NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

JULY 2024 | VOLUME 3 | ISSUE 7

FASTEST

FVIIa for Acute hemorrhagic Stroke Administered at Earliest Time

Issue Contents:

Message from Dr. Naidech

The summer heat is relentless, and so is FASTEST. There are now 489 enrolled patients at 91 sites. Congratulations to sites that have enrolled this month and to the highest enrolling sites! Memorial Hermann Texas Medical Center, Houston, and the University of Calgary - Foothills Medical Centre are our top enrolling sites in North America. Internationally, the National Cerebral and Cardiovascular Center in Japan and Tubingen University Hospital in Germany lead the board. Keep up the great work!

Andrew M Naidech, MD MSPH
Northwestern University
Feinberg School of Medicine

Please join us for the *FASTEST* Monthly Webinar

Wednesday July 17th, 2:00-3:00 pm EST

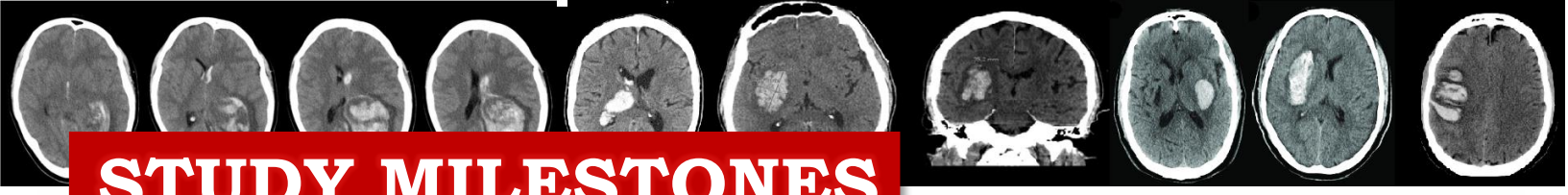
- Dr. Mari-Carmen Lichti from Clinic Frankfurt Höchst, Germany will be presenting their case.
- Dr. Christopher Lewandowski and his team from Henry Ford Health System, Germany will be presenting their case.
- Brief trial update.
- Dr. Broderick will be discussing reporting protocol violations, serious adverse events (SAE), and the CIRB submission.
- Pharmacy update on new IP shipment in US.

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 = **489**

- US Randomizations: **133**
- International randomizations: **356**
  - Japan = **224**
  - Canada = **59**
  - Spain =**34**
  - Germany = **28**
  - UK = **11**

Randomization last month = **15**

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, July 17th, @ 2:00-3:00 pm EST**

FASTEST study team office hours: **Monday, July 29th, @ 1:00-2:00 pm.**

Important Notes

Study Drug Update:

Please note: To help reduce drug wastage due to temperature excursions and to manage kit allocation effectively in the event of a shortage, we will only be shipping one kit to sites that have not enrolled a subject in the past three months.

Thank you for your understanding and cooperation.

Sites Without Enrollment or Screening for Few Months:

The latest version of the newly updated **Data Collection Guidelines V5** can now be found in WebDCU in Project Documents. Please use this document going forward for any CRF related questions in WebDCU. Please let us know if you have any questions.

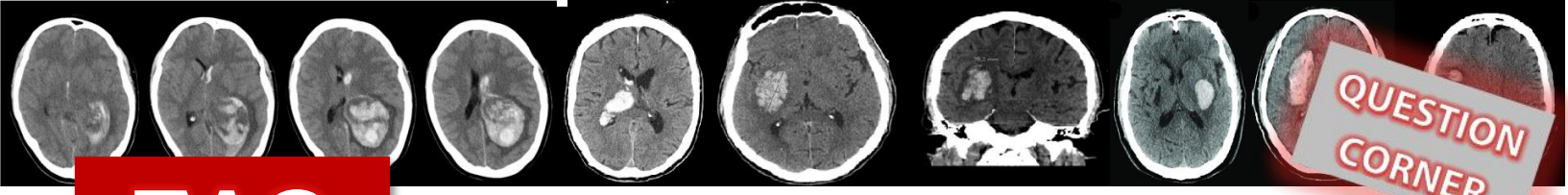
Updating Changes on the 1572:

We are seeing a lot of changes to the DoA's recently as the Fellows change over. Please make sure you are reflecting these changes on the 1572. The current 1572 template is in the Toolbox in WebDCU.

