NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

MARCH 2023 | VOLUME 2 | ISSUE 3

FASTEST

FVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Walsh

I am proud to be a member of the University of Cincinnati FASTEST site at which we have had 4 enrollments. Our success has been thanks to a robust team effort including our Clinical Research Coordinators (CRCs) who perform 24/7 screening/enrollment in the emergency department, the Lead Study Coordinator, and our Stroke Team physicians on call. A tool that helps us to more promptly identify ICH patients, including from CTs performed in both the ED and our Mobile Stroke Unit, is our Stroke Team's utilization of Viz.ai and its ICH alerts. The CRCs are excellent about quickly identifying potential FASTEST subjects in the ED and immediately contacting team members including the Site-PI, Lead Coordinator, and Stroke Team Physician on call. Our Lead Coordinator has expertly filled many critical roles including training and supervision of the CRCs. Finally, we have noted the strengths of EFIC and ongoing learning by retrospectively discussing not only our actual enrollments but also the "near enrollments." Thank you to our team at UC for your efforts and dedication to the FASTEST study!

Kyle B. Walsh, MD, MS
Associate Professor,
Department of Emergency Medicine
Neurointensivist and Stroke Team Member
University of Cincinnati

Please join us for the *FASTEST* Monthly Webinar

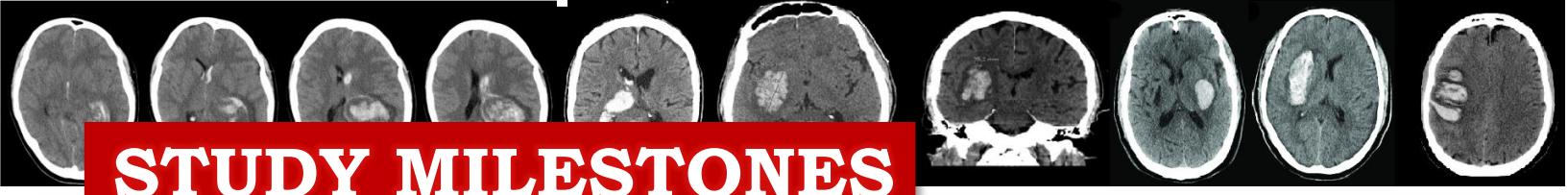
Wednesday March 15th, 2:00-3:00 pm EST

- Northwestern Medicine Central DuPage Hospital Winfield, IL team will be presenting their first enrollment case via MSU.
- *FASTEST* Pharmacy will update on Study Drug Inventory and old drug destruction.
- NDMC will review changes in the recently updated Data Collection Guidelines.

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=40q90l8dB9QtZj9P5aZ0BeWkvzCsNx1WgQL9cFmISHQ%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: **56** (**28** USA, **26** OUS: **4** Germany, **14** Japan, **3** Spain, **5** Canadian, **1** UK)

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

Total Randomization = **133**

- US Randomizations: **34**,
- International randomizations: **99** (**19** Canadian, **7** Germany, **64** Japan, **9** Spain)

Randomization last month = **23**
Total Screen Failures = **407**
Subjects Randomized by MSU = **3**
Subjects Terminated Early = **0**
eConsent Used = **1**
Remote Consent Used = **2**

CALENDAR OF EVENTS

Upcoming *FASTEST* Monthly Webinar: **Wednesday, March 15th @ 2:00-3:00 pm EST**

FASTEST study team office hours: **Monday, March 13th and 27th @ 2:00 pm EST**

FASTEST @ ISC 2023

IMPORTANT NOTE

Attention site PIs, Site Pharmacists and PSCs,

1. **Upcoming Database Freeze:** For the upcoming DSMB meeting the database will be freezed on **Monday, March 13TH !**
   Please submit all case report forms, respond to queries, and report all screen failure by next **Friday, March 10TH 2023.**

2. **Regarding Study Drug Inventory:** Your current inventory of FASTEST study drug includes kits that are expiring on **Thursday, 30th-March-2023**, these kits will no longer be dispensable to subjects after 30th-March-2023.

