NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

JULY 2022 | VOLUME 1 | ISSUE 4

FASTEST

EVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Dowlatshahi

The momentum is building! Summer 2022 is seeing more and more FASTEST sites launching across the world. I'm excited to see the enrollment emails coming in; a friendly competitive spirit is emerging. I encourage our onboarding sites to keep pushing forward and leverage this momentum. Consider working with your ED staff and CT techs to keep the drug close by to minimize delays. In Ottawa, we keep it in our CT scanner room so we can treat as soon as a patient comes off the gurney. Each site is encouraged to explore local solutions to reduce door to needle times – we've all done this before for ischemic stroke. Let's do it again and change the future of ICH.

Dar Dowlatshahi MD PhD

Vice Chair Research, Department of Medicine
University of Ottawa, Canada
FASTEST Canadian National PI

Please join us for the FASTEST Monthly Webinar

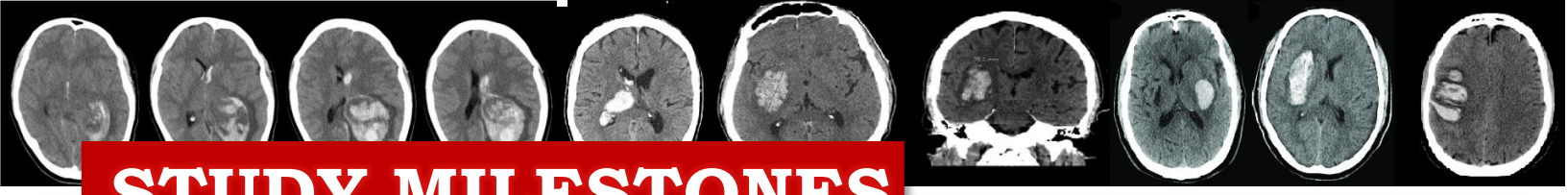
Wednesday July 20th, 2:00-3:00 pm EST

- Dr. Broderick will be discussing "Ischemia in intracerebral hemorrhage: A comparative study of small-vessel and large-vessel diseases".
- Dr. Royya Modir from UCSD Medical Center - Hillcrest Hospital, San Diego, CA. will be presenting their recent case and sharing their experience.

Zoom:
https://ucincinnati.zoom.us/j/96899791261?pwd=d1VtcEppL0RoTkFxQTV1WW54SERaZz09

To join Zoom Meeting -- Meeting ID: 968 9979 1261
Passcode: 710245 or call in. To find your local number, go to https://ucincinnati.zoom.us/u/addjGYPaHx

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



STUDY MILESTONES

Total Sites Released to Enroll: **25** (**12** USA, **2** Germany, **9** Japan, **1** Spain, **1** Canadian)

Total Randomization = **13**

- US Randomizations: **9**,
- International randomizations: **4** (2 Canadian, 2 Germany)

Randomization this month (last 30 days) = **3**

Total Screen Failures = **51**

Subjects Randomized by MSU = **0**

Subjects Terminated Early = **0**

eConsent Used = **0**

Remote Consent Used = **0**

CALENDAR OF EVENTS

Upcoming *FASTEST* Monthly Webinar: **Wednesday, July 20th @ 2:00-3:00 pm EST**

Upcoming EFIC panel review dates for EFIC plans: **Mondays, July 11th and 25th, and August 8th and 22nd 2022**

FASTEST study team office hours: **Monday, July 18th @ 2 pm EST**

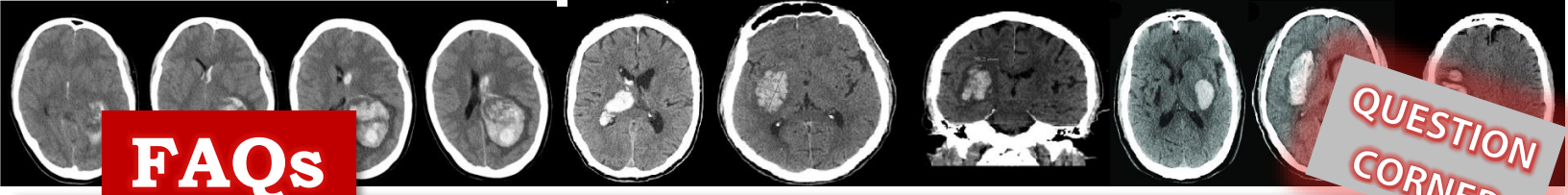
SAVE THE DATE!!

