NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

OCT 2024 | VOLUME 3 | ISSUE 10

FASTEST

FVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Dowlatshahi

What a journey! It is an absolute honour to be part of a global effort that offers treatment for what was once thought to be the untreatable stroke. Our Canadian sites have rallied to offer hope to patients unfortunate enough to experience an intracerebral hemorrhage, yet fortunate enough to reach a world-class comprehensive stroke centre. We are creating the pathway to deliver what we believe will become the standard of care in a few short years. Let's keep pushing!

Dar Dowlatshahi MD PhD
Vice Chair of Research,
Department of Medicine
University of Ottawa, Canada
FASTEST Canadian National PI

Please join us for the *FASTEST* Monthly Webinar

Wednesday October 16th, 2:00-3:00 pm EST

- Dr Yolanda Silva Blas from Girona University Hospital, Girona, Spain will be discussing her case.
- Dr. Broderick will be discussing the recent protocol amendments and upcoming futility analysis.
- NDMC will review site quality report cards.

Join Zoom Meeting

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

Meeting ID: 992 3691 0048

Recoding of the Webinar can be accessed here

https://www.nihstrokenet.org/trials/fastest/webinar
Password **Faster**

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 = **558**

- US Randomizations: **155**
- International randomizations: **403**
  - Japan = **247**
  - Canada = **73**
  - Spain =**38**
  - Germany = **29**
  - UK = **16**

Randomization last month = **21**

Total Screen Failures = **2085**

Subjects Randomized by MSU = **17**

Subjects Terminated Early = **4**

eConsent Used = **27**

Remote Consent Used = **23**

CALENDAR OF EVENTS

Upcoming *FASTEST* Monthly Webinars: **Wednesday, October 16th @ 2:00-3:00 pm EST**

FASTEST study team office hours: **Monday, November 11th, @ 1:00-2:00 pm.**

IMPORTANT NOTES

Upcoming Data Freeze: In preparation for the upcoming database freeze ahead of the next DSMB meeting, please complete any outstanding data items including overdue CRFs and visits, unresolved DCRs, and open rule violations by **Thursday, October 24th**.

To view any outstanding data/CRFs for your site, select [**Subject CRF List**] under the [**Data Management**] tab. Select '**Data Due or Open DCR**' from the Page Actions drop down box in the top right-hand corner.

Please reach out to us if you have any questions.

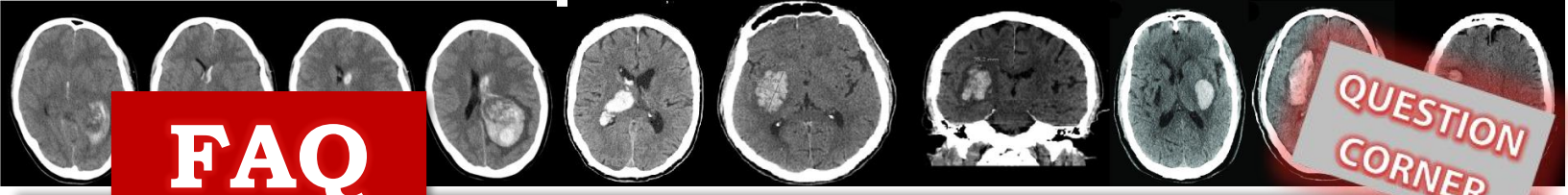
Site Performance Report Cards: The site-specific report cards to evaluate the performance of sites participating in the FASTEST trial were sent out last week. Please note that StrokeNet will also be issuing trial-specific report cards to gauge the performance of its participating sites moving forward. Please reach out to us if you have any questions.

MOP Updated: The updated version of the MOP (V3.1) is now available in the toolbox on WebDCU. A copy with the highlighted changes has also been provided with this newsletter.

FAQ

Q: It was brought to our attention that a recently enrolled subject has an AVM that may be the cause of the hemorrhage, which was not apparent on the initial scans according to the site PI. How should this be classified and reported?

A: ICH due to an AVM is an exclusion criterion. In this case, as the AVM was not apparent on the initial scan and was only diagnosed after enrollment, the subject technically does not meet eligibility criteria. However, according to the protocol language, this does not require reporting as an eligibility violation to the CIRB.



However, the sites should update and report this accordingly in the **F101 Eligibility form** as outlined below:

Secondary ICH related to other known causes *Trauma, aneurysm, arteriovenous malformation (AVM), coagulopathy, etc.*	○ No ◉ Yes	*Q22 must be No or this subject is not eligible.* *Response: AVM identified after randomization. AVM not known before randomization.*

Please upload all images (scheduled or unscheduled) related to this subject for our review. Kindly let us know when images are uploaded. Moving forward, we wanted to emphasize the need for increased diligence in ensuring that all eligibility criteria are met.