Please follow these steps below to prevent dispensing expired kits to subjects:

- **7 days prior to** the expiration of a study drug kit, all sites will receive an automated email from WebDCU™ notifying them of the expiring kit(s) in their inventory.
- Sites will receive the email daily until the expiring study drug kit is removed from WebDCU. Sites should check regularly for this email starting **Thursday, 23-MARCH-2023**.
- All clinical performing sites should receive new kits prior to the automated expiration email sent from WebDCU.
- To reduce waste, sites should not destroy expiring study drug until AFTER the first email notice goes out (i.e., 7 days prior to expiration).
- Once all sites have received new drug, and after receiving the first email notice (7-day prior to expiration date email) study drug may be destroyed per CPS policy and procedures and all old drugs can be destroyed and removed from WebDCU (refer to **FASTEST WebDCU instructions for removing drug** in WebDCU™ - Go to **Toolbox-->Project Documents--> WebDCU Instructions for Expiring Study Drug**).

3. **Issues Table:** 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

#	Issue ID	RCC	Site	Subject	Subject ID's affected	Is the issue affiliated with an existing protocol deviation?	Is the issue affiliated with an existing AE?	Protocol Deviation/Exception/Violation	Unanticipated Problem	Non-compliance	Other	Form Complete, Pending NCC Review?	Potentially reportable based on site response above	Type of protocol deviation classified by the NCC	Meets cIRB criteria for reporting determined by the NCC	Status	CIRB Report
1	9	Regents of the University of Minnesota	M Health Fairview Southdale Hospital, Edina, MN	1124				☑				Yes	No				

New Sites... Welcome Aboard!

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

Vancouver General Hospital, Vancouver, BC, Canada

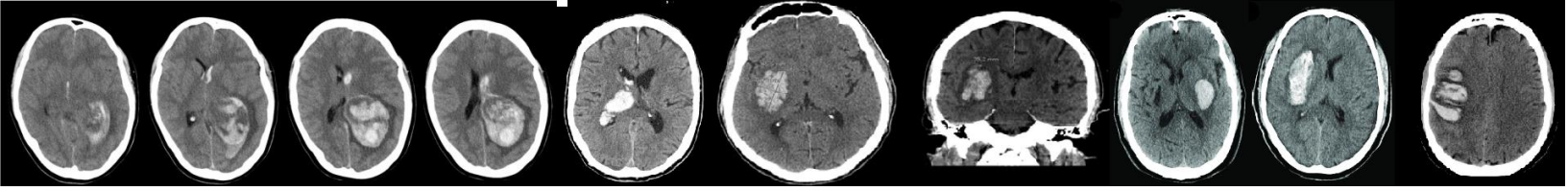
Site PI:
Ming Yin Dominic TSE, MD

Providence St. Vincent Medical Center, Portland, OR

Site PI:
Ted J. Lowenkopf, MD

Regions Hospital, St Paul, MN

Site PI:
Michael E. Brogan, MD



Bellvitge University Hospital, Barcelona, Spain

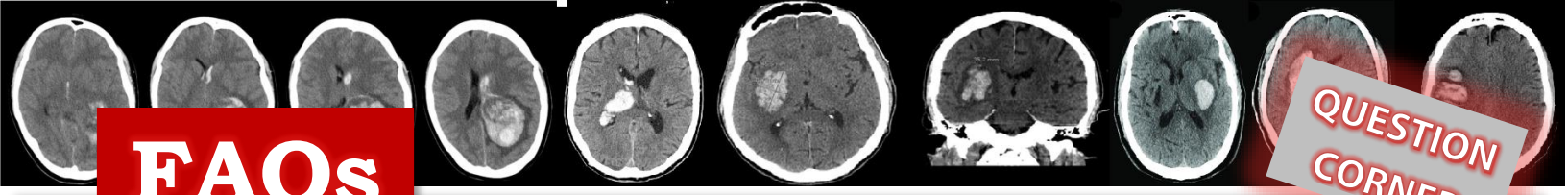
Site PI:
Pere Cardona Portela, MD

Congratulations on First Enrollment!!