FASTEST Investigator's Meeting

Monday November 7th, 2022

2:00 - 4:00 pm EST

Dr. Broderick and the StrokeNet NCC would like to invite all *FASTEST* investigators to attend the Annual *FASTEST* Investigator's Meeting to be held in the November 2022. The meeting will be held virtually. The invite and meeting link will be sent to all *FASTEST* investigators in November.



FAQs

QUESTION CORNER

Q: There is hematoma expansion/growth in our patient without clinically significant neurological deterioration/ worsening (24 hrs. NIHSS unchanged from baseline NIHSS?
A: Hematoma expansion/growth without clinically significant neurological deterioration/worsening should be documented as non-serious AE. This is similar to how we document the rise in troponin levels without clinically significant deterioration as non-serious AE.

Q: Do we also report AE and what is the timeline to report the Non-serious AEs?
A: All non-serious adverse events observed by the investigator or reported by the participant will be recorded from the time of randomization through **Day 4.** Kindly make note that these non-serious adverse events need to be reported in WebDCU™ within **5 days** of the site investigator's awareness of the event.

Q: Can we use our own temp. monitoring logs?
A: All areas where study drug is stored (including MSUs) must be monitored continuously for temperature excursions and the temperature monitoring system, at a minimum, must provide a daily minimum and maximum temperature. Sites may use their own institution-specific or electronic study drug temperature monitoring log to document temperature readings if such temperature log is deemed equivalent. The original Study Drug Temperature Log must be filed in the master file at the site and available for monitoring visits.

Q: Who can compound the study drug?
A: Trained Pharmacy staff, physicians (PI AND Sub-I) and trained Coordinators with a **medical license** including drug compounding within their scope of practice can compound and prepare study drug for administration. There is no need to delegate this responsibility on the DoA and should be a study team determination. Training on compounding study drug video can be found in the WebDCU training campus under the FASTEST project WebDCU™ Campus - Training Center (musc.edu).

Q: What is the timeline to report SAEs?
A: All SAEs must be reported in WebDCU™ within **24 hours** of site investigator's awareness of the event and must be followed for the duration of the study follow-up or until resolution, whichever comes first. Kindly note that all SAEs will be recorded from the time of randomization through **Day 90**. However, mortality is reported through end of study **(day 180).** Kindly remember that Death due to the natural history of ICH will be recorded as a non-related SAE. Additionally, all serious but known complications of ICH (i.e., malignant brain edema) will be recorded as non-related SAEs. Please refer to our study MOP sent to all the participating sites earlier.

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

Congratulations on First Enrollment!!

Universitätsklinikum Tübingen

Congratulations Dr. Sven Poli and his team at the Tübingen University Hospital, Tübingen, Germany 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.

