stroke Association Professor of Stroke Medicine
University of Nottingham
Emeritus NIHR Senior Investigator

Please join us for the *FASTEST* Monthly Webinar

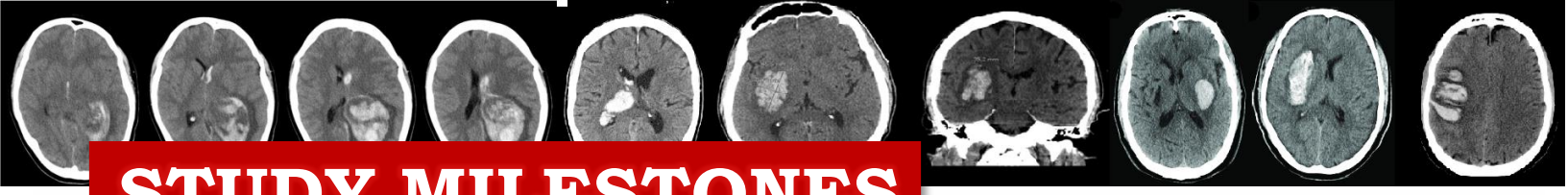
Wednesday October 19th, 2:00-3:00 pm EST

- Dr. Sven Poli from Tubingen University Hospital, Tubingen, Germany will be presenting their case and sharing their experience of enrollments at their center.
- FASTEST pharmacy will give a presentation addressing issues with study drug administration and syringes.
- NCC will be discussing the e-Consent process in detail.
- Many important issues will be discussed by the PI, and NDMC in the upcoming webinar.

Join Zoom Meeting
https://nam11.safelinks.protection.outlook.com/?url=https%3A%2F%2Fucincinnati.zoom.us%2Fj%2F95768343105%3Fpwd%3DZjYwZ0tNakxsN01qMmhPOE15N21Jdz09&data=05%7C01%7Cquadrisd%40ucmail.uc.edu%7C7b2505f4647443dd6b2e08da7ec1eb4c%7Cf5222e6c5fc648eb8f0373db18203b63%7C1%7C0%7C637961668587750683%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTil6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=40q90l8dB9QtZj9P5aZ0BeWkvzCsNx1WgQL9cFmlSHQ%3D&reserved=0

Meeting ID: 957 6834 3105
Passcode: 111641

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



STUDY MILESTONES

Total Sites Released to Enroll: **45** (**21** USA, **24** OUS: **4** Germany, **14** Japan, **1** Spain, **4** Canadian, **1** UK)

Total MSUs Released to Enroll: **6** (**5** US and **1** OUS)

Total Randomization = **67**

- US Randomizations: **18**,
- International randomizations: **49** (**11** Canadian, **3** Germany, **32** Japan, **3** Spain)

Randomization last month = **17**
Total Screen Failures = **311**
Subjects Randomized by MSU = **1**
Subjects Terminated Early = **0**
eConsent Used = **0**
Remote Consent Used = **0**

CALENDAR OF EVENTS

Upcoming *FASTEST* Monthly Webinar: **Wednesday, December 21st @ 2:00-3:00 pm EST**

FASTEST study team office hours: **Monday, December 19th @ 2:00 pm EST**

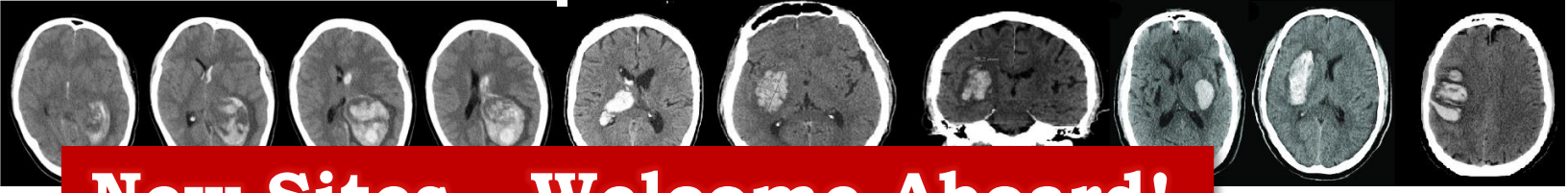
Important Note

Annual Continuous Review:
For all U.S. sites that have cIRB approval please submit your continuing review form to Advara before **Dec 16th for review.**