Reporting Protocol violation and SAEs:

Please do NOT report events (PV, PD or AE) to the cIRB until after the NCC project manager review. We will inform you if any event needs to be reported to the cIRB and/or regulatory authority.

- Protocol deviations/violations and all study-related issues should be reported in the 'issues table' for NCC review. The NCC will review these issues and then instruct sites if Advarra reporting is required.
- SAEs should only be reported in WebDCU for IMSM review. If IMSM finds an SAE reportable to the cIRB, the site will be instructed to report the SAE to Advarra. No SAEs should be reported to Advarra directly until instructed by NCC.



FAQ

Q: In WebDCU, the COVID-19 Assessment CRF is posted at the End of Study. If my subject had a positive COVID-19 test during the study, do I need to also submit an Adverse Event CRF?
A: Review the date of the positive test and the date of randomization/infusion.
-If the date of PCR test with positive results is between randomization and Day 4, complete Form 104: Adverse Event.
-If the date of PCR test with positive results is after Day 4 through Day 90, complete Form 104: Adverse Event only if the event is serious.

Q: For the 90-day visit we attempted to contact the subject, the subject's spouse, & son via telephone call, voice messages, text messages and e-mail numerous times with no response. one time they answered and hung up on our team. Looking at the subject's medical record we can see they have been coming in to occupational and speech therapy appointments at another campus, so they are alive. And from those notes I can infer their mRS is likely a 2. However, the subject does have a significant history of methamphetamine use (came to ED shortly after being discharged from index ICH encounter because heart was "racing" after using meth) and no-shows to appointments. After looking at the MOP we are still unsure what my next steps should be in this situation. Please advise me on what we should do at this time?
A: If possible, your team should try to follow up with the subject at their occupational and speech therapy appointments at the other campus. However, it is acceptable to use the mRS derived from the subject's medical record. Please ensure to note in the comment section on why the mRS was obtained without RFA. Assessing the mRS without obtaining RFA will be considered a minor protocol deviation. Therefore, this would need to be reported in the issues table for our review. Please document all efforts and attempts to contact the subject within the study follow-up window. The subject will not be considered lost to follow-up until all attempts have been made from the 180-day follow-up (+ 14 days) up to day 240 as described in the MOP.

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.

New Sites... Welcome Aboard!

The following new site was **released to enroll** in the *FASTEST* study during the last month.

Arnau de Vilanova University Hospital, Lleida, L, Spain

Site PI: Francisco PURROY

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**
2. **Prisma Health Greenville Memorial Hospital, Greenville, SC**

Great job on sites receiving CIRB approval under prospective consent.

1. **Jackson Memorial Hospital, Miami, FL**
2. **Arrowhead Regional Medical Center, Colton, CA**
3. **Temecula Valley Hospital, Temecula, 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	1 Subject
Nakamura Memorial Hospital, Sapporo, Japan	1 Subject
St. Michaels Hospital, Toronto, ON, Canada	1 Subject
Charite University Medicine Berlin, Berlin, Germany	1 Subject
Tubingen University Hospital, Tubingen, Germany	1 Subject
Memorial Hermann Memorial City Medical Center, Houston, TX	1 Subject
Wake Forest Baptist Medical Center, Winston-Salem, NC	1 Subject
Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA	1 Subject
The Queen's Medical Center, Honolulu, HI	1 Subject
University of Cincinnati Medical Center, Cincinnati, OH	1 Subject
WellStar Kennestone Hospital, Marietta, GA	1 Subject
Hospital Universitari Germans Trias i Pujol, Barcelona, B, Spain	1 Subject
Bellvitge University Hospital, Barcelona, B, Spain Barcelona, B, Spain	1 Subject
Girona University Hospital, Girona, GI, Spain	1 Subject
Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom	1 Subject

Memorial Hermann Texas Medical Center, Houston, TX is the top enrolling site in USA with ***23 enrollments*** so far followed by Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA with ***14 enrollments***.

