NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

APRIL 2023 | VOLUME 2 | ISSUE 4

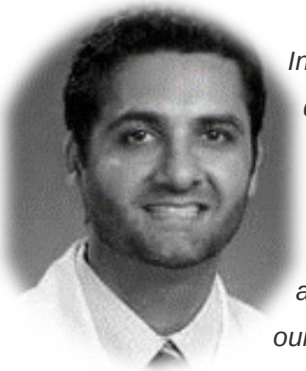
FASTEST

FVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Sangha



Intracerebral hemorrhage continues to be a disease without an emergent intervention that can change the course of a patient's life. The FASTEST trial is truly a global concerted effort to help enroll patients into a study that aims to change the course for our patients. In areas of high-density Comprehensive Stroke Centers, such as Los Angeles County, it can be difficult to recruit patients due to a dilutional effect. At the Kaiser Permanente, Los Angeles Medical Center we have employed a few strategies to enroll patients including: 24/7 screening and enrollment, using telemedicine in the emergency department to help obtain consent after hours and on weekends and calling the pharmacy team up front to inform them of a possible FASTEST patient while the clinical and study team verify the inclusion/exclusion criteria. Kudos to all the FASTEST investigators for working together to reduce ICH related morbidity.

Navdeep S. Sangha, MD

Clinical Associate Professor,
Co-Assistant Chief, Department of Neurology
Kaiser Permanente, Los Angeles Medical Center

Please join us for the *FASTEST* Monthly Webinar

Wednesday April 26th, 2:00-3:00 pm EST

- Case Discussion
- DSMB meeting review
- Review of verbal consent process
- Review of acceptable screen failures

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%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%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: **63** (**33** USA, **30** OUS: **5** Germany, **14** Japan, **4** Spain, **5** Canadian, **2** UK)

Total MSUs Released to Enroll: **7** (**6** US and **1** OUS)

Total Randomization = **160**

- US Randomizations: **47**
- International randomizations: **113** (**22** Canadian, **9** Germany, **68** Japan, **14** Spain)

Randomization last month = **21**
Total Screen Failures = **499**
Subjects Randomized by MSU = **6**
Subjects Terminated Early = **0**
eConsent Used = **3**
Remote Consent Used = **3**

CALENDAR OF EVENTS

Upcoming *FASTEST* Monthly Webinar: **Wednesday, April 26th @ 2:00-3:00 pm EST**

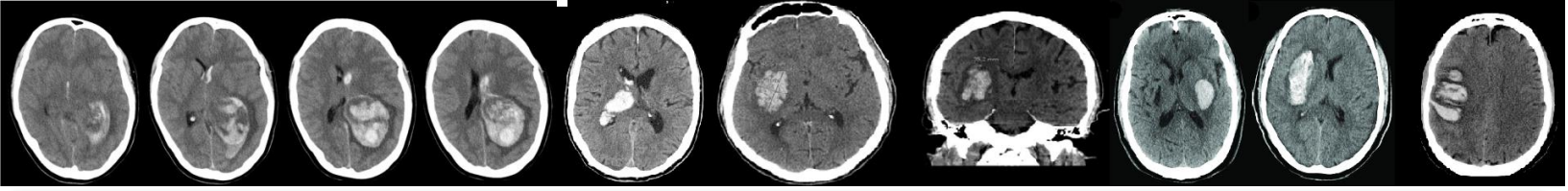
FASTEST study team office hours: **Monday, April 10th and 24th @ 2:00 pm EST**

FAQs

QUESTION CORNER

Q: We hat needs to be reported in the 'Issues Table' in WebDCU?
A: The Issues Table has been created in WebDCU to report Protocol Deviations/Violations, Unanticipated problems, Serious or Continuing Non-Compliance or any audits with findings at your site.

Click on **"Add New"** on the top right corner to add your issue



Q: What is the correct way of reporting an SAE in the WebDCU? How do we report 'death' SAE? Do we create a new CRF?
A: All SAE's (e.g., worsening/expansion of ICH, Neurological deterioration, PE, UTI, Respirator failure, Basilar Artery Occlusion, Hyponatremia etc.) need to be reported in **Form 104** separately.

