NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

AUGUST 2024 | VOLUME 3 | ISSUE 8

FASTEST

FVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Gioia

"Time is Brain" in acute ICH management, and the FASTEST trial embraces this concept entirely, understanding the importance of ultrafast management in acute ICH as the best chance to help our patients. It feels like a new dawn in ICH research given recent positive trials in acute ICH management, and the FASTEST trial is well placed to answer the question whether rapidly-administered haemostatic treatment will prevent expansion and improve outcomes. While the enrollment window is tight, the pragmatic design of the trial meant that our first enrollment into the trial was seamless. Keeping study drug in a locked box in the trauma bay for quick access was a good strategy, along with my quick availability as site-PI to help the on-call team randomize the patient off hours. As a team we are excited about the trial, and eagerly await the next patient.

Laura C. Gioia MD MSc
Vascular neurologist/Stroke Neurologist (CHUM)
Clinical Assistant Professor
(University of Montreal)

Please join us for the *FASTEST* Monthly Webinar

Wednesday August 21st, 2:00-3:00 pm EST

- Professor Poli and his team from Tubingen University Hospital, Germany will be presenting their case.
- Professor Jan Purrucker and his team from University Hospital Heidelberg, Germany will be presenting their case.
- Brief trial spotlight on our high enrolling sites Kaiser Permanente, Memorial Herman and Calgary.

Join Zoom Meeting

https://ucincinnati.zoom.us/j/99236910048

Meeting ID: 992 3691 0048

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

STUDY MILESTONES

Total Sites Released to Enroll: **91** (**52** USA, **39** OUS: **6** Germany, **14** Japan, **6** Spain, **9** Canadian, **4** UK)

Total MSUs Released to Enroll: **12** (**10** US and **2** OUS)

Total Randomization = **511**

- US Randomizations: **139**
- International randomizations: **372**
  - Japan = **232**
  - Canada = **62**
  - Spain =**35**
  - Germany = **29**
  - UK = **14**

Randomization last month = **21**

Total Screen Failures = **1943**

Subjects Randomized by MSU = **16**

Subjects Terminated Early = **3**

eConsent Used = **223**

Remote Consent Used = **20**

CALENDAR OF EVENTS

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

FASTEST study team office hours: **Monday, August 26th, @ 1:00-2:00 pm.**

Important Notes

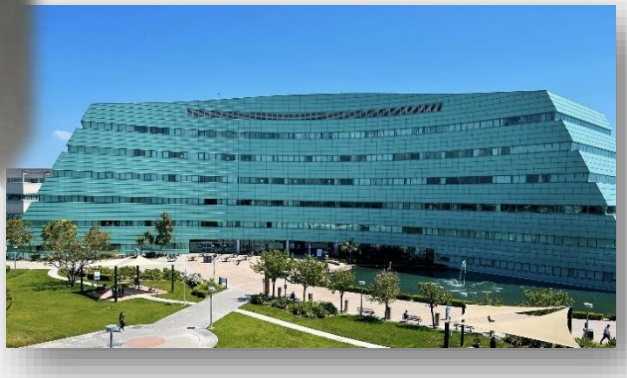
FASTEST study MOP Updated: The FASTEST study Manual of Procedures (MOP) has been updated. The newly revised *MOP Version 3* is now available in the Toolbox on WebDCU. We have also attached version 3 of the MOP to this newsletter, with the changes highlighted for your reference.

Calibration of Emerald Loggers: For sites using the Emerald temperature loggers provided by NCC for their ED and MSUs, please note that we will be replacing the current loggers with newly calibrated ones by the end of August.

New Sites... Welcome Aboard!

Kaiser Permanente South Bay Medical Center, Harbor City, CA

Site PI:
Navdeep SANGHA



Kaiser Permanente Baldwin Park Medical Center, Baldwin Park, CA

Congratulations on 1st Enrollment!!

Congratulations to Dr. Alejandro BUSTAMANTE RANGEL and his team at the Hospital Universitari Germans Trias i Pujol, Barcelona, B, Spain for enrolling their first subject in FASTEST.