Congratulations to Dr. Toshiyuki FUJINAKA and his team at the NHO Osaka National Hospital, Osaka, Japan for enrolling their first subject in *FASTEST*.

Congratulations to Dr. Yolanda SILVA and her team at the Girona University Hospital, Girona, Spain for enrolling their first subject in *FASTEST*.

Congratulations to Dr. Joan MARTI FABREGAS and his team at the Santa Creu and Sant Pau Hospital, Barcelona, Spain for enrolling their first subject in *FASTEST*.



FAQs

QUESTION CORNER

Q: Who is allowed to order the FASTEST study drug to be administered to a study candidate. Does it have to be somebody who is listed as an investigator on the protocol? Can the study drug be ordered by the Neurology resident who is working with the patient, even if the resident is not listed on the protocol.
A: If the study procedures are approved/done under the supervision of someone on the DOA with the appropriate permissions it is acceptable. Ordering the study drug after discussing eligibility with the study PI or Sub-I for enrollment into the trial or administration of study drug under their supervision by a resident or RN (licensed personnel) are acceptable.

Therefore, if the neurology resident has discussed the case (inclusion and exclusion criteria) with the study PI or Sub-I, which we assume will be the attending and/or the stroke fellows and they deem the patient eligible to be enrolled into the FASTEST trial then it should be Ok for the resident to order the study drug. However, kindly make sure that the residents mention in their EMR notes that the patient was discussed for possible enrollment in the FASTEST trial with Dr. XYZ so that it is clear and documented that the (decision for) enrollment was approved/ done under the supervision of the study PI or Sub-I (on the DOA).

Q: We have missed the baseline troponin draw for our new enrollment last night. This happened due to miscommunication with nurse at the time participant was enrolled. Should the PSC document this in "Issues" in WebDCU?
A: Yes, this is a protocol violation, and you will need to document this in the "Issues table" in the WebDCU and upload a NTF for review. All Protocol Deviations, Violations, Unanticipated problems, Serious or Continuing Non-Compliance need to be filed We will get back to you and let you know if this needs to be reported to IRB or not. In either case a NTF will be required to be uploaded onWebDCU.

Q: We have 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 query accordingly.

Q: Exclusion criteria #2 states 'Secondary ICH related to know causes (trauma, aneurysm, etc.), oral anticoagulant use within past 7 days. A patient presented to us with ICH and on Apixaban. They were emergently treated with Kcentra to reverse Apixaban. It wasn't directly noted if the Apixaban was the cause of ICH but it doesn't sound like it was (the patient was on it since 2021 for PE). With the way the exclusion criteria is worded, would this patient be eligible if the care team/PI did not think the Apixaban was the cause of the ICH?
A: As per the protocol if the subject has been on oral anticoagulant use within past 7 days they cannot be enrolled. In the current situation you mentioned the pt was on Apixaban since 2021 for PE, so this disqualifies the patient for enrollment already, irrespective of the antidote administration.

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.

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. **Ascension St. John**
2. **Barnes Jewish (St. Louis University)**
3. **Regions MC MN**
4. **Providence St. Vincent**
5. **Bellvitge University Hospital, Barcelona, Spain**
6. **Vancouver General Hospital, Vancouver, BC, Canada**

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

1. **Mayo Jacksonville**
2. **University of Alabama**
3. **UC Davis**
4. **Mt. Sinai**
5. **St. Joseph MC**
6. **Thomas Jefferson**
7. **Medical College of South Carolina**

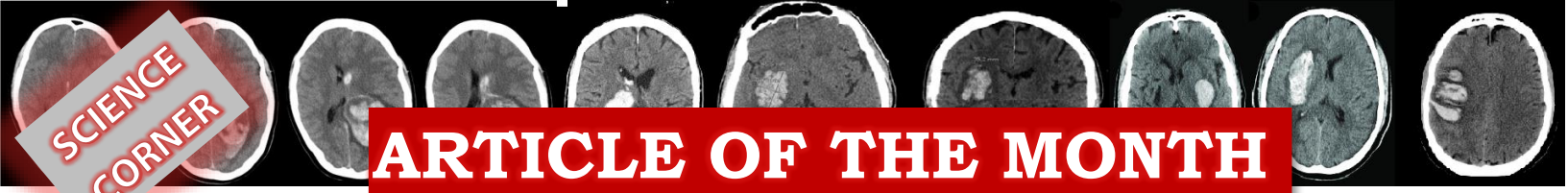
Top Enrolling Site

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!