All reported SAEs need to be followed up till **resolution or death** and the CRF (Form 104) needs to be updated accordingly. The From 104 has the option for it in Q 7 and Q8.

Q20	Randomized on *Derived by WebDCU, 24-hour local time*	09-Feb-2022 14:13
Q05	Date of onset	10-Feb-2022
Q06	Time of onset	00:45
Q07	Outcome	○ Resolved ○ Resolved with sequelae ○ Continuing (Follow up is required) ○ Continuing at end of study (No follow up is required) ◉ *Continuing at time of death* ○ Unknown
Q08	Date of resolution	

Example:

- If **during the hospital stay** an SAE leads to worsening of ICH/hematoma expansion and then eventually (few days-weeks later) to death, then it should be reported in the same CRF. The updated CRF will be sent to independent medical safety monitor for review again.
- If a new additional SAE occurs **during the hospital stay,** then it should be reported in a separate Form 104 and followed up similarly till **resolution or death.**
- If **during the hospital stay** the subject passes away (due to one of the reported SAE), no need to report the death as a separate SAE. Update the CRF of the SAE that caused death **to include a description of events that lead to the subject's death.** Adverse event names cannot be **"Death"** since that is an outcome.
- If death occurs during follow up period at 30, 90, 180 days (after the patient has been discharged) and the site gets aware of it **then** report this fatality as a **separate/new SAE**.

Q: We forgot to draw troponin before enrollment. The baseline troponin draw was completed afterward at 01:45 pm, whereas the FASTEST IP was administered at 12:53 pm. Can this result still be entered as baseline troponin draw in F105?
A: Since you don't have the baseline troponin value, kindly enter the one you have and leave a note in the "General comments" at the bottom of the **F105 Laboratory Tests**. NDMC will review it and probably create a DCR query for protocol violation. Answer their DCR query accordingly and enter this in the 'Issues Table' in WebDCU for NCC review. This is a major protocol deviation and will be required to report to the IRB.

Q: And does the use of Kcentra affect their eligibility?
A: Since we are using a pro-coagulant drug and studying its effects on ICH outcomes, therefore any other treatment/drug within 24 hours that might affect the study results renders the patient ineligible for enrollment in the trial. We have an amendment submitted with FDA and awaiting approval in which we have added an exclusion criterion for further clarification: *"Pro-coagulant drugs within 24 hours prior to patient enrollment into the FASTEST trial (example, tranexamic acid or aminocaproic acid etc.)"*. Once approved all sites will be updated accordingly.

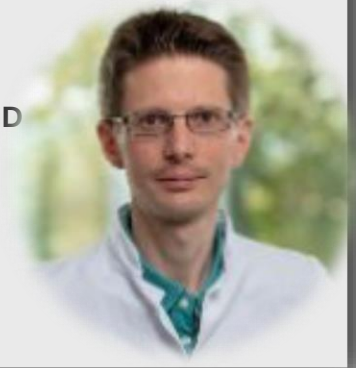
Please send in your questions and we will address them accordingly and share with others in the next Newsletter.

New Sites... Welcome Aboard!

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

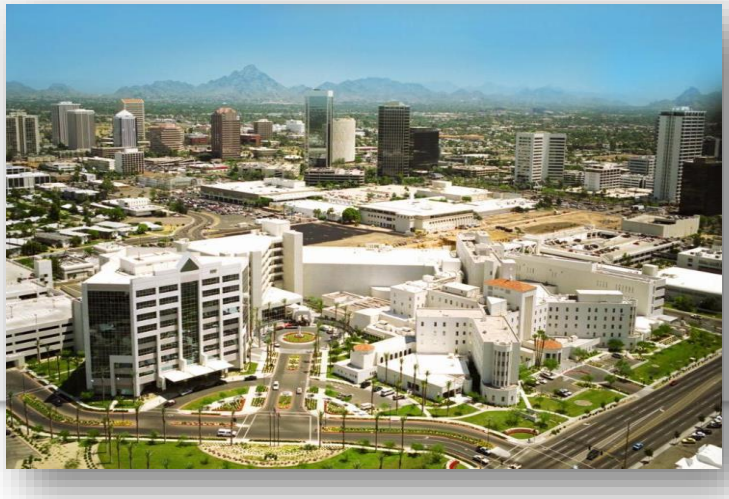
University Hospital Heidelberg, Heidelberg, Germany

