NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

JUNE 2022 | VOLUME 1 | ISSUE 3

FASTEST

EVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Naidech

One of life's greatest gifts is the opportunity to work hard at work worth doing. We have been chipping away at the margins of treatment for intracerebral hemorrhage (ICH) for years for small numbers of patients, such as ICH in the presence of anticoagulant medications. FASTEST is a once-in-a-career opportunity to show efficacy of a medication for spontaneous ICH. FASTEST has been launched and is recruiting in StrokeNet. It's crucial we support this rigorous trial to determine if acute hemostatic treatment is efficacious for patients soon after ICH symptom onset. Our patients are counting on us.

Andrew M Naidech, MD MSPH

Professor
Northwestern University
Feinberg School of Medicine
Department of Neurology
Physician Informatics Director,
Northwestern Memorial Healthcare

Please join us for the *FASTEST* Monthly Webinar

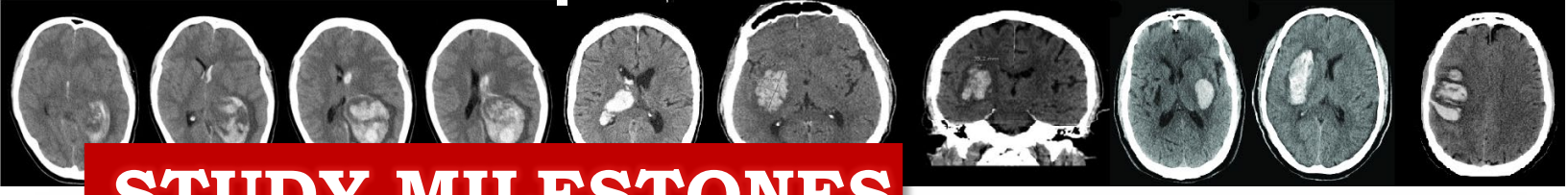
Wednesday June 22nd, 2:30-3:30 pm EST

- FASTEST PIs will present and discuss the 2022 updated Guidelines for the Management of ICH.
- NDMC will review AE and SAE reporting in WebDCU and use of Data Collection Guidelines for primary study coordinators and research managers.
- Betsy Casillo will review the Advarra process for recording reportable events (AE & SAE) in CIRBI and the process for requesting translations for our participating sites.

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: **14** (**9** USA, **2** Germany, **1** Japan, **1** Spain, **1** Canadian)

Total Randomization = **10**

- US Randomizations: **8**,
- International randomizations: **2** (2 Canadian)

Randomization this month (last 30 days) = **2**

Total Screen Failures = **26**

Subjects Randomized by MSU = **0**

Subjects Terminated Early = **0**

eConsent Used = **0**

Remote Consent Used = **0**

CALENDAR OF EVENTS

Upcoming *FASTEST* Monthly Webinar: **Wednesday, June 22nd @ 2:30-3:30 pm EST**

Upcoming EFIC panel review dates for EFIC plans: **Mondays, June 13th and 27th 2022**

FASTEST study team office hours: **Monday, June 20th @ 2 pm EST**

QUESTION CORNER

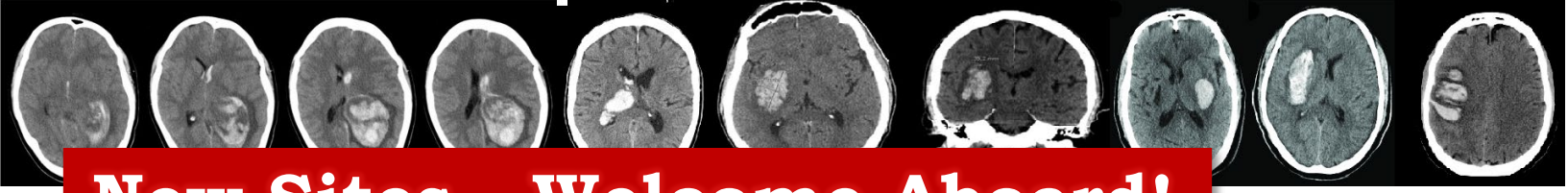
FAQs

Q: Who can compound the study drug?
A: Trained Pharmacy staff 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.

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 hese non-serious adverse events need to be reported in WebDCU™ within **5 days** of the site investigator's awareness of the event.

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

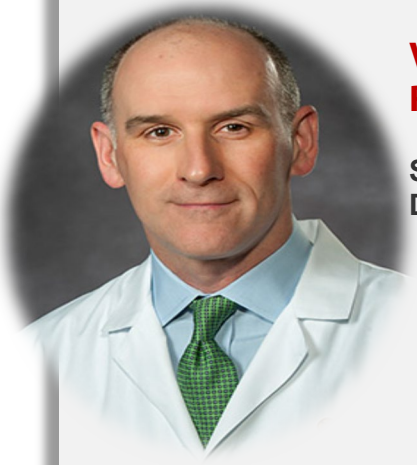


New Sites... Welcome Aboard!

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

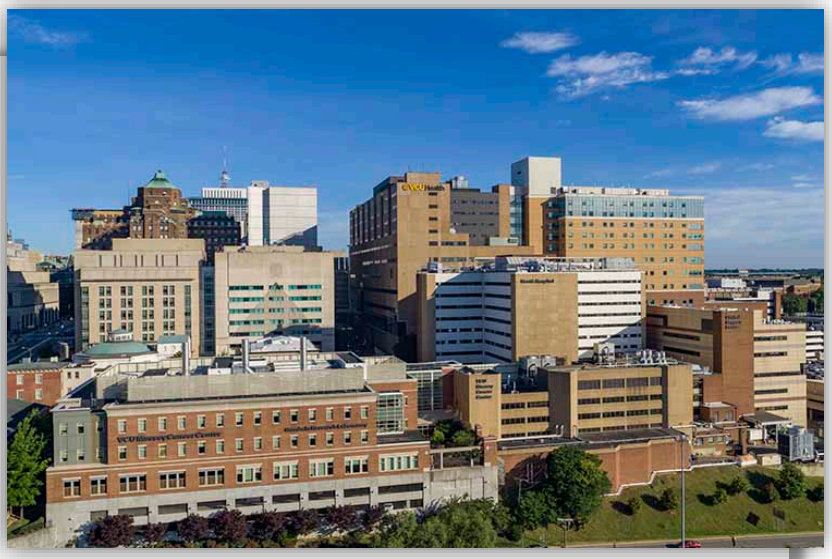
Northwestern Memorial Hospital, Chicago, IL

Site PI:
Babak S. Jahromi, MD, PhD



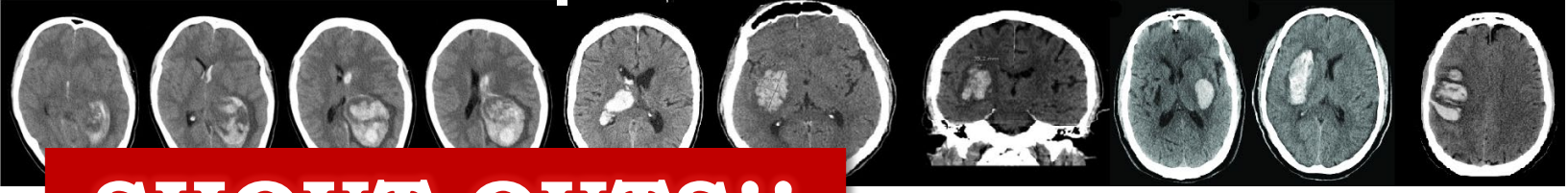
VCU Medical Center, Richmond, VA

Site PI:
Dennis J. Rivet, MD



Vall d'Hebron University Hospital (VHUH)

Site PI:
Carlos A. Molina, MD, PhD



SHOUT OUTS!!

Congratulations to all our US sites that have completed their EFIC reports and gained Advarra full study approval. Advarra shared that the FASTEST sites reviewed have been strong! Well done!

Thank you to the 5 sites preparing for readiness**:**

1. **Stoney Brook**
2. **UMass**
3. **University of Chicago**
4. **Memorial City**
5. **University of Utah**
6. **The Queens MC**

Thank you to both sites that have submitted to Advarra for CIRB review**:**

1. **Mills Peninsula**
2. **Providence St. Vincent**

Thank you for the 4 sites preparing for Advarra CIRB submission:

1. **North Shore**
2. **Prisma Health**
3. **University of Minnesota**
4. **Fairview Southdale**

Welcome to new sites that have officially joined FASTEST

1. **UF Health Shands**
2. **Intercoastal/Sarasota Memorial**
3. **Santa Barbara Cottage Hospital Link Neuroscience Institute**

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. Memorial Hermann Hospital Texas Medical Center — 1 Subject
2. UC Irvine Medical Center, Orange, CA — 1 Subject

SCIENCE CORNER

RESEARCH ARTICLE OF THE MONTH

2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage: A Guideline From the American Heart Association/American Stroke Association

Originally published5 17 May 2022 / https://doi.org/10.1161/STR.0000000000000407 / Stroke. 2022;0:10.1161/STR.0000000000000407

TOP 10 TAKE-HOME MESSAGES FOR THE MANAGEMENT OF PATIENTS WITH SPONTANEOUS INTRACEREBRAL HEMORRHAGE GUIDELINE

1. The organization of health care systems is increasingly recognized as a key component of optimal stroke care. This guideline recommends development of regional systems that provide initial intra-cerebral hemorrhage (ICH) care and the capacity, when appropriate, for rapid transfer to facilities with neurocritical care and neurosurgical capabilities.

2. Hematoma expansion is associated with worse ICH outcome. There is now a range of neuroimaging markers that, along with clinical markers such as time since stroke onset and use of antithrombotic agents, help to predict the risk of hematoma expansion. These neuroimaging markers include signs detectable by noncontrast computed tomography, the most widely used neuroimaging modality for ICH.

3. ICHs, like other forms of stroke, occur as the consequence of a defined set of vascular pathologies. This guideline emphasizes the importance of, and approaches to, identifying marers of both microvascular and macrovascular hemorrhage pathogeneses.

4. When implementing acute blood pressure lowering after mild to moderate ICH, treatment regimens that limit blood pressure variability and achieve smooth, sustained blood pressure control appear to reduce hematoma expansion and yield better functional outcome.

5. ICH while anticoagulated has extremely high mortality and morbidity. This guideline provides updated recommendations for acute reversal of anticoagulation after ICH, highlighting use of pro-tein complex concentrate for reversal of vitamin K antagonists such as warfarin, idarucizumab for reversal of the thrombin inhibitor dabigatran, and andexanet alfa for reversal of factor Xa inhibitors such as rivaroxaban, apixaban, and edoxaban.

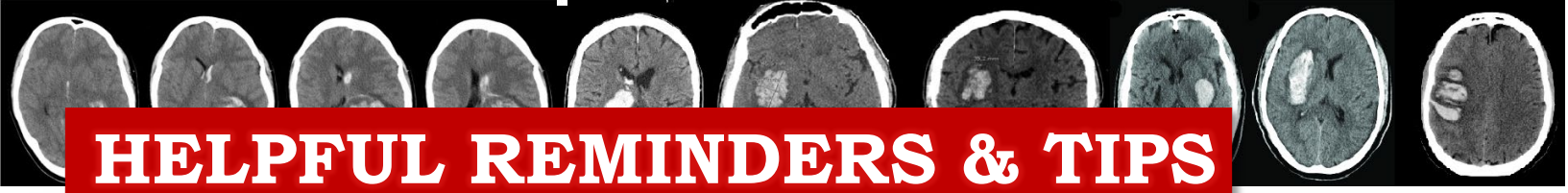
6. Several in-hospital therapies that have historically been used to treat patients with ICH appear to confer either no benefit or harm. For emergency or critical care treatment of ICH, prophylactic corticosteroids or continuous hyperosmolar therapy appears to have no benefit for outcome, whereas the use of platelet transfusions outside the setting of emergency surgery or severe thrombocytopenia appears to worsen outcome. Similar considerations apply to some prophylactic treatments historically used to prevent medical complications after ICH. Use of graduated knee- or thigh-high compression stockings alone is not an effective alone is not an effective prophylactic therapy for prevention of deep vein thrombosis, and prophylactic antiseizure medications in the absence of evidence for seizures do not improve long-term seizure control or functional outcome.

7. Minimally invasive approaches for evacuation of supratentorial ICHs and intraventricular hemorrhages, compared with medical management alone, have demonstrated reductions in mortality. The clinical trial evidence for improvement of functional out-come with these procedures is neutral, however. For patients with cerebellar hemorrhage, indications for immediate surgical evacuation with or without an external ventricular drain to reduce mortality now include larger volume (>15 mL) in addition to previously recommended indications of neurological deterioration, brainstem compression, and hydrocephalus.

8. The decision of when and how to limit life-sus-taining treatments after ICH remains complex and highly dependent on individual preference. This guideline emphasizes that the decision to assign do not attempt resuscitation status is entirely dis-tinct from the decision to limit other medical and surgical interventions and should not be used to do so. On the other hand, the decision to implement an intervention should be shared between the physician and patient or surrogate and should reflect the patient's wishes as best as can be discerned. Baseline severity scales can be useful to provide an overall measure of hemorrhage severity but should not be used as the sole basis for limiting life-sustaining treatments.

9. Rehabilitation and recovery are important determinants of ICH outcome and quality of life. This guide-line recommends use of coordinated multidisciplinary inpatient team care with early assessment of dis-charge planning and a goal of early supported dis-charge for mild to moderate ICH. Implementation of rehabilitation activities such as stretching and functional task training may be considered 24 to 48 hours after moderate ICH; however, early aggressive mobilization within the first 24 hours after ICH appears to worsen 14-day mortality. Multiple randomized trials did not confirm an earlier suggestion that fluoxetine might improve functional recovery after ICH. Fluoxetine reduced depression in these trials but also increased the incidence of fractures.

10. A key and sometimes overlooked member of the ICH care team is the patient's home caregiver. This guideline recommends psychosocial education, practical support, and training for the care-giver to improve the patient's balance, activity level, and overall quality of life.



HELPFUL REMINDERS & TIPS

For Project Managers and Study Teams

- **Regarding Serious Adverse Event (SAE) reporting:** Due to the nature of the trial we would like all primary study coordinators and research managers to be vigilant about the adverse event reporting. Kindly make sure that all SAEs are reported in WebDCU™ **within 24 hours** of site investigator's awareness of the event.
  The name of person who assesses an AE, both serious and non-serious is entered in the **AE CRF** and **should be a qualified investigator**.

- **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.

- **Regarding Temp. monitoring device for MSU:** We are happy to inform that StrokeNet NCC has started shipping out temp. monitoring devices for the MSUs. These Emerald devices will also have a calibration certificate which will need to be updated after every 1.5 years.

- **Regarding 24-hour CT imaging:** Also make sure that the 24-hour CT scan is requested and performed. **Some sites missed out on that as the orders were put in by the study PI at those sites but were canceled by the critical care or stroke team because they weren't aware of the study. Kindly make sure it doesn't get missed out.**

- **Regarding Troponin:** Kindly note that serum Troponin is required at **baseline (standard of care)** and **24 hours (not standard of care).**

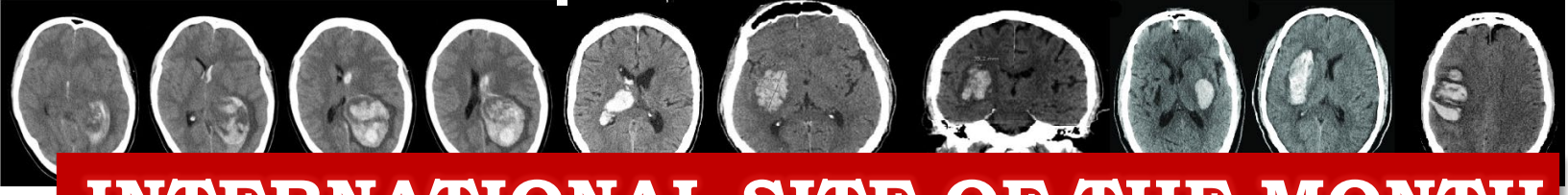
- **Regarding CT imaging before going to the OR:** Kindly Note that if the patient is going to be taken to OR for surgery by Neurosurgery team after getting enrolled into the study, please make sure that a **CT scan is taken before going to the OR** which is also **standard of care** in this situation.

- **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

- **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

Vall d'Hebron University Hospital (VHUH), Horta, Barcelona, Spain

The Vall d'Hebron University Hospital is a public and university affiliated hospital founded in 1955. It belongs to the Catalan Health Institute and is the hospital complex with the highest volume of interventions in Catalonia, Spain. It is located at the bottom of Collserola, at the north of Barcelona, and its influence area includes the districts of Horta-Guinardó, Nou Barris and Sant Andreu.

In actuality, it is the most important hospital complex in Catalonia. A study from 2009 places the Vall d'Hebron University Hospital among the four most important reference centers in Spain, and one of the twenty most important hospitals in the country.

Site PI: Carlos A. Molina, MD, PhD

Professor Carlos Molina has been the Chair of the Stroke Unit at the Vall d'Hebron Hospital in Barcelona for more than 17 years.He has considerable experience in the diagnosis and treatment of acute ischemic and hemorrhagic stroke. He is a recognized and well-known leader in reperfusion therapies for acute ischemic stroke and secondary stroke prevention. Moreover, Professor Carlos Molina has conducted several multi-center clinical trials and prospective registries for acute stroke. He has more than 460 papers in peer-review journals (H-index 56), mainly in the field of non-invasive evaluation of reperfusion in acute stroke. Dr. Molina is Section Editor of the Stroke Journal and a member of the executive committee for several stroke trials on acute stroke and secondary stroke prevention.

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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