The Memorial Hermann TMC team enrolling Fastest subject with the help of stroke fellows on the last day of their current fellow/resident year. From left Jacob Sambursky (fellow), ED nurse, Oriana Sanchez (fellow), Dr. Grotta, and Manuela Ochoa (resident).

Effects of Achieving Rapid, Intensive, and Sustained Blood Pressure Reduction in Intracerebral Hemorrhage Expansion and Functional Outcome

David Rodriguez-Luna, MD, PhD, Olalla Pancorbo, RN, MSc, Laura Llull, MD, PhD, Yolanda Silva, MD, PhD, Luis Prats-Sanchez, MD, PhD, Mari´an Muchada, MD, PhD, Salvatore Rudilosso, MD, PhD, Mikel Terceño, MD, PhD, Anna Ramos-Pachon, MD, Mar Hernandez Guillamon, PhD, Pilar Coscojuela, MD, ´ Jordi Blasco, MD, Santiago Perez-Hoyos, BSc, PhD, Angel Chamorro, MD, PhD, and Carlos A. Molina, MD, PhD, for the RAINS Study Group

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Background

The time taken to achieve blood pressure (BP) control could be pivotal in the benefits of reducing BP in acute intracerebral hemorrhage (ICH). We aimed to assess the relationship between the rapid achievement and sustained maintenance of an intensive systolic BP (SBP) target with radiologic, clinical, and functional outcomes.

Methods

Rapid, Intensive, and Sustained BP lowering in Acute ICH (RAINS) was a multicenter, prospective, observational cohort study of adult patients with ICH <6 hours and SBP ≥150 mm Hg at 4 Comprehensive Stroke Centers during a 4.5-year period. Patients underwent baseline and 24-hour CT scans and 24-hour noninvasive BP monitoring. BP was managed under a rapid (target achievement ≤60 minutes), intensive (target SBP <140 mm Hg), and sustained (target stability for 24 hours) BP protocol. SBP target achievement ≤60 minutes and 24-hour SBP variability were recorded. Outcomes included hematoma expansion (>6 mL or >33%) at 24 hours (primary outcome), early neurologic deterioration (END, 24-hour increase in NIH Stroke Scale score ≥4), and 90-day ordinal modified Rankin scale (mRS) score. Analyses were adjusted by age, sex, anticoagulation, onset-to-imaging time, ICH volume, and intraventricular extension.

Results

We included 312 patients (mean age 70.2 ± 13.3 years, 202 [64.7%] male). Hematoma expansion occurred in 70/274 (25.6%) patients, END in 58/291 (19.9%), and the median 90-day mRS score was 4 (interquartile range, 2–5). SBP target achievement ≤60 minutes (178/312 [57.1%]) associated with a lower risk of hematoma expansion (adjusted odds ratio [aOR] 0.43, 95% confidence interval [CI] 0.23–0.77), lower END rate (aOR 0.43, 95% CI 0.23–0.80), and lower 90-day mRS scores (aOR 0.48, 95% CI 0.32–0.74). The mean 24-hour SBP variability was 21.0 ± 7.6 mm Hg. Higher 24-hour SBP variability was not related to expansion (aOR 0.99, 95% CI 0.95–1.04) but associated with higher END rate (aOR 1.15, 95% CI 1.09–1.21) and 90-day mRS scores (aOR 1.06, 95% CI 1.04–1.10).

Discussion

Among patients with acute ICH, achieving an intensive SBP target within 60 minutes was associated with lower hematoma expansion risk. Rapid SBP reduction and stable sustention within 24 hours were related to improved clinical and functional outcomes. These findings warrant the design of randomized clinical trials examining the impact of effectively achieving rapid, intensive, and sustained BP control on hematoma expansion.

Classification of Evidence

This study provides Class III evidence that in adults with spontaneous ICH and initial SBP ≥150 mm Hg, lowering SBP to <140 mm Hg within the first hour and maintaining this for 24 hours is associated with decreased hematoma expansion.