UMass Memorial Medical Center, Worcester, MA

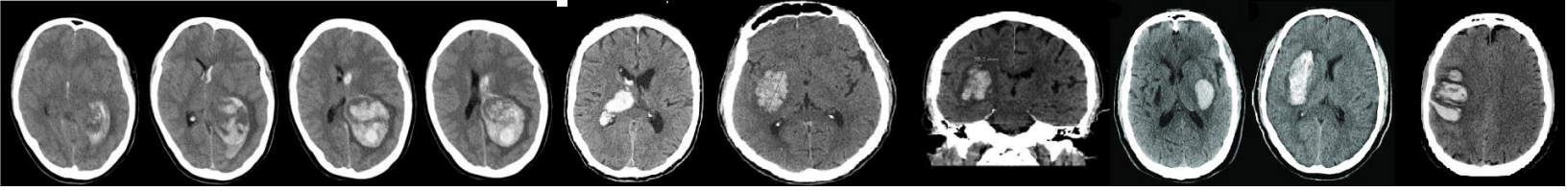
Site PI:
Adalia H. Jun-O'Connell, MD

Stony Brook University Hospital, Stony Brook, NY

Site PI:
Jason Mathew, DO

University of Chicago Medical Center, Chicago, IL

Site PI:
Christopher L. Kramer, MD



Nakamura Memorial Hospital, Sapporo, Japan

Site PI: Kenji Kamiyama MD

Kyorin University Hospital, Tokyo, Japan

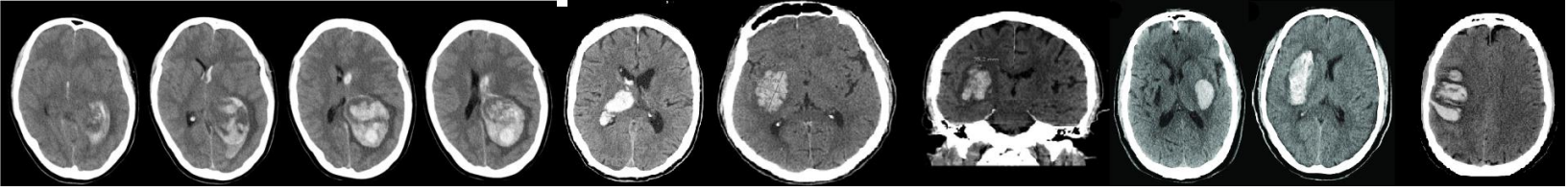
Site PI: Teruyuki Hirano, MD, PhD

Kobe City Medical Center General Hospital, Kobe, Japan

Site PI: Nobuyuki Sakai MD

Kyushu Medical Center, Fukuoka, Japan

Site PI: Yasushi Okada MD



Jichi Medical University Hospital, Shimotsuke, Japan

Site PI: Shigeru Fujimoto MD, PhD

Gifu University Hospital, Gifu, Japan

Site PI: Toru Iwama MD

Kagoshima City Hospital, Kagoshima, Japan

Site PI: Fumio Miyashita MD

Niigata City General Hospital, Niigata, Japan

Site PI: Kenichi Morita, MD, PhD

SHOUT OUTS!!

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

Thank you to the 4 sites preparing for readiness**:**

1. **Central DuPage**
2. **University of Utah**
3. **The Queens MC**
4. **Memorial City**

Thank you for the 2 sites preparing for Advarra CIRB submission:

1. **University of Minnesota**
2. **Fairview Southdale**

Welcome to new sites that have officially joined FASTEST

1. **University of Buffalo**
2. **UC Davis**
3. **Mayo Clinic Jacksonville**

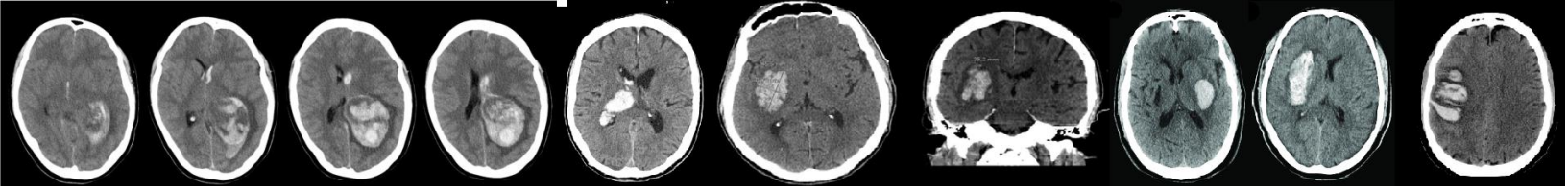
Top Enrolling Site

Congratulations to **Memorial Hermann Hospital-Texas Medical Center** for being the highest enrolling site in the study.