Site PI:
Jan Christoph Purrucker, MD



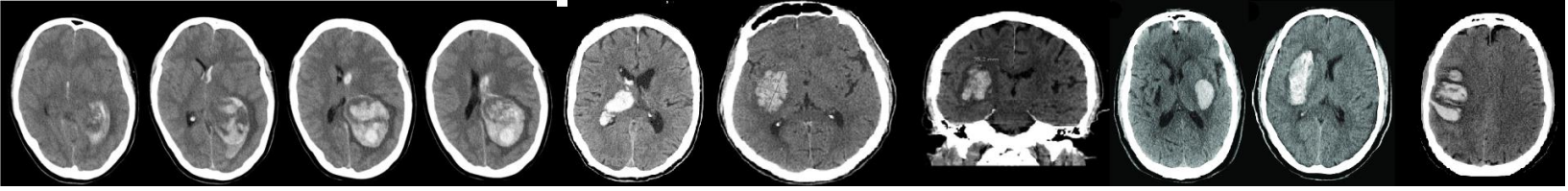
Mount Sinai West, New York, NY

Site PI:
John W. Liang, MD



St. Joseph's Hospital and Medical Center, Phoenix, AZ

Site PI:
Supreet Kaur, MD



UC Davis Medical Center, Sacramento, CA

Site PI:
Lara L Zimmermann, MD

University of Alabama Hospital, Birmingham, AL

Site PI:
Elizabeth J. Liptrap, MD

Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom

Site PI:
Tudor Gheorghiu, MD

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. **University of Alabama (UAB)**
2. **UC Davis, CA**
3. **St. Joesph AZ, MSU site**
4. **Mt. Sinai, NY**
5. **Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom**
6. **University Hospital Heidelberg, Heidelberg, Germany**

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

1. **Cedar Sinai, CA**
2. **WellStar, GA**
3. **Ronald Reagan, CA**

Top Enrolling Site

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

Subjects enrolled = 19!!

Congratulations to Enrolling Sites last Month!

Kobe City Medical Center General Hospital, Kobe, Japan	**3 Subjects**
Iwate Prefectural Central Hospital, Morioka, Japan	**1 Subject**
Niigata City General Hospital, Niigata, Japan	**1 Subject**
Kagoshima City Hospital, Kagoshima, Japan	**1 Subject**
Santa Creu and Sant Pau Hospital, Barcelona, Spain	**1 Subject**
Vall d'Hebron Hospital, Barcelona, Spain	**1 Subject**
Girona University Hospital, Girona, Spain	**1 Subject**
Clinic Frankfurt Hoechst, Frankfurt, Germany	**1 Subject**
Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA	**1 Subject**
Memorial Hermann Texas Medical Center, Houston, TX	**2 Subjects**
M Health Fairview University of Minnesota Medical Center, Minneapolis, MN	**1 Subject**
Riverside Methodist Hospital, Columbus, OH	**1 Subject**
Hamilton General Hospital, Hamilton, ON, Canada	**2 Subjects**
Vancouver General Hospital, Vancouver, BC, Canada	**2 Subjects**
Ottawa Hospital, Ottawa, ON, Canada	**1 Subject**

SCIENCE CORNER

ARTICLE OF THE MONTH

Acute Microbleeds and Microinfarcts Within the Perihematomal Area After Intracerebral Hemorrhage

Laurent Puy, MD, PhD; Antoine Rauch , MD, PhD; Vincent Deramecourt, MD, PhD; Charlotte Cordonnier, MD, PhD; Vincent Bérézowski, PhD