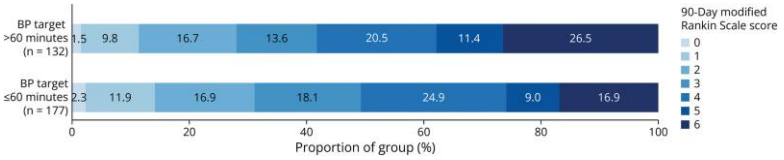


Figure 2 Modified Rankin Scale Scores at 90 Days Based on Achievement of Systolic Blood Pressure Target Within 60 Minutes

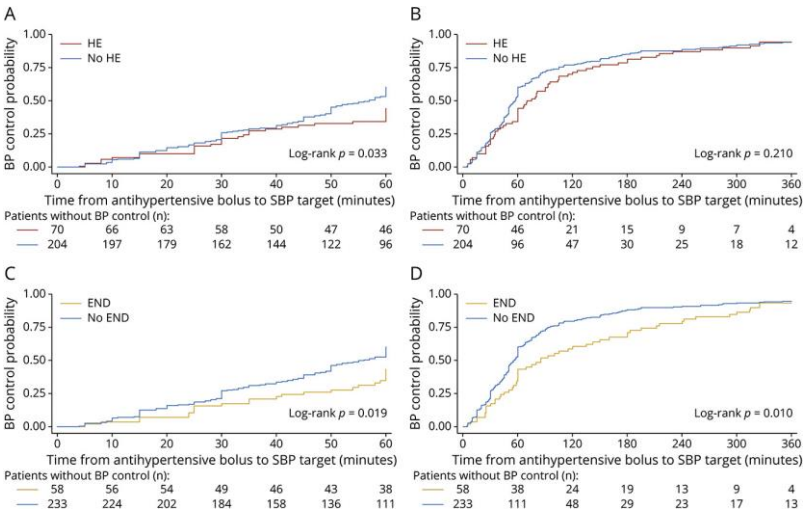
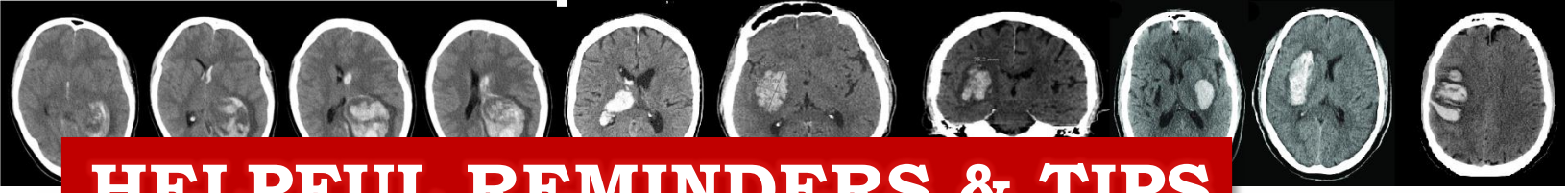


Figure 1 Kaplan-Meier Curves of Blood Pressure Control Probability Based on the Occurrence of Hematoma Expansion and Early Neurologic Deterioration



HELPFUL REMINDERS & TIPS

For Project Managers, Study Coordinators & Study Teams

- **REDCap Alerts:** There will be following alerts for FASTEST sites in REDCap:
  - •Incomplete Records
  - •Remote Attestation
  - •WebDCU Subject ID

  These alerts were sent out 05-15-2024 at about 10 AM and will continue every day until the site addresses the matter.

- **New data base change:**

  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.

Q12		Type of event	○ Acute myocardial infarction ○ Acute cerebral infarction ○ Acute pulmonary embolism ○ Other adverse event	R
Q31	*If Q12 is 'Acute cerebral infarction'*	Type of acute cerebral infarction *Clinically silent new DWI positive small region on MRI is less than 1cm diameter* *Clinically silent new moderate- or large-sized ischemic lesion on CT or MRI is greater than or equal to 1 cm*	○ Clinically silent new DWI positive small region on MRI ○ Clinically silent new moderate- or large-sized ischemic lesion on CT or MRI ○ Any new cerebral infarction on MRI or CT that is accompanied by clinical worsening	W

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/