Subjects enrolled = 5!!

Congratulations to the Enrolling Sites Past Month (30 days)!

1. Tubingen University Hospital, Tubingen, Germany — 2 Subjects
2. UCSD Medical Center - Hillcrest Hospital, San Diego — 1 Subjects



Use of Lipid-Lowering Drugs After Intracerebral Hemorrhage

Ashkan Shoamanesh and Magdy Selim

Originally published 6 Jun 2022 / https://doi.org/10.1161/STROKEAHA.122.036889 / Stroke. 2022;53:2161–2170

Hyperlipidemia is common in patients with intracerebral hemorrhage (ICH). Accumulating evidence indicates that patients with ICH are at risk for future hemorrhage recurrence, cardiovascular disease, and ischemic stroke and highlights the importance of secondary prevention of vascular events after ICH. Although the benefits of intensive treatment of hyperlipidemia for reducing ischemic cardiac and vascular events in patients with ischemic stroke are well established, the benefit versus harm in patients with ICH are less clear. Epidemiological studies suggest that hyperlipidemia is protective against ICH and that intensive lowering of lipids is associated with increased risk for ICH. Similarly, although currently available lipid-lowering treatments have been thoroughly studied in patients with ischemic cardiac and vascular disease, only few randomized trials of these therapies included a very small number of patients with history of ICH. Thus, limiting any definitive conclusions regarding the safety and net benefit of these treatments in ICH populations. Currently, there is no consensus regarding the optimal strategy for management of hyperlipidemia after ICH. In this article, we review relevant literature to outline the competing risks and benefits of lipid-lowering treatments in this vulnerable patient population. We suggest a treatment paradigm based on available data but note that data from dedicated randomized trials are needed to build the necessary evidence to guide optimal lipid-lowering strategy in patients with a history of ICH.

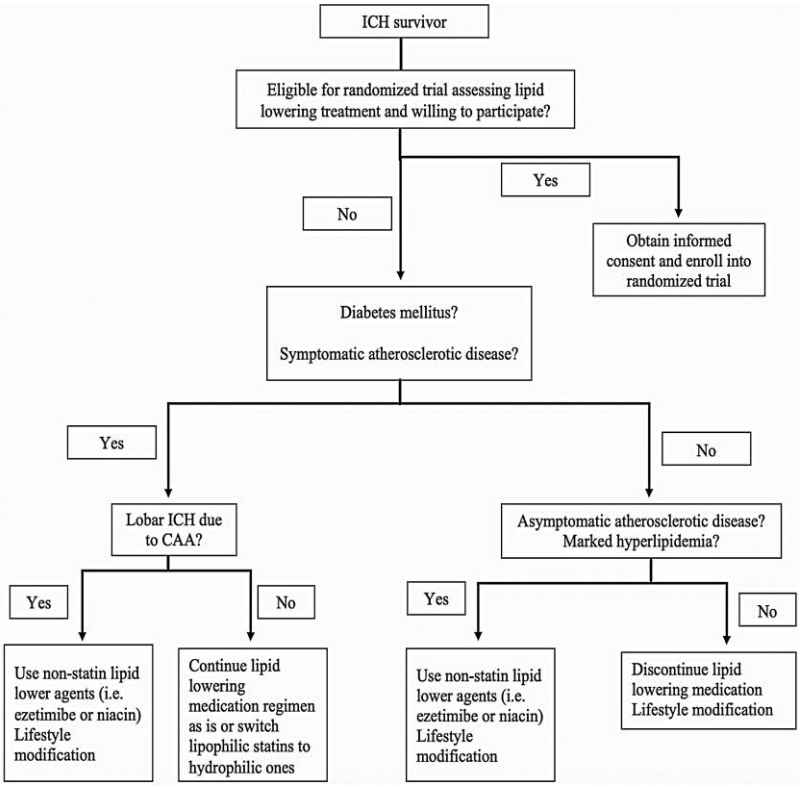


Figure: Proposed treatment algorithm for hyperlipidemia after intracerebral hemorrhage (ICH) based on the totality of available evidence. CAA indicates cerebral amyloid angiopathy.