CTA amendments:
If you site has not return the signed CTA amendment. Please get it back to us as priority. Kindly reach out to Emily Stinson (stinsoey@ucmail.uc.edu) if you have any questions.

REDCap – eConsent Access & Training:
Please have the REDCap administrative users for your site view the REDCap training video and fill out the required training attention at the end. This will help us maintain our part 11 compliance requirements. https://redcap.link/StrokeNet_eConsent_Training.

Kindly send us the **2 or 3 individuals** who you want to have administrative access to manage eConsent at your site in REDCap. We have a new training requirement for admin users now. Please have the administrative users view the training video and fill out the required training attention at the end. This will help us maintain our part 11 compliance requirements.



New Sites... Welcome Aboard!

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

Temple University Hospital, Philadelphia, PA

Site PI:
Nina T. Gentile, MD

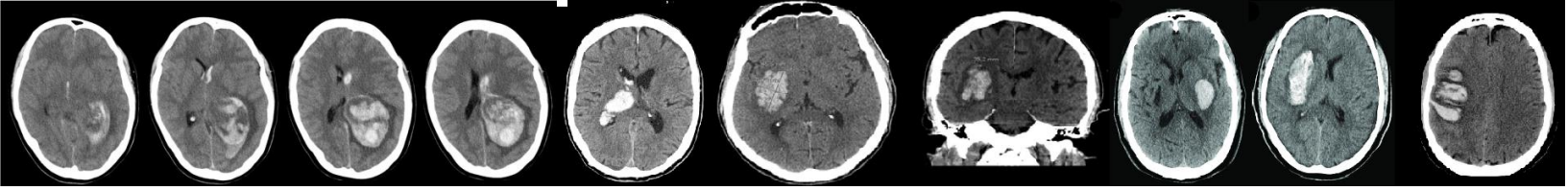
Sunnybrook Health Sciences Center, Toronto, ON, Canada

Site PI:
Houman Khosravani, MD PhD

Congratulations on First Enrollment!!

Congratulations to Dr. Takayuki HARA and his team at the Toranomon Hospital, Tokyo, Japan for enrolling their first subject in *FASTEST*.

Congratulations to Dr. Naoto KIMURA and his team at the Iwate Prefectural Central Hospital, Morioka, Japan for enrolling their first subject in *FASTEST*.



Congratulations to Dr. Mouhammad JUMAA and his team at the Toledo Hospital, Toledo, OH for enrolling their first subject in *FASTEST*.

Congratulations to Dr. Chung-Huan SUN and his team at the The Queen's Medical Center, Honolulu, HI for enrolling their first subject in *FASTEST*.

FAQs

QUESTION CORNER

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.

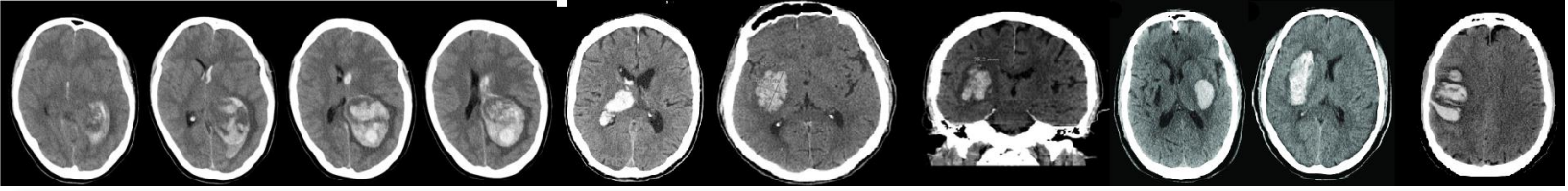
Q: Can we use the GCS from the ER staff?
A: Yes, as long as the GCS from the ER staff (licensed physician or nurse) is recorded in your EMR notes.