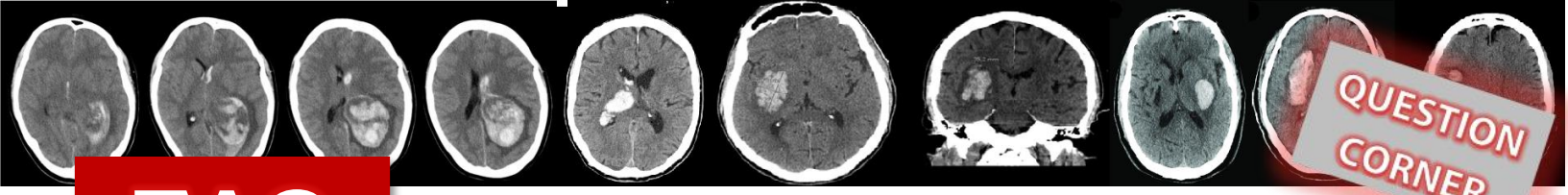
Congratulations to Dr. Pierre BORCZUK and his team at the Massachusetts General Hospital, Boston, MA for enrolling their first subject in FASTEST.

Congratulations to Dr. Shigeru FUJIMOTO and his team at the Jichi Medical University Hospital, Shimotsuke, Japan for enrolling their first subject in FASTEST.

Congratulations to Joji KURAMATSU and his team at the University Hospital Erlangen, Erlangen, Germany for enrolling their first subject in FASTEST.

Congratulations to Dr. Laura GIOIA and her team at the University of Montreal Hospital, Montreal, QC, Canada for enrolling their first subject in FASTEST.

Congratulations to Dr. Mustapha EZZEDDINE and his team at the Wake Forest Baptist Medical Center, Winston-Salem, NC for enrolling their first subject in FASTEST.



FAQ

Q: Our subjects SID-A and SID-B, both have missed their 180-day visits and are out of window?
A: A subject is not considered LTFU until it is **240 days** after randomization. Therefore, **SID-A** was considered LTFU as of July 12th while **SID-B** is not LTFU until August 29th. Kindly refer to the FASTEST study MOP Version 3 (pg. 45).

For **SID-A**, please add the Day 180 visit and enter Data collected = **'No'** for F137 and F144 and enter into General Comments the reason why it wasn't collected. Please also complete the End of Study visit and indicate LTFU on F126. Please note that being unable to complete the mRS or EQ-5D assessments at Day 180 visit constitutes a major protocol violation. Kindly report this in the issues table in WebDCU and ensure that the documented attempts to complete the 180-day follow-up are also included. Kindly refer to the table provided in the FASTEST MOP Version 3 on page 55-56 for guidelines.

For **SID-B**, they will not be considered lost to follow-up until August 29th. The Day 180 visit may be done via telephone if you are able to connect with subject before August 29th. Kindly make sure to document all attempts made to collect the Day 180 mRS or EQ-5D assessments from this patient up until that date. If you are unable to gather the required information in person or over the phone by Day 240, this too will need to be reported as a major protocol violation in the issues table in WebDCU.

Q: We just had a new FASTEST enrollee and had a few questions on what the preferred way of finalizing consent with our subject would be. When they arrived, they were non-decisional. The first family member to arrive was their son who is bilingual, we began the consent discussion with them until the wife showed up who is predominantly Spanish speaking. By the time she had showed we had been discussing enrollment with the son who was agreeable to enrolling the subject. After discussing the enrollment amongst themselves they decided they would like to move forward and the wife signed the consent form but it is the English version. Now that there has been more time to get everything sorted out, since she is primarily Spanish speaking we were wondering if it would be acceptable to use this English consent form, if we should finalize the short form consent process with them, or wait until we have the fully translated Spanish ICF?
A: First this is not an easy consenting scenario to work through. While we feel like you went through the proper process of consenting a non-English speaking LAR, using the bilingual son as an interpreter we are assuming that the non-English speaking LAR (subject's wife) could also not be able to read English. If this is the case, we would recommend reconsenting the non-English LAR with a Spanish consent.

There is no immediate urgency since we do have a signed English consent, but we would like for you to request via the Advarra portal a fully translated Spanish consent. Once you receive this, we would suggest re-consenting the LAR with the Spanish consent. This would help demonstrate a good faith effort to protect/educate/consent the human subject/LAR in their language.