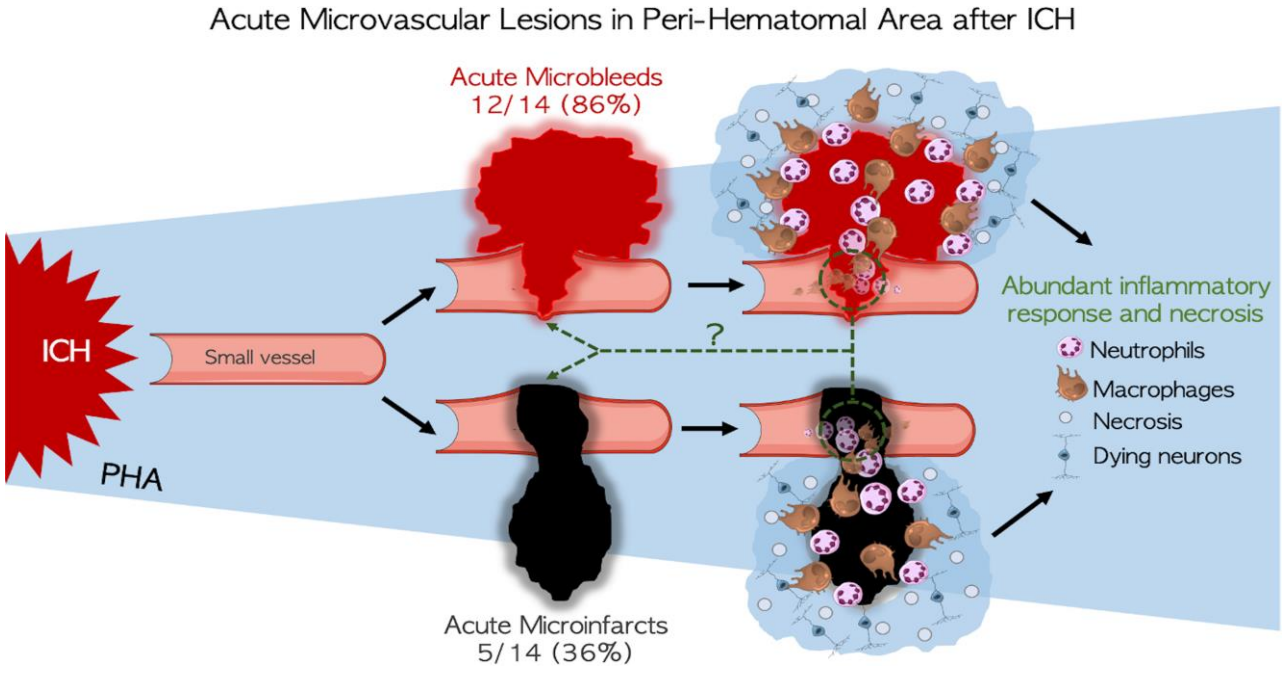
Originally published13 Feb 2023 / https://doi.org/10.1161/STROKEAHA.122.040908 / Stroke. 2023;54: e58–e62

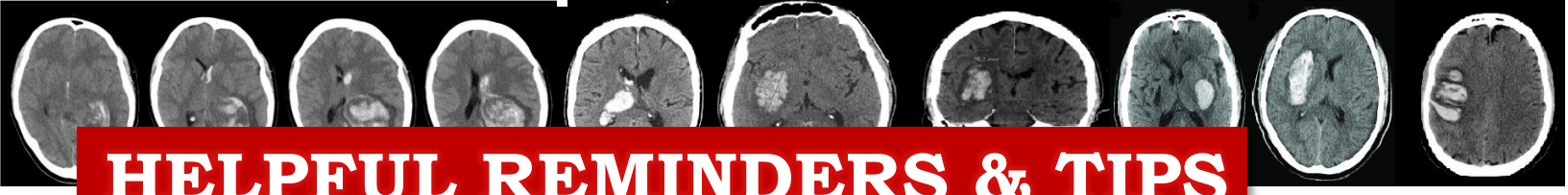
Background:
To further our understanding of the pathophysiology of spontaneous intracerebral hemorrhage (ICH) and related injury, we provided a postmortem neuropathological examination of acute microvascular lesions (microbleeds and microinfarcts) within the perihematomal area.