Q: If the data (ex. NIHSS, mRS, GCS etc.) is recorded in our EMR, you won't be expecting the hard copy NIHSS form to be in our subject binder, correct?
A: Please refer to the FASTEST Data Collection Guidelines on page 3. As per the guidelines specially the first two points (as below), the eCRFs should serve as the source document and can be used for site monitor review.

- Unless otherwise indicated, data can be directly entered into eCRFs, whereby the eCRF becomes the source document. A general comment should indicate that the eCRF is the source document to assist site monitors and reduce data clarification requests.
- eCRFs should be completed utilizing documentation from the legal medical record or other source data, whether it is paper or electronic. These source documents should be retained for site monitor review.

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 queriers 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: Does the "rounding" rules apply to the drug dose? The patient's weight was 52.8, but we used the line for 51-52 kg for the dosing. It ended up being a 0.1 difference in dose. (The syringe only gives .5 marking, so it was hard to gauge the 0.1 anyway).

A: Yes, as explained above, **the rounding rule can be applied to the drug dose.** Estimated wait is appropriate to use, especially since we can't always wait for a stroke patient to be weighed. But since in this current example the weight of the patient was 52.8 (almost 53), it should have been rounded off as 53 kg. However, using 52 kg will not be of any harm to the patient or the study. As emphasized above, **we do require the study team to eventually enter the actual weight for the patient.**

Q: Is it required to utilize the histidine syringe provided OR it's okay to utilize our local syringe to administer study drugs for FASTEST?

A: We encourage sites to **stock appropriately sized syringes from local inventory alongside the study drug kits** (ex: 10 ml syringe) for two reasons:

1) To draw up the appropriate dose accurately - The volume on the histidine syringe provided is measured in 0.5ml increments (see picture). However. According to the dosing table and administration instructions, drug is given in 0.1 ml increments (example: for patient weight 90 kg, per USA and Canadian dosing card, dose administered should be 7.2 ml) A standard 10ml syringe is marked in 0.2ml increments and can be used for more accurate administration.

2) To administer study drug through incompatible needleless connector - The prefilled Histidine glass syringe provided in the kit (see picture) is compatible with a standard Luer-lock connector. However, some needleless connectors for intravenous catheters are incompatible with the glass diluent syringes (for example, certain connectors with an internal spike, such as Clave®/MicroClave®, InVision-Plus®, InVision-Plus CS®, InVision-Plus® Junior®, Bionector®), and their use can damage the connector and affect administration. In these scenarios, once the study drug is reconstituted (most likely you will need the two vials), leave the histidine syringe attached until it is ready for use. When it's ready to use, obtain an appropriate sized syringe from local inventory, remove the pre-filled histidine syringes from the study vials and use the "local" syringe to draw up the appropriate dose accurately.

Q: if we have a subject that needs 2 syringes, how do the other sites handle that. Do they try to put them into one syringe before doing the bolus, or do they just remove the first one and then attach the second one after the first is done.

A: The two syringes issue has been confusing for some sites. We are recommending that sites use the two histidine diluent syringes for mixing the drug only. Once the vial is reconstituted with the histidine, we recommend that the histidine syringe be removed, and the actual dose of drug be drawn up with a single 10ml syringe from the site's local inventory. So, say a patient needed 8.2ml of drug, they would reconstitute the two vials with the histidine syringes, remove the histidine syringes, and then use a single 10ml syringe to draw up 5ml from one vial and 3.2ml from another. This is advantageous because you only need one syringe for the dose, and the 10ml syringes are marked in 0.2ml increments so it is easier to draw up a specific dose.