Q: How do we enter SAE which happened between 24h and day 30 when we still in between? And I am not sure if the patient is going to survive to day 30?
A: Please enter the SAE according to the date closest to the relevant time point. For example, an SAE occurring on day 6 (while still in the hospital) it should be reported within the 24-hour timeline. If the SAE occurs on day 20, it should be reported with the 30-day follow-up. Typically, sites follow up with patients after discharge at 30, 90, and 180 days. If it is discovered during these follow-ups that the patient visited the ER or a doctor for a serious issue, it should be reported at the corresponding follow-up.

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

SHOUT OUTS!!

Congratulations to US sites that have completed EFIC and will be submitted to the CIRB for review/approval for emergency consent.

1. **Medical University of South Carolina University Hospital, Charleston, SC Parneet**

Great job on new sites being released to enrolled:

1. **Kaiser Permanente Baldwin Park Medical Center, Baldwin Park, CA**
2. **Kaiser Permanente South Bay Medical Center, Harbor City, CA**

The Top Enrolling Site

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

Subjects enrolled = 56!!

Congratulations to Enrolling Sites last Month!

Toranomon Hospital, Tokyo, Japan	2 Subject
National Cerebral and Cardiovascular Center, Osaka, Japan	2 Subject
Japanese Red Cross Kyoto Daini Hospital, Kyoto, Japan	1 Subject
KMU University Hospital, Osaka, Japan	1 Subject
Iwate Prefectural Central Hospital, Morioka, Japan	1 Subject
Niigata City General Hospital, Niigata, Japan	1 Subject
Kobe City Medical Center General Hospital, Kobe, Japan	1 Subject
Vancouver General Hospital, Vancouver, BC, Canada	2 Subject
Ottawa Hospital, Ottawa, ON, Canada	1 Subject
University of Calgary - Foothills Medical Centre, Calgary, AB, Canada	1 Subject
University Hospital Augsburg, Augsburg, Germany	1 Subject
Memorial Hermann Memorial City Medical Center, Houston, TX	1 Subject
Prisma Health Greenville Memorial Hospital, Greenville, SC	1 Subject
Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA	2 Subject
Bellvitge University Hospital, Barcelona, B, Spain Barcelona, B, Spain	1 Subject
Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom	3 Subject

SCIENCE CORNER

ARTICLE OF THE MONTH

Early minimally invasive intracerebral hemorrhage evacuation: a phase 2a feasibility, safety, and promise of surgical efficacy study

Timothy J Kleinig, Amal Abou-Hamden, John Laidlaw, Leonid Churilov, Christopher Paul Kellner, Teddy Wu, J Mocco, Hui Lau, Alexios Adamides, Bhadrakant Kavar, James Dimou, Jennifer Cranefield, Amy McDonald, Stephanie Plummer, Stephen Davis, Bruce C V Campbell

J Neurointerv Surg. 2024 May 21;16(6):555-558. DOI: 10.1136/jnis-2023-020446

Background

Surgical treatment of intracerebral hemorrhage (ICH) is unproven, although meta-analyses suggest that both early conventional surgery with craniotomy and minimally invasive surgery (MIS) may be beneficial. We aimed to demonstrate the safety, feasibility, and promise of efficacy of early MIS for ICH using the Aurora Surgiscope and Evacuator.

Methods

We performed a prospective, single arm, phase IIa Simon's two stage design study at two stroke centers (10 patients with supratentorial ICH volumes ≥20 mL and National Institutes of Health Stroke Scale (NIHSS) score of ≥6, and surgery commencing <12 hours after onset). Positive outcome was defined as ≥50% 24-hour ICH volume reduction, with the safety outcome lack of significant ICH reaccumulation.

Figure 1 Aurora system consists of the Surgiscope and Evacuator (A), which is obtainable in 100 and 130 mm lengths. The Evacuator is connected to suction (controllable via the index finger) and contains a whisk to break up tough clot (controllable by the thumb). The whisk is rotated into the clot, away from brain tissue. The Surgiscope has a camera at the apex and LED lights at the tip, and is shown with the obturator in situ. The Evacuator is inserted into the Surgiscope (B) and protrudes distal to the tip for optimal clot engagement. Bleeding can be controlled by monopolar cautery applied to the shaft. Permission granted by Integra LifeSciences Corporation, Princeton, New Jersey, USA.