National Cerebral and Cardiovascular Center, Osaka, Japan	**4 Subjects**
Toranomon Hospital, Tokyo, Japan	**3 Subjects**
Kobe City Medical Center General Hospital, Kobe, Japan	**2 Subjects**
Iwate Prefectural Central Hospital, Morioka, Japan	**3 Subjects**
Kyorin University Hospital, Tokyo, Japan	**1 Subject**
NHO Osaka National Hospital, Osaka, Japan	**1 Subject**
Santa Creu and Sant Pau Hospital, Barcelona, Spain	**2 Subjects**
Vall d'Hebron Hospital, Barcelona, Spain	**1 Subject**
Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA	**1 Subject**
Girona University Hospital, Girona, Spain	**1 Subject**
University of Cincinnati Medical Center, Cincinnati, OH	**1 Subject**
M Health Fairview Southdale Hospital, Edina, MN	**1 Subject**
Hamilton General Hospital, Hamilton, ON, Canada	**1 Subject**
University of Calgary - Foothills Medical Centre, Calgary, AB, Canada	**2 Subjects**



SCIENCE CORNER

ARTICLE OF THE MONTH

Time Course of Early Hematoma Expansion in Acute Spot-Sign Positive Intracerebral Hemorrhage: Prespecified Analysis of the SPOTLIGHT Randomized Clinical Trial

Fahad S. Al-Ajlan, David J. Gladstone, Dongbeom Song, Kevin E. Thorpe, Rick H. Swartz, Kenneth S. Butcher, Martin del Campo, Dar Dowlatshahi, Henrik Gensicke, Gloria Jooyoung Lee, Matthew L. Flaherty, Michael D. Hill, Richard I. Aviv and Andrew M. Demchuk and SPOTLIGHT Investigators

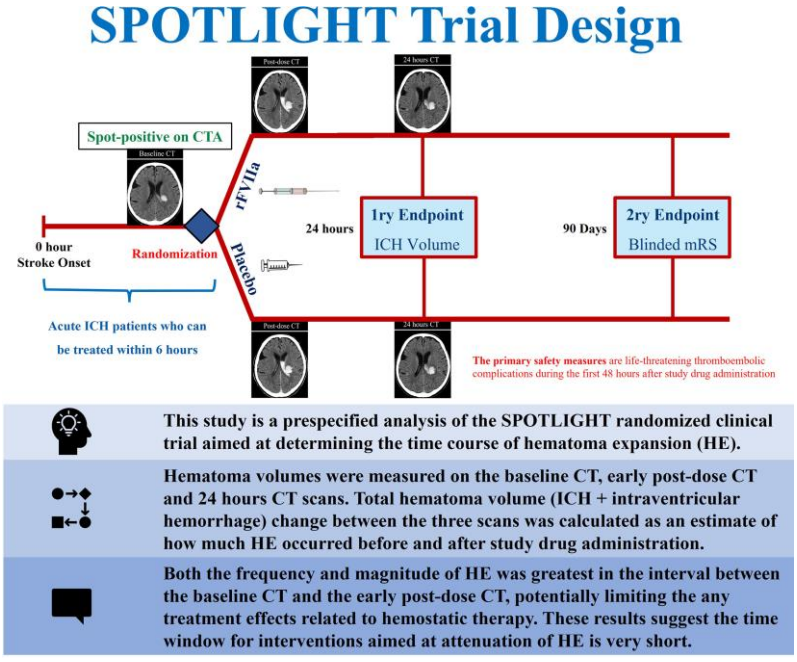
Originally published 9 Feb 2023/ https://doi.org/10.1161/STROKEAHA.121.038475 / Stroke. 2023;54:715–721

Background:

In the SPOTLIGHT trial (Spot Sign Selection of Intracerebral Hemorrhage to Guide Hemostatic Therapy), patients with a computed tomography (CT) angiography spot-sign positive acute intracerebral hemorrhage were randomized to rFVIIa (recombinant activated factor VIIa; 80 µg/kg) or placebo within 6 hours of onset, aiming to limit hematoma expansion. Administration of rFVIIa did not significantly reduce hematoma expansion. In this prespecified analysis, we aimed to investigate the impact of delays from baseline imaging to study drug administration on hematoma expansion.