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.

1. **Temple University**
2. **Sunnybrook Health Science Center Canada**

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

1. **Riverside Methodist**
2. **OSU**
3. **Barnes Jewish**
4. **Ascension St. Johns**

Top Enrolling Site

Congratulations to **National Cerebral and Cardiovascular Center, Osaka, Japan** for being the highest enrolling sites in the study.

Subjects enrolled = 10!!

Congratulations to the November Enrolling Sites!

National Cerebral and Cardiovascular Center, Osaka, Japan	**5 Subject**
Kobe City Medical Center General Hospital, Kobe, Japan	**3 Subject**
Kyorin University Hospital, Tokyo, Japan	**1 Subject**
Japanese Red Cross Kyoto Daini Hospital, Kyoto, Japan	**1 Subject**
Toranomon Hospital, Tokyo, Japan	**1 Subject**
Grady Memorial Hospital, Atlanta, GA	**1 Subject**
Toledo Hospital, Toledo, OH	**1 Subject**
University of Calgary - Foothills Medical Centre, Calgary, AB, Canada	**2 Subject**
Kagoshima City Hospital, Kagoshima, Japan	**1 Subject**
The Queen's Medical Center, Honolulu, HI	**1 Subject**

Looking forward to 1st Enrollment from UK!

SCIENCE CORNER

RESEARCH ARTICLE OF THE MONTH

Prehospital Blood Pressure and Clinical and Radiological Outcomes in Acute Spontaneous Intracerebral Hemorrhage

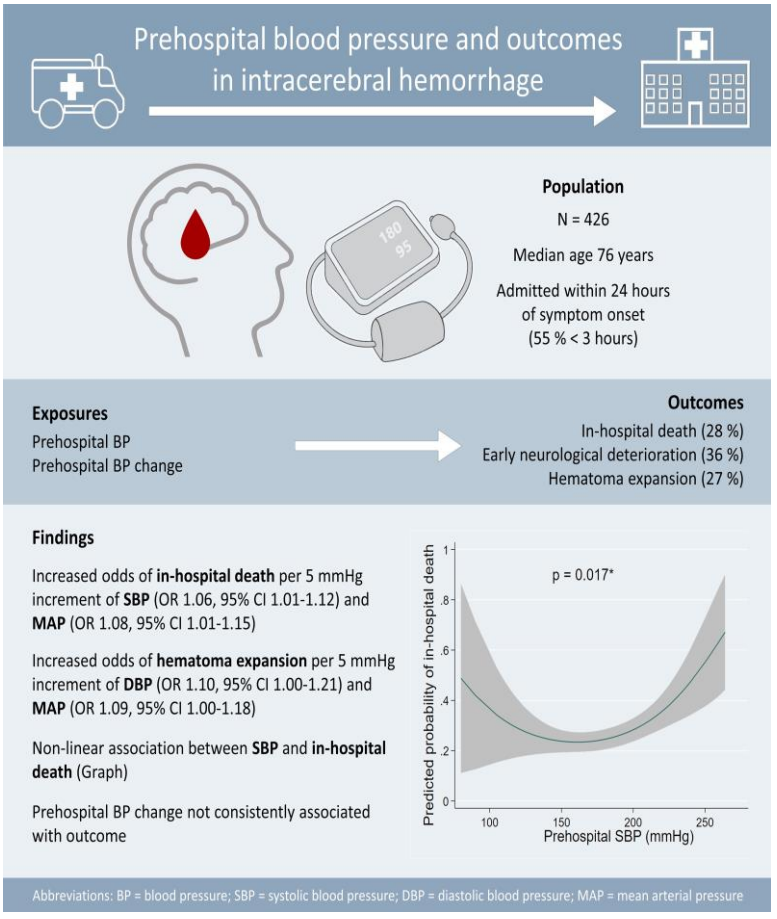
Kristin Tveitan Larsen, Maiken Nordahl Selseth, Silje Holt Jahr, Vigdis Hillestad, Nojoud Koubaa, Else Charlotte Sandset, Ole Morten Rønning and Espen Saxhaug Kristoffersen

