NIH StrokeNet

PREVENTION | TREATMENT | RECOVERY

Biweekly Update
8-May 2020

StrokeNet Enrollment Update

ARCADIA	440/1100	CREST 2	1653/2480
Sleep SMART	253/3062	CREST H	139/500
TRANSPORT2	11/129	MOST	33/1200
I-ACQUIRE	22/240	ARCADIA-CSI	52/500
ASPIRE	0/700	SATURN	0/1480

StrokeNet Trial Updates

I-ACQUIRE

We hope that everyone is staying well and safe! Thank you for your continued effort and flexibility during this uncertain time.

As of March 17, 2020 all enrollment and randomization have been suspended.
At that time we had **8** sites released to enroll and a total of **22** randomized subjects:

- Ann Arbor, MI - C.S. Mott Children's Hospital - **1** participant randomized
- Boston, MA - Boston Children's Hospital - **7** participants randomized
- Cincinnati, OH - Cincinnati Children's Hospital Medical Center - **3** participants randomized
- Columbus, OH - OSU Martha Morehouse Medical Plaza- **1** participant randomized
- La Jolla, CA – USCD Health La Jolla – **4** participants randomized
- New Haven, CT - Yale New Haven Children's Hospital - **2** participants randomized
- Philadelphia, PA - Children's Hospital Of Philadelphia (CHOP)
- Roanoke, VA - Fralin Biomedical Research Institute - **4** participants randomized

Save the date – Our next PI/Co-I/Coordinator Webinar will be Thursday 14 May (12-1pm ET).

Our next PI and Coordinator call will be on **Monday, May 11th at 11am.** If anyone has topics they would like to discuss during the call, please send them to Julia Gonzalez, (Julia.jackson@duke.edu).

Risk mitigation plan for reopening Transport2 at sites is currently under review. A final plan is set to be distributed to sites as soon as possible.

NINDS has asked that we track the impact of COVID-19 on our enrolling sites. In response, a new module has been added to WebDCU called **COVID-19 Impact Assessment** under the **Project Management** tab. Each site will need to complete this assessment for their site. The site will indicate on this form what restrictions are in place that come from their local site and when each of those restrictions went into effect. Each site should complete this form, regardless of the fact that enrollment is halted for all StrokeNet studies. The purpose of this tool is for us to know the individual restrictions at each site in response to COVID-19.

Please note: this assessment only needs to be completed for sites that were previously released to enroll. If you already completed this assessment, please edit your initial entry to answer the new questions that have been added. For questions or concerns, please reach out to Patty Hutto huttoja@musc.edu

Please make sure you have completed your BlueCloud recertification training by logging into the website: http://duke-transport2.trainingcampus.net. Individuals who have expired or about to expire training have been sent reminder emails. **Note this is for the scoring of the Fugl Meyer, not the video training.** Annual renewal is now being tracked in WebDCU, which will notify coordinators directly when any of their staff have outdated training.

As a reminder, subject randomization is currently on hold, but please continue to pre-screen patients in a remote setting. Subjects who are scheduled for any future follow-up assessments will have to be held and noted as a deviation.

To date, Moss Rehab, University of Kentucky, University Southern California, Medstar, Emory University, and University of Cincinnati have randomized subjects. MUSC, Barnes Jewish, Burke, University of Texas, University Alabama, and Baystate are all open to enrollment. Cleveland VA has a fully executed CTA and CIRB approval, and currently working through their local IRB submission. Duke has received IRB approval, and is finalizing study start-up activities. UPMC has received CIRB approval and is still pending a signed CTA. There are eleven subjects randomized in the trial. Five have completed the study, and six have completed the intervention phase and are in the follow-up period.

Thank you for your continued effort and flexibility during this time of uncertainty.

MOST
Multi-Arm Optimization of Stroke Thrombolysis

The StrokeNet Central Institutional Review Board has approved MOST's request to resume enrollment activities at all sites. Understandably, local situations are varied across the country and you should not restart enrollment activities at your site until your institution and local IRB determine that it is safe and feasible. The COVID Impact Assessment survey in WebDCU™ should be updated in real-time to reflect the current status of research at your institution.