Methods:

Hematoma volumes were measured on the baseline CT, early post-dose CT, and 24 hours CT scans. Total hematoma volume (intracerebral hemorrhage + intraventricular hemorrhage) change between the 3 scans was calculated as an estimate of how much hematoma expansion occurred before and after studying drug administration.



Results:

Of the 50 patients included in the trial, 44 had an early post-dose CT scan. Median time (interquartile range) from onset to baseline CT was 1.4 hours (1.2–2.6). Median time from baseline CT to study drug was 62.5 (55–80) minutes, and from study drug to early post-dose CT was 19 (14.5–30) minutes. Median (interquartile range) total hematoma volume increased from baseline CT to early post-dose CT by 10.0 mL (−0.7 to 18.5) in the rFVIIa arm and 5.4 mL (1.8–8.3) in the placebo arm (P=0.96). Median volume change between the early post-dose CT and follow-up scan was 0.6 mL (−2.6 to 8.3) in the rFVIIa arm and 0.7 mL (−1.6 to 2.1) in the placebo arm (P=0.98). Total hematoma volume decreased between the early post-dose CT and 24-hour scan in 44.2% of cases (rFVIIa 38.9% and placebo 48%). The adjusted hematoma growth in volume immediately post dose for FVIIa was 0.998 times that of placebo ([95% CI, 0.71–1.43]; P=0.99). The hourly growth in FFVIIa was 0.998 times that for placebo ([95% CI, 0.994–1.003]; P=0.50).

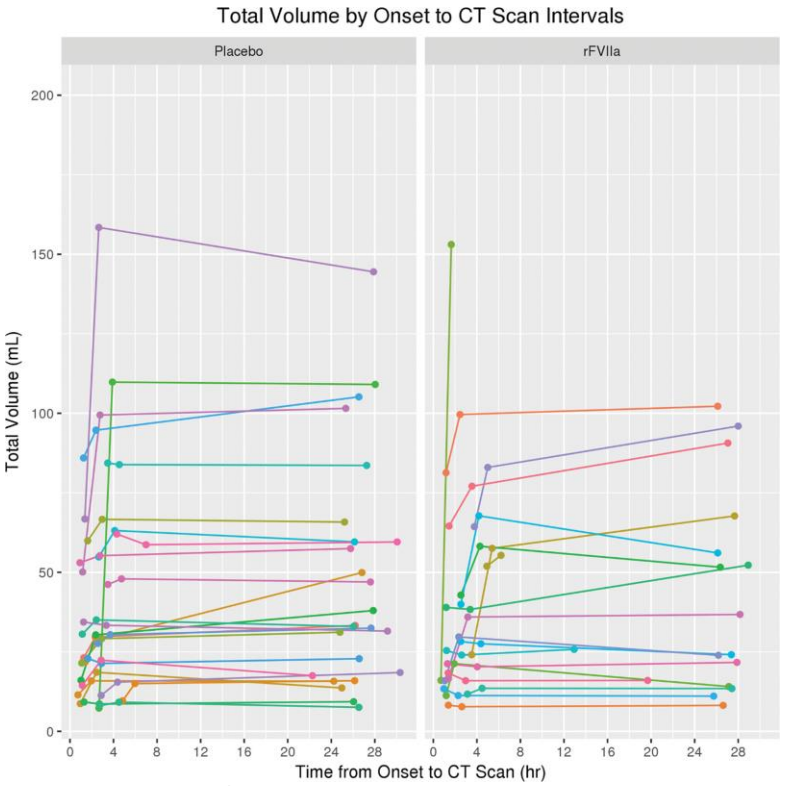
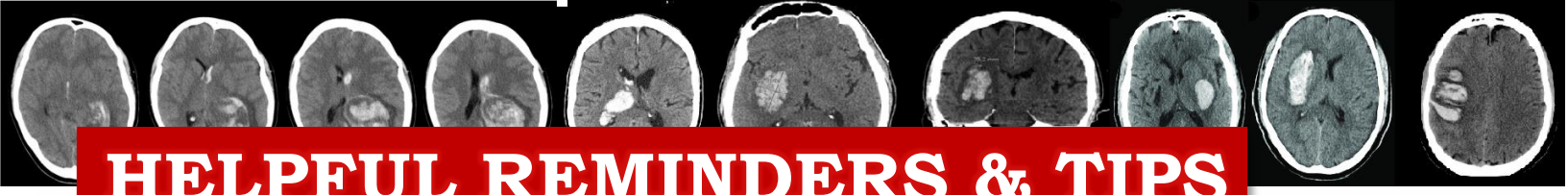