How Then to Approach the Management of Hyperlipidemia in Patients With ICH?

The Figure outlines our suggested treatment algorithm derived from the totality of available evidence at present. We emphasize the uncertainties in our suggestions in the absence of direct evidence from randomized controlled trials to inform the best strategy for statin use in patients with ICH. When approaching ICH survivors with hyperlipidemia we endorse that they first be considered for participation in randomized clinical trials addressing optimal lipid-lowering treatment in this population. Next, we base our decision based on the presence/absence of diabetes, and history of symptomatic atherosclerotic disease (coronary, peripheral, or stroke/TIA from large artery atherosclerotic disease). In patients without these comorbidities, we would not use statin but may consider alternative agents such as ezetimibe in cases with markedly elevated cholesterol levels or documented asymptomatic atherosclerotic disease. In patients with deep ICH and history of familial hypercholesterolemia, diabetes, or symptomatic atherosclerotic disease, we would continue the patient's pre-ICH lipid-lowering regimen with a preference for avoiding high-intensity dosing and switching lipophilic statins to hydrophilic ones. In patients with lobar ICH and suspected cerebral amyloid angiopathy, and history of diabetes or symptomatic atherosclerotic disease, we favor avoiding statins and using alternative lipid-lowering treatments, e,g, ezetimibe, instead. If the use of statins is considered, we suggest avoiding high-intensity dosing and lipophilic statins. We do not favor the use of PCSK9 inhibitors as alternatives to statins except in patients with familial hypercholesterolemia at the present time given paucity of data regarding the use of PCSK9 inhibitors in patients with history of ICH and the uncertainty regarding the role of excessive reduction in cholesterol levels with these drugs in predisposing to ICH recurrence. In all cases, we ensure to maintain strict long-term blood pressure control to a target of <130/80 mm Hg to reduce the risk of ICH recurrence.