Q: We received notification that our FASTEST patient presented to the ED on Friday for elevated blood pressure. They are currently receiving home health care and during their visit on Friday they noticed elevated BP's in the 180's. They were advised to go to ED for further work up. They were noted to be asymptomatic and given hydralazine to help better control their BP, discharged on same day. Wanted to touch base to see if this is something that would qualify as an SAE or if regular AE documentation would suffice?

A: The decision to classify an event as either an AE or SAE is ultimately at the discretion of the site's PI, regardless of the event's grade. Typically, if the event results in a change in treatment, hospitalization, or even an ED visit, during which the subject required medical or surgical intervention will fall under the SAE category. Kindly refer to the study MOP **page 48 -54** for detailed description of the reporting requirements.

1. Reportable Event Definitions

1.1 Adverse Event (AE)

An AE is defined as any untoward event or complication that was not previously identified, or that occurs with greater frequency or severity than previously reported, which occurs during the protocol intervention or during the follow-up period, whether or not considered related to the protocol intervention.

For the FASTEST trial, non-serious adverse events will be reported from the time of randomization through Day 4.

1.2 Serious Adverse Event (SAE)

AEs are classified as either serious or non-serious. An SAE is any adverse event that results in any of the following outcomes or actions:

- Death due to any cause.
- A life-threatening adverse experience (i.e., the subject was at immediate risk of death from the event as it occurred).
- Inpatient hospitalization or prolongation of existing hospitalization. (Hospitalizations scheduled before enrollment for an elective procedure or treatment of a pre-existing condition that has not worsened during participation in the study is not considered a serious adverse event).
- A persistent or significant disability/incapacity (i.e., a substantial disruption of one's ability to conduct normal life functions).
- A congenital anomaly/birth defect; and,
- An important medical event that may not result in death, be life-threatening, or require hospitalization, but may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition (e.g., a new diagnosis of cancer made after study enrollment is considered an important medical event)
- Has suspicion of transmission of infectious agents.

An adverse event that does not meet any of the criteria for seriousness listed above should be regarded as a non-serious AE.

All SAEs will be recorded from the time of randomization through Day 90. Any fatality will be reported through Day 180.

Please note that **all AEs** must be reported within the **first 4 days of enrollment**, while **SAEs** must be reported **up to 90 days**, and mortality events should be reported up to day 180 (see below). These reports must be submitted within **24 hours of the study team becoming aware of the event**.

In this case, the subject was enrolled in the trial on **August 1st**, and the event occurred on **September 13th** during which the subject received medical intervention (hydralazine) for BP management. This should be reported in WebDCU as an SAE. **Please remember that reporting an SAE after 24 hours of awareness of event constitutes a protocol deviation.**

SHOUT OUTS!!

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

1. **Mayo Clinic Saint Marys Campus, Rochester, MN**

Great job on sites recently released to begin enrolling.

1. **Health Sciences Centre, Winnipeg, MB, Canada**

The Top Enrolling Site

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

Subjects enrolled = 63!!

Congratulations to Enrolling Sites last Month!

National Cerebral and Cardiovascular Center, Osaka, Japan	3 Subject
Kagoshima City Hospital, Kagoshima, Japan	1 Subject
Toranomon Hospital, Tokyo, Japan	1 Subject
Gifu University Hospital, Gifu, Japan	2 Subject
Vancouver General Hospital, Vancouver, BC, Canada	4 Subject
University of Alberta Hospital, Edmonton, AB, Canada	1 Subject
St. Michaels Hospital, Toronto, ON, Canada	1 Subject
John Radcliffe Hospital, Oxford, United Kingdom	1 Subject
Memorial Hermann Memorial City Medical Center, Houston, TX	1 Subject
Toledo Hospital, Toledo, OH	1 Subject
Jackson Memorial Hospital, Miami, FL	1 Subject
M Health Fairview Southdale Hospital, Edina, MN	1 Subject
Massachusetts General Hospital, Boston, MA	1 Subject
Memorial Hermann Memorial City Medical Center, Houston, TX	1 Subject
Girona University Hospital, Girona, GI, Spain	1 Subject

SCIENCE CORNER

ARTICLE OF THE MONTH

Decompressive craniectomy plus best medical treatment versus best medical treatment alone for spontaneous severe deep supratentorial intracerebral haemorrhage: a randomised controlled clinical trial