In order to resume MOST activities, please indicate that your institutional policies regarding COVID-19 allow subject enrollment and treatment on the COVID Impact Assessment. By doing so, each site confirms the following statements:

• We will minimize participant and study staff COVID-19 exposure, transmission, and infection, including:

  o Screening individuals for COVID-19 symptoms and exposure prior to study visits.

  o Avoiding potential transmission by asymptomatic infected individuals.

  o Taking other study-specific precautions for research visits.

  o Using remote study visits when feasible.

• We will verify that study visits or procedures will not contribute to shortage of resources, such as essential clinical staff and Personal Protective Equipment (PPE) that are needed to take care of COVID-19 infected patients.

• We will verify that study procedures would not interfere with clinical procedures put in place to treat COVID- 19 patients.

From the CREST-2 Clinical Coordinating Center:

CREST-2

CREST-2		CREST-2 StrokeNet
CEA	870	378 (44% of total)
CAS	783	133 (17% of total)
Total	**1653**	**511 (31% of total)**

Re-Initiation of Enrollment: The Clinical Coordinating Center has submitted to CIRB to open enrollment for the trial. We are very excited to re-initiate recruitment as we have heard from several CREST-2 sites that they have patients waiting to be randomized! Once a response is received from CIRB, we will send out a communication to our sites. In addition to this, we will also be circulating an enrollment survey to get an idea of how sites anticipate recruitment will be at their institution moving forward. We understand that recent events will likely impact research operations but we're very hopeful that CREST-2 will be successful with your help!

Continuing Review: The CREST-2 Continuing Review date is set for May 13th.

Thank you for your participation in Sleep SMART. We hope you are doing well, especially during this difficult time.

The NCC regulatory specialist will be making the amendment v5.0 changes to your site-specific ICD and will submit those to the CIRB on your behalf. Once you receive your site CIRB approval letter with the approved ICD please upload those to WebDCU as soon as possible and submit to your local IRB for acknowledgement, if required.

As of March 24, 2020, when Sleep SMART was suspended, 752 subjects were enrolled and 253 subjects were randomized.

Sites not yet released to enroll:

We want to encourage all sites that have not yet been released to enroll to continue to work toward site activation.

If your institutional guidelines allow, please proceed with start-up activities:

- CIRB submission
- Finalize the Clinical Trial Agreement and FusionHealth DUA and Consignment agreement
- Upload site and people documents to WebDCU
- Complete online trainings (https://webdcu.musc.edu/campus/)
- Complete readiness call
- Please review the site to-do checklist found in the WebDCU toolbox

Sites that have already enrolled:

Don't forget these important reminders:

1. Please perform the 3- and 6-month follow-up visits by telephone within the assessment window(!), by a blinded study team member: 90 days (-14 days, +30 days), 180 days (-14 days, +60 days).
    - If a blinded study team member is not available, but the assessment can still be done within window by an unblinded study team member, please take advantage of that opportunity and report performance by the unblinded investigator.
2. If the window for the 3-month visit ends and you have not been able to reach a subject, please continue to reach out to him/her until the 6-month window begins. Please pursue 6-month assessments out to 3 months past the 6 month assessment time point before considering the subject lost to follow-up.
3. If you can't get in touch with the subject by phone to schedule the outcome assessment, please check the consent form to see if you have permission to contact him/her by text or email. Alternative contacts may also be found in the back of the consent. Sleep SMART also has a letter template available on our website (https://www.nihstrokenet.org/sleep-smart-trial/research-team "unable to reach letter template") and for those on the verge of being lost to follow-up, a lost to follow-up letter.
4. Please review the changes to the revised MOP, recently released.
5. Please check "Alerts" in WebDCU to find unresolved queries.
6. Visit our website: www.nihstrokenet.org/sleep-smart-trial/research-team to review helpful materials.
7. Please remember to report AEs. If you need guidance, please refer to the Sleep SMART MOP. Please recall that the only AEs that should be reported between consent and randomization are:

- All SAEs (fatal and non-fatal) that are definitely related or stand a reasonable possibility to be related to the Nox T3 sleep apnea test or the aCPAP run-in night procedures (within 5 days of awareness of event for non-fatal; within 24 hours of awareness for fatal)
- All non-serious AEs of special interest (see protocol 8.3.8) that are definitely related or stand a reasonable possibility to be related to the Nox T3 sleep apnea test or the aCPAP run-in night procedures (within 5 days of awareness of event)
- Primary outcome events (ischemic stroke, ACS, and deaths) (within 5 days of awareness of event)

8. All responses to Data Clarification Requests (DCRs) must be submitted within 5 days of query generation, except those associated with Serious Adverse Events, which must be answered within 24 hours of query generation. Site payments are contingent upon the subject's data being entered, submitted, and all DCRs addressed.
9. For stroke outcome events, please be sure to upload documentation in the outcome packets that provides information about new stroke symptoms, including focal neurological symptoms and signs on exam, and associated dates.

Save the date-Our next PI and coordinator webinar will be Wednesday, May 20, 2020 from 1-2 EST. We will focus on the most recent CIRB amendment.

ASPIRE

- Enrollment and randomization activities were suspended on March 20, 2020
- Screening activities are continuing as permitted by local institutional policies
- Our protocol allows consent via telephone/telehealth contact. Methods to implement remote consent and randomization are being developed for consideration by the cIRB.
- We would like to encourage all sites that have not been released to enroll to continue to work on startup activities:
    - cIRB submission
    - Finalizing clinical trial agreement
    - Uploading startup documents to WebDCU
    - Receiving study drug and lab kits
    - Completing readiness calls
        - Sites with CTA & cIRB can schedule a readiness call https://doodle.com/poll/rnnu37hfvmca36z9
- 99 executed CTAs and 85 sites with cIRB approval
- 44 sites released to enroll
- ASPIRE next Webinar is May 27, 2020 3:00p-4:00p EDT https://nihstrokenet.adobeconnect.com/trials/ To take part in the conversation dial 1 (877) 621-0220 Pass Code: 745694

ARCADIA

Looking forward to a safe and productive new normal!

The ARCADIA protocol Version 5 has been cIRB approved! Many of the changes to the new protocol were made to reflect the new realities of life (and clinical trials) in the era of COVID-19. For example:

1. We extended our time window for eligibility from 120 days to 180 days from stroke.
2. First dose of study medication is now required within 48 hours of randomization, rather than 24 hours (allows for shipping of first dose of study drug).
3. We allow remote/virtual consenting and remote randomization, as sites are able.
4. Clarified that study-specific procedures do not need to be performed in person.
5. Added COVID-19 as an Adverse Event of Special Interest.

The NCC is now working on submitting the site-specific informed consent documents to the cIRB for approval. We will keep coordinators and PIs informed as to next steps.

We are also working on approval for our restart plan. The focus of the plan will be to allow those sites that are capable of resuming research activities to do so, beginning with randomizing those patients who were found eligible prior to the pause. We hope that we will be able to begin recruiting/consenting new patients ~June 1. Details will follow, so please be on the lookout for communications from Rebeca and Pam.

Key points to remember:

- Now that the randomization window has been extended to 180 days, we continue to ask that sites not close out subjects that are beyond their 120-day randomization window in the expectation that we will be able to re-consent and randomize them once the pause is lifted overall and at your site.
- We have also submitted a request for additional financial support to address the research challenges caused by this pandemic at the sites, including support for the additional effort required to consent and screen patients who may not become eligible for randomization, as well as support for shipping of drug to patients. More information to come once these are approved.
- In the meantime, please continue screening and keeping lists of potential participants that we can contact after the consent/randomization pause is lifted.
- Please also keep in touch with patients to be sure they are weathering the crisis, and that their study-related medications continue.
- As personnel changes and new staff comes onboard often, we ask that you communicate with all of your team members.