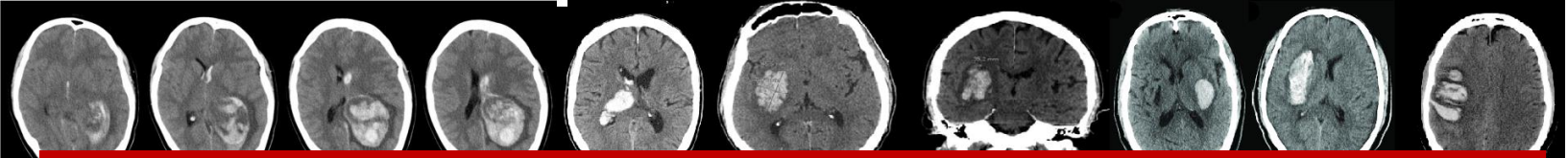
HELPFUL REMINDERS & TIPS

For Project Managers and Study Teams

- Newly approved study wide documents available in the Tool Box in WebDCU
  - **Condensed Radio advertisement** less than 60 sec. Can be used for sites still working on EFIC public disclosures. **REMINDER:** All radio advertisements recordings need to be submitted for CIRB approval prior to ad running.
  - **Consent conversation script**- This is **NOT** a consent document but a script of a conversation that can be used to help explain EFIC and emergency consent to LAR's and/or subjects.
- **Screen failure logs: Please update the screen failure logs in WebDCU screen failure data is very important to the study.**
- **CTA Amendments:** Please make sure the amended CTA's have been returned to UC for execution.
- eICD templates are being sent to CIRB approved sites that have the amended CTA's fully executed.
- **Uploading of documents:** Please remember to pull approval letters and CIRB approved documents from the CIRBI portal and upload them to WebDCU. It is the sites responsibility to keep their site documents updated and uploaded to WebDCU. If you have questions about where to upload your documents please reach out to Emily Stinson stinsoey@ucmail.uc.edu
- **Study team office hours:** Please join the FASTEST study team office hours. Calendar invites have been sent out. This is an informal meeting to answer questions and provide additional training and support. We will meet biweekly on **Monday's at 2pm EST each month.** We highly recommend that you attend regularly as we plan to touch on many topics. We especially encourage new study coordinators to join to help get acclimated to FASTEST as well as spend time collaborating with different FASTEST study sites.
- **As you are completing EFIC events, please complete the CC and PD forms in WebDCU™**. The updated EFIC Forms Resource Guide is available in WebDCU™ (in the Toolbox under Project Documents) and is a very helpful tool for completing these forms. The FASTEST webinar from March 16th, 2021 (available at https://www.nihstrokenet.org/fastest/webinars) can provide additional tips. If you have questions in completing the forms, please feel free to reach out to the NCC. The NCC is also happy to review the forms and provide guidance and feedback along the way to ensure completeness.

From the *FASTEST* Central Pharmacy Team

- **Temperature excursion and monitoring: Please be very vigilant about temperature excursion and temperature monitoring documentation.**
- **Study Drug Shipment:** The Central Pharmacy will ship FASTEST study drugs few days prior to the readiness call. *FASTEST* IP will be shipped refrigerated. The initial study drug shipment will contain a total of two study drug kits to sites with one enrolling location (ED or MSU) and four study drug kits to sites that have two enrolling locations (ED+MSU) or 2 Eds
- **For the US sites**: Please upload the following regulatory documents into WebDCU for your site pharmacy to receive IP:
  - Institutional Pharmacy License
  - Institutional Drug Destruction Policy/SOP
  - Clinical Site Drug Shipping Address, Phone Number, and Contact Person
  - Adding Pharmacy Personnel to WebDCU DOA



INTERNATIONAL SITE OF THE MONTH

Tübingen University Hospital, Tübingen, Germany

Founded in 1805, the Tübingen University Hospital is one of the 34 university hospitals in Germany that contribute to the successful combination of high-performance medicine, research and teaching. More than 400,000 in - and outpatients from around the world benefit from this connection of science and practice each year. Its experts collaborate across disciplines and offer state-of-the-art research-based treatment to all patients. The University Hospital does research to improve diagnostics, therapies, and healing processes.

Medical research in the Neurosciences is part of the University of Tübingen's Excellence Cluster. UKT scientists are members of the Werner Reichardt Centre for Integrative Neurosciences (CIN) and carry out research at the Hertie Institute for Clinical Brain Research (HIH). They also work closely with the Faculty of Medicine. Oncology and Immunology, Infection Biology, Vascular Medicine, and Diabetes are further focus areas of research at the UKT. The University Hospital is a reliable partner in four of the six German Centres for Health Research (DZG) created by the Federal Government.

As the region's largest employer, the University Hospital employs around 9,000 full and part-time employees. With around 600 apprentices in over ten different professions, the University Hospital Tübingen is the largest provider of apprenticeships in the region.

Site PI: Dr. Sven Poli,

MD MSc FESO FWSO FAHA

Dr. Poli is the Vice Medical Director at Department of Neurology & Stroke at University of Tübingen. The research focus of Dr. Poli's Stroke and Neuroprotection Laboratory is to find new and to optimize existing neuroprotective strategies that can help minimize brain damage after stroke. Dr. Poli and his team study and characterize molecular mechanisms involved in ischemic-hypoxic damage and reperfusion-reoxygenation-induced neuronal death. His aim is to provide translational research with a close link to clinical application.

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 ***FASTES*** study please visit : https://www.nihstrokenet.org/fastest/home

For prior ***FASTES*** 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/

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