Originally published 17 Oct 2022 / https://doi.org/10.1161/STROKEAHA.121.038524 / Stroke. 2022;53:3633–3641

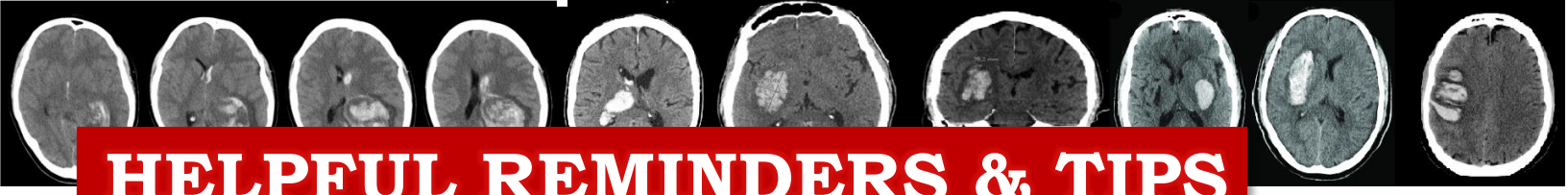
Background:
High blood pressure (BP) is associated with poor outcome in acute spontaneous intracerebral hemorrhage. Little is known about the predictive value of prehospital BP in intracerebral hemorrhage. We aimed to investigate the relationship between prehospital BP and clinical and radiological outcomes.

Methods:
This is a retrospective, hospital-based study of all adult intracerebral hemorrhage patients admitted within 24 hours of symptom onset to a large primary stroke centre during 2012 to 2019. The first prehospital and on-admission BP were recorded as systolic BP, diastolic BP, mean arterial pressure, and pulse pressure. The absolute differences between prehospital and on-admission BP were calculated (BPchange). Primary outcomes were in-hospital death, early neurological deterioration, and hematoma expansion. Associations between prehospital BP, BPchange, and outcomes were explored by regression with adjustment for relevant confounders.

Results:
We included 426 patients aged median 76 (interquartile range 67–85) years and 203 (48%) were female. Median prehospital systolic BP was 179 (interquartile range 158–197) and diastolic BP was 100 (interquartile range 86–112) mm Hg. In-hospital death occurred in 121/426 (28%), early neurological deterioration in 107/295 (36%), and hematoma expansion in 50/185 (27%) patients. There were linear associations between 5 mm Hg increment of prehospital systolic BP (odds ratio 1.06, [95% CI, 1.01–1.12]) and mean arterial pressure (odds ratio 1.08, [95% CI, 1.01–1.15]) and in-hospital death, and between 5 mm Hg increment of prehospital diastolic BP (odds ratio 1.10, [95% CI, 1.00–1.21]) and mean arterial pressure (odds ratio 1.09, [95% CI, 1.00–1.18]) and hematoma expansion. There was a nonlinear association between prehospital systolic BP and in-hospital death. No consistent associations between prehospital BP change and outcomes were found.



Conclusions:
In patients with acute intracerebral hemorrhage, elevated prehospital BP parameters were associated with in-hospital death and hematoma expansion. Changes in prehospital BP were not consistently associated with outcome. A possible U-shaped association between prehospital BP and in-hospital death needs further investigation.



HELPFUL REMINDERS & TIPS

For Project Managers and Study Teams

- **Pharmacy documents in Toolbox:** Any documents that are pharmacy/drug related will be categorized as "pharmacy" in the toolbox starting on/before **2/1/2023**.

- **Adding new study members:** Please update your DOA logs and upload the training documents to WebDCU as soon as you add a new study member to your FASTEST study team. All sites currently released to enroll kindly make sure your DOAS are up to date.