We are thinking of you all on the frontlines, as well as our ARCADIA participants. Please keep safe!

Webinar: Our next PI and coordinator webinar will be May 26th at 2 PM Eastern--save the date! We're asking that at least 1 person from each site attend the monthly webinar and pass the information along to their team. Also, please send suggestions for topics you'd like discussed.

If you miss out on a webinar, you will soon be able to find the slides on the StrokeNet website (https://nihstrokenet.org/intranet/minutes/trial-webinars).

ARCADIA•CSI
Cognition & Silent Infarcts

The ARCADIA-CSI Study Team is wishing all of our sites the best during this challenging time. We are thinking of you all and hoping you and your families are staying safe and healthy.

At this time, enrollment continues to be suspended. However, the study team is working diligently on an amendment that will allow sites to remote consent. The amendment was submitted this past week at the Prime level. Site submissions will follow Prime level cIRB approval.

The continuing review has been approved. Approval documents were sent out on Monday. Prime level approval documents have been placed in WebDCU under the Toolbox>protocol documents. Please let us know if you have any questions.

For already-enrolled CSI patients, who have not had their neurocognitive assessment, the SRU follow-up telephone exams to patient homes has begun. You will need to make reservations 7-14 days before the assessment. If you need a shorter time window, please contact the SRU at the University of Alabama Birmingham.

Please contact Tashia Harris, herndotl@ucmail.uc.edu or Stephanie Kemp, skemp@standford.edu with any questions.

RPPR Follow-up

After careful consideration by NINDS Grants Management and Program staff, we have determined that all NIH StrokeNet Regional Coordinating Centers will have their human subjects coding changed to “NO” human subjects. In order to facilitate this process, we ask that you do the following:

1. Please indicate “NO” human subjects on the FY 2020 RPPR
2. Please indicate “YES” to human subjects changes. In the explanation of changes, please indicate that there is **no change to the human subjects work on this award from what was originally proposed. This is a correction to the human subjects coding, as this award supports the salaries of staff to coordinate administrative activities of this Regional Coordinating Center, and does not involve direct human subjects research.**
3. Please request the release of any outstanding year 2 restricted funds so that the restriction can be lifted prior to the year 3 award. If you are unsure of the process, please contact Joanna.vivalda@nih.gov for guidance.

Important ESO/WSO News

As you are likely aware, the ESC/WSO Conference, jointly organised by the European Stroke Organisation and the World Stroke Organization, has been rescheduled for 7-9 November, 2020, in Vienna, Austria. Although ESO-WSO has been postponed, there have been many recent advances in stroke care, and the need to provide high quality care for people with stroke is as critical now as ever.

Therefore, there will be a **"Large Clinical Trials" session, online on May 13,** where results from large clinical trials will be revealed**.**

Wednesday, May 13, 2020, at 13:00 pm CET.
The major trial results that will be presented:

Efficacy of Fluoxetine: A Randomized Controlled Trial in Stroke (Effects) – **Erik Lundström (Sweden)**

Assessment of Fluoxetine in Stroke Recovery (Affinity): Results of a Double-blind, Placebo-controlled, Randomised Trial – **Graeme Hankey (Australia)**

A Randomized Trial of Direct Endovascular Thrombectomy Versus Thrombectomy Preceded by Intravenous Alteplase in Acute Ischemic Stroke – **Jianmin Liu (China)**

The Basilar Artery International Collaboration Study (Basics): A Randomized Controlled Trial of Endovascular Therapy in Basilar Artery Occlusion – **Wouter Schonewille (Netherlands)**

Ascot Trial: The Effect of Randomisation to Atorvastatin or Placebo, and Amlodipine-based or Beta-blocker-based Regime on 20-year Incidence of Stroke or Dementia – **William Whiteley (UK)**

The webinar is FREE of charge. The ink to participate will be online at https://eso-wso-conference.org/eso-wso-may-webinar/ on **13-May.**

Coordinator Webinar

Coordinator Webinars are a