Jürgen Beck, Christian Fung, Daniel Strbian, Lukas Bütikofer, Werner J Z'Graggen, Matthias F Lang, Seraina Beyeler, Jan Gralla, Florian Ringel, Karl Schaller, Nikolaus Plesnila, Marcel Arnold, Werner Hacke, Peter Jüni, Alexander David Mendelow, Christian Stapf, Rustam Al-Shahi Salman, Jenny Bressan, Stefanie Lerch, Arsany Hakim, Nicolas Martinez-Majander, Anna Piippo-Karjalainen, Peter Vajkoczy, Stefan Wolf, Gerrit A Schubert, Anke Höllig, Michael Veldeman, Roland Roelz, Andreas Gruber, Philip Rauch, Dorothee Mielke, Veit Rohde, Thomas Kerz, Eberhard Uhl, Enea Thanasi, Hagen B Huttner, Bernd Kallmünzer, L Jaap Kappelle, Wolfgang Deinsberger, Christian Roth, Robin Lemmens, Jan Leppert, Jose L Sanmillan, Jonathan M Coutinho, Katharina A M Hackenberg, Gernot Reimann, Mikael Mazighi, Claudio L A Bassetti, Heinrich P Mattle, Andreas Raabe, Urs Fischer, on behalf of the SWITCH study investigators*

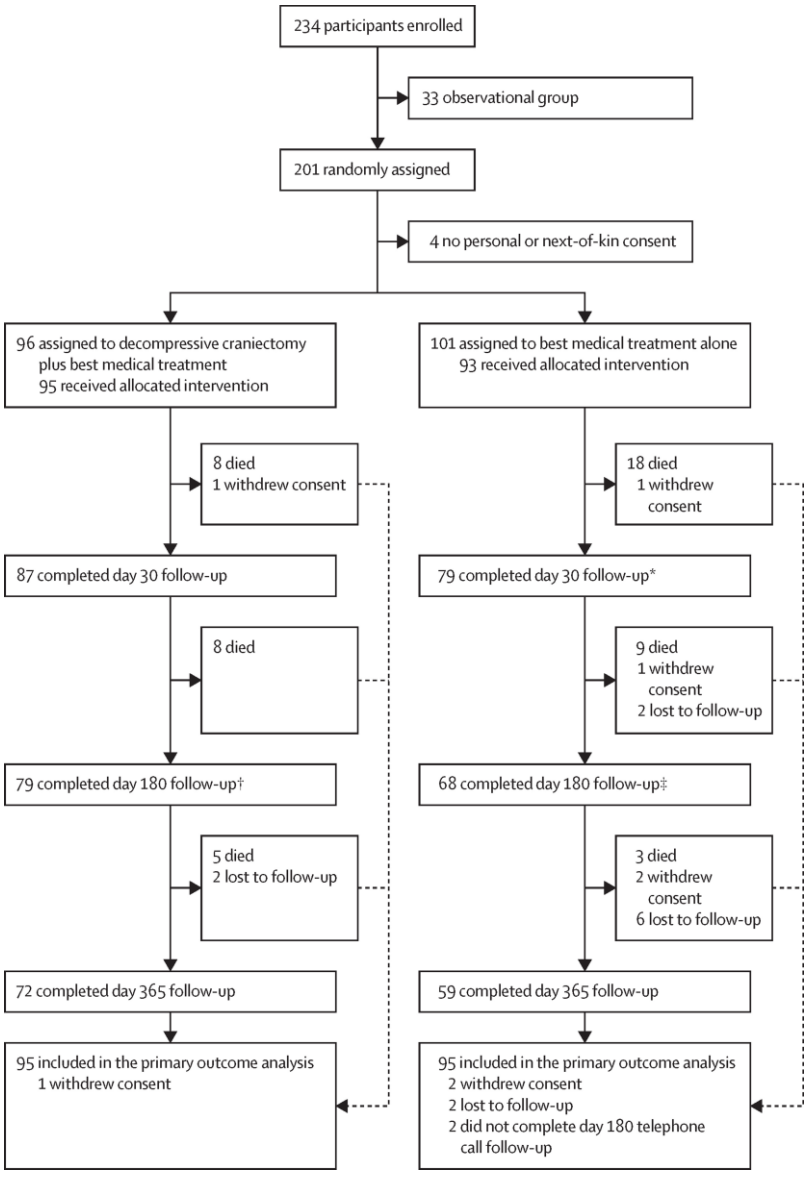
Lancet. 2024 Jun 1;403(10442):2395-2404. DOI: 10.1016/S0140-6736(24)00702-5.