Results

From December 2019 to July 2020, we enrolled 10 patients at two Australian Comprehensive Stroke Centers, median age 70 years (IQR 65-74), NIHSS score 19 (IQR 19-29), ICH volume 59 mL (IQR 25-77), at a median of 227 min (IQR 175-377) post-onset. MIS was commenced at a median time of 531 min (IQR 437-628) post-onset, had a median duration of 98 min (IQR 77-110), with a median immediate postoperative hematoma evacuation of 70% (IQR 67-80%). A positive hematoma evacuation of 70% (IQR 67-80%). A positive outcome was achieved in 5/5 first stage patients and in 4/5 second stage patients. One patient developed significant 24-hour ICH reaccumulation; otherwise, 24 hour stability was observed (median reduction 71% (IQR 61-80), 5/9 patients <15 mL residual). Three patients died, unrelated to surgery. There were no surgical safety concerns. At 6 months, the median modified Rankin Scale score was 4 (IQR 3-6) with 30% achieving a score of 0-3.

Table 1 Cohort baseline variables (n=10)

Variable	Median (IQR) or No/total No
Age (years)	70 (65–74)
Men	7/10
Premorbid modified Rankin Scale score	0 (0–0)
Known hypertension	7/10
Baseline antiplatelet	1/10
Last known well to hospital arrival (min)	157 (70–261)
National Institutes of Health Stroke Scale score	19 (19–25)
Glasgow Coma Scale	13 (11–14)
Intraventricular hemorrhage	6/10
Spot sign on neuroimaging	3/10
Putaminal location	7/10
Arteriolosclerotic etiology	8/10

Table 2 Trial workflow and outcomes

Variable	Median (IQR) or No/total No
Onset to enrollment (min)	227 (175–377)
Onset to surgery (min)	531 (437–628)
Hospital arrival to surgery (min)	353 (250–469)
Early theater return	1/10
Procedure duration (min)	98 (77–110)
Preoperative volume (mL)	59 (25–77)
24 hours postoperative volume (mL)	12 (5–25)
≤15 mL residual at 24 hours	5/10
≤10 mL residual at 24 hours	5/10
≥50% ICH reduction (postoperative)	10/10
≥50% ICH reduction (24 hours)	9/10
Evacuation percentage (24 hours)*	71 (61–80)
Mortality (28 days)	3/10
Mortality (90 days)	3/10
Mortality (180 days)	3/10
mRS (90 days)	4 (4–6)
mRS (180 days)	4 (3–6)

*Excludes patient with ICH reaccumulation.
ICH, intracerebral hemorrhage; mRS, modified Rankin Scale.

Conclusion

In this study, early ICH MIS using the Aurora Surgiscope and Evacuator appeared to be feasible and safe, warranting further exploration.

Trial registration number: ACTRN12619001748101.

HELPFUL REMINDERS & TIPS

For Project Managers, Study Coordinators & Study Teams

- **Data Collection Guidelines:**
  Data Collection Guidelines V5 can be found in the Toolbox in WebDCU.
  Fastest MOP V3 has been added to the Toolbox in WebDCU.

- **Adverse Events reporting reminders:**
  - Non-serious AEs should be reported from the time of study drug infusion through Day 4.
  - Serious AEs and AEs of special interest should be reported from the time of study drug infusion through Day 90.
  - Any fatality should be reported as an AE through Day 180. If death occurs, the AE name should be the event leading to death.
  - All SAEs should be submitted on F104 within 24 hours from time of knowledge.

- ***F246 – Informed Consent – Regained Capacity***
  - If the subject does regain capacity at some point during the trial or at end of study, but signed informed consent was not obtained, please enter the reasoning for why consent was not obtained into (Q09) 'Reason signed informed consent not obtained'.
  - If the subject does not regain capacity during the trial or at end of study, please enter the reason why into the General Comments section.
  - We will query for further information if needed.

- ***F104 Adverse Events***
  We have had a recent database change impacting **F104 Adverse Events**. This update includes the additional question (Q31) shown below. If (Q12) *Type of event = 'Acute cerebral infarction'*, you will be prompted to answer (Q31).

  The attached PDF is Version 7 of the form and can be used as the printable form. This can also be found in the CRF Collection Schedule in WebDCU.

  Any already submitted Adverse Event forms will have warning violations triggered on forms where (Q12) = Acute Cerebral Infarction. Please update your CRFs to answer (Q31) if needed.

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/