- **Reporting SAE within 24 hours:** We would like to emphasize all sites on the timely reporting of the SAEs. Kindly note that all SAEs must be reported in WebDCU™ **within 24 hours** of site awareness of the event and must be followed for the duration of the study follow-up or until resolution, whichever comes first.

- **CRF Completion within 24 hours:** We would like to emphasize all sites on the timely completion of the case report forms (CRFs) **within 24 hours** of the visit (Baseline, 1-hour, 24-hour, Day 4/ Discharge). For the follow-up visits (Day 30, Day 90, Day 180, and End of study) which have a window of ±14 days please fill out the CRS as soon as the follow up visit has been completed.

- **Clarification regarding Emerald Temp Loggers:** We would like to clarify the misperception among sites receiving the Emerald loggers from StrokeNet NCC for their MSUs and EDs that the NCC is not responsible to track or note any temperature excursions. We are ONLY providing technical assistance to set up the loggers for the respective sites. Like any other trial, **it is the sole responsibility of the site to note any temperature excursions** and inform us duly so that NOVO can be informed accordingly.

- **Syncing & Accessing Data from the Cloud:** Kindly ask the MSU staff to sync the Temp loggers regularly so that the data can be uploaded to the cloud. **You can download the PDF of the monthly temp log from the cloud for study records and internal or external audits.** No need to fill out a temp log manually. If the PSC or the MSU staff having any issues with the device kindly notify FASTEST Project Manager, Syed Quadri quadrisd@ucmail.uc.edu to further assist you with troubleshooting the device.

- **Requesting 48 hrs recording from the data logger:** We are asking all sites receiving the Emerald loggers to send us a 48 hrs recording/data after placing the device in the MSU or ED and before moving the study drug. This is to make sure that the temp. logger is set up properly and recording the data. Once we give approval you can move the drug to the MSU or ED.

- **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

Hamilton General Hospital, Hamilton, ON, Canada

The Hamilton General Hospital (HGH) is a major teaching hospital in Downtown Hamilton, Ontario, Canada, affiliated with the Michael G. DeGroote School of Medicine at McMaster University. Founded in 1848, Hamilton General Hospital (HGH) was the first hospital in Hamilton. It became a part of Hamilton Health Sciences in 1996 when Hamilton General, Henderson General, McMaster University Medical Centre, McMaster Children's Hospital and Chedoke Hospital merged.

HGH is one of the largest cardiac surgical centers in Canada, performing over 1,600 open heart surgeries annually. HGH is also one of the largest trauma, neurosurgery, and stroke centers in Canada. They perform over 1000 neurosurgical procedures annually. It is an accredited center of Distinction in Stroke Services for demonstrating clinical excellence in Acute Stroke Services and Inpatient Stroke Rehabilitation

Site PI: Ashkan Shoamanesh, MD

Dr. Shoamanesh is the founding Director of the Hemorrhagic Stroke Research Program within the Stroke and Cognition Program at the Population Health Research Institute at Hamilton Health Sciences. He is an Associate Professor of Medicine (Neurology) at McMaster University, where he holds the Marta and Owen Boris Chair in Stroke Research and Care.

Dr. Shoamanesh main research focus is the characterization of hemorrhage-prone cerebral small vessel disease and the optimization of clinical care in this patient population. Towards this aim, he leads as principal investigator of the global phase III ENRICH-AF trial (NCT03950076) investigating optimal stroke prevention in intracranial hemorrhage survivors with atrial fibrillation at over 300 sites in 22 countries and is the founding chair of the Canadian Hemorrhagic Stroke Trials InitiatiVE (CoHESIVE; www.phri.ca/cohesive/). He additionally serves on the Steering and/or Executive Committees of several public and industry funded international randomized trials targeting secondary stroke prevention and the reversal of anticoagulant-related hemorrhage.

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/

NIH StrokeNet
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