Background

It is unknown whether decompressive craniectomy improves clinical outcome for people with spontaneous severe deep intracerebral haemorrhage. The SWITCH trial aimed to assess whether decompressive craniectomy plus best medical treatment in these patients improves outcome at 6 months compared to best medical treatment alone.

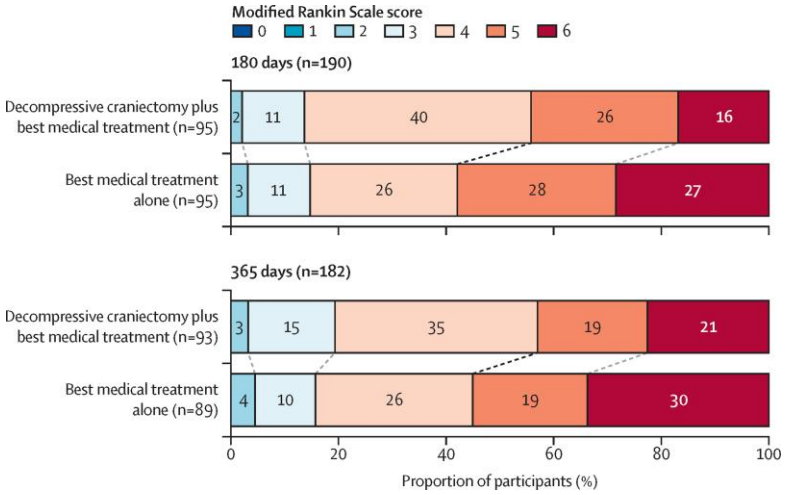
Methods

In this multicentre, randomised, open-label, assessor-blinded trial conducted in 42 stroke centres in Austria, Belgium, Finland, France, Germany, the Netherlands, Spain, Sweden, and Switzerland, adults (18– 75 years) with a severe intracerebral haemorrhage involving the basal ganglia or thalamus were randomly assigned to receive either decompressive craniectomy plus best medical treatment or best medical treatment alone. The primary outcome was a score of 5–6 on the modified Rankin Scale (mRS) at 180 days, analysed in the intention-to-treat population. This trial is registered with ClincalTrials.gov, NCT02258919, and is completed.



Findings

SWITCH had to be stopped early due to lack of funding. Between Oct 6, 2014, and April 4, 2023, 201 individuals were randomly assigned and 197 gave delayed informed consent (96 decompressive craniectomy plus best medical treatment, 101 best medical treatment). 63 (32%) were women and 134 (68%) men, the median age was 61 years (IQR 51–68), and the median haematoma volume 57 mL (IQR 44–74). 42 (44%) of 95 participants assigned to decompressive craniectomy plus best medical treatment and 55 (58%) assigned to best medical treatment alone had an mRS of 5–6 at 180 days (adjusted risk ratio [aRR] 0·77, 95% CI 0·59 to 1·01, adjusted risk difference [aRD] −13%, 95% CI −26 to 0, p=0·057). In the per-protocol analysis, 36 (47%) of 77 participants in the decompressive craniectomy plus best medical treatment group and 44 (60%) of 73 in the best medical treatment alone group had an mRS of 5–6 (aRR 0·76, 95% CI 0·58 to 1·00, aRD −15%, 95% CI −28 to 0). Severe adverse events occurred in 42 (41%) of 103 participants receiving decompressive craniectomy plus best medical treatment and 41 (44%) of 94 receiving best medical treatment.



Conclusion

SWITCH provides weak evidence that decompressive craniectomy plus best medical treatment might be superior to best medical treatment alone in people with severe deep intracerebral haemorrhage. The results do not apply to intracerebral haemorrhage in other locations, and survival is associated with severe disability in both groups.

HELPFUL REMINDERS & TIPS

For Project Managers, Study Coordinators & Study Teams

- **For Upcoming Database Freeze:**
  - In preparation for the upcoming database freeze ahead of the next DSMB meeting, please complete any outstanding data items including overdue CRFs and visits, unresolved DCRs, and open rule violations by Thursday, **October 24th**.
  - To view any outstanding data/CRFs for your site, select [Subject CRF List] under the [Data Management] tab. Select 'Data Due or Open DCR' from the Page Actions drop down box in the top right-hand corner.
  - Please reach out to Susanna Steinmuller (crestett@musc.edu) or Evan Tomaschek (tomascheke@musc.edu) with any data questions.

- **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/