Figure 1: Evolution of total hematoma volume measured with 3 computed tomography (CT) scans over the 24 h in the placebo and treatment arms**.** In most patients, the hematoma expansion occurred between the baseline and early post-dose CT scan. rFVIIa indicates recombinant activated factor VIIa.

Conclusions:

In the SPOTLIGHT trial, the adjusted hematoma volume growth was not associated with Factor VIIa treatment. Most hematoma expansion occurred between the baseline CT and the early post-dose CT, limiting any potential treatment effect of hemostatic therapy. Future hemostatic trials must treat intracerebral hemorrhage patients earlier from onset, with minimal delay between baseline CT and drug administration.



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

- **IMPORTANT:** Upcoming database freeze **Monday, March 13TH !**
  - **Please submit** all case report forms, respond to queries, and report all screen failure by next **Friday, March 10TH**.
  - To view overdue CRFs and open queries in WebDCU, select the [Data Management] tab, then [Subject CRF List]. Select [Data Due or Open DCR] from the drop-down box in the right-hand corner.
- **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.

- **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.

- **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

Sunnybrook Health Sciences Center, Toronto, ON, Canada

Sunnybrook Health Sciences Centre (SHSC) is a nationally leading and internationally recognized academic health sciences center located in Toronto, Ontario, Canada. It is the largest trauma center in Canada and one of two trauma centers in Toronto, the other being St. Michael's Hospital. Sunnybrook is a teaching hospital fully affiliated with the University of Toronto. With 1.3 million patient visits annually, Sunnybrook has established itself across three campuses.

When members of Canada's military returned from battle during the Second World War, their medical and health-care needs began to surpass the ability of the existing military hospitals to provide care. Therefore, leading to establishment of Canada's largest veteran's hospital. It is home to Canada's largest veterans center, in the Kilgour Wing and the George Hees, which cares for World War II and Korean War veterans.

In partnership with Sunnybrook Research Institute, the hospital leads the way in groundbreaking research that changes the way patients are treated around the world. Over 200 scientists and clinician-scientists conduct more than $100 million of breakthrough research each year. Sunnybrook has made surgical breakthroughs in its history, including the world's first non-invasive opening of the blood–brain barrier to deliver chemotherapy more effectively for brain tumor.

Site PI:
Houman Khosravani, MD PhD

Dr. Khosravani is assistant professor of medicine, at University of Toronto. His interests are quality improvement at different levels of care relevant to hyper-acute stroke management and inpatient stroke services, focusing on improvement of door-to-needle times for thrombolysis. He is also working on understanding and improving factors that are relevant to a successful thrombectomy program in a comprehensive stroke center. He is medical director of the inpatient stroke unit, and interested in development of stroke pathways, the overlap between internal medicine and inpatient stroke neurology, and development of a framework for excellence in comprehensive neurovascular care.

Dr. Khosravani is an active member of Thrombosis Canada and interested in the implementation of stroke-best practices in antithrombotics and anticoagulation. He also has a strong interest in utilizing computation and computer science to facilitate delivery of safe and high-quality acute stroke care.

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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