Methods:
We included all consecutive cases (2005–2019) from the Lille University Hospital brain bank of ICH patients who died within the first month. Paraffin-embedded tissue sections from the perihematomal area were processed for several stainings and immunolabelings to investigate the presence of acute microbleeds and microinfarcts in the perihematomal area and to characterize surrounding neuronal and systemic inflammatory reaction (macrophages and neutrophils).

Results:
We included 14 ICH cases (median age, 78 years; 10 females). Acute microbleeds were observed in the perihematomal area in 12/14 patients (86%, ranging from 1 through >10) and microinfarcts in 5/14 (36%, ranging from 1 through 4). Microbleeds were observed whatever the delay from ICH onset to death was, while most cases with acute microinfarcts were observed between day 3 and day 7 (n=3/5). Both lesions were characterized by an abundant accumulation of systemic inflammatory cells and necrotic areas.

Conclusions:
Acute microbleeds and microinfarcts might contribute to the propagation of secondary brain tissue damages after ICH. Our examinations also question the potential role of massive systemic inflammatory cells recruitment in the genesis of these microvascular injuries.





HELPFUL REMINDERS & TIPS

For Project Managers and Study Teams

- **WHAT IS NEW IN THE TOOLBOX?**
  We have recently added following two documents to WebDCU Toolbox:
  1. FASTEST WebDCU instructions for removing drug.
  2. New version of the Data Collection Guidelines.

- Jama Olsen from NDMC will be working with the international CRO monitors to be sure they are familiar with the Issues Table in the WebDCU and will be able to instruct sites what to report in it if need be. Kindly reach out to Jama for any queries or clarification about the Issues Table at olsen@musc.edu.

- **SAE reporting:** Please report SAEs within **24 hours** of the knowledge of even. Kindly note that SAE are not reported until you press the **"Submit CRF"** option. Once submitted within 24 hours these CRFs can always be updated later accordingly as more information/details about the SAE are gathered.

- **Follow-up labs and imaging:** The follow-up non-contrast CT of the head and Serum troponin need to be obtained at **24±6 hours from stroke onset/last known well** as per the study Table of Events.

- **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.

- **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

Vancouver General Hospital, Vancouver, BC, Canada

Vancouver General Hospital (VGH) is a renowned medical facility located in Vancouver, Canada. Founded in 1906, it is one of the largest and most respected hospitals in the country, with a long history of providing high-quality patient care, education, and research. VGH is part of the Vancouver Coastal Health Authority and serves as a tertiary referral center for patients from across British Columbia, as well as a regional center for specialized services such as trauma, neurosurgery, and cancer care. The hospital has a dedicated team of healthcare professionals, including physicians, nurses, and allied health staff, who work tirelessly to ensure that patients receive the best possible care. With a commitment to innovation and excellence, Vancouver General Hospital continues to lead the way in healthcare and is a vital part of the community it serves.

VGH is a hub for cutting-edge research. The hospital has a long history of research excellence, dating back to the early 20th century, when it was one of the first hospitals in Canada to establish a dedicated research department. Today, VGH is home to several renowned research centers, including the Centre for Heart Lung Innovation, the Centre for Clinical Epidemiology and Evaluation, and the Centre for Health Evaluation and Outcome Sciences, to name just a few. These centers translational research, with a particular emphasis on areas such as cardiovascular disease, cancer, and infectious diseases. The hospital also collaborates closely with leading academic institutions and research organizations, both locally and internationally, to ensure that its research efforts are at the forefront of medical knowledge. With its commitment to research excellence and innovation, Vancouver General Hospital is a leader in medical research and a vital contributor to the global scientific community.

Site PI:
Ming Yin Dominic TSE, MD

Dr. Dominic Tse is a Clinical Assistant Professor in the UBC Division of Neurology.
He received his MBCHB from the University of Auckland, New Zealand. He completed residency in Adult Neurology at Auckland City Hospital followed by a stroke fellowship at the University of Calgary. He joined the Vancouver Stroke Program as a stroke neurologist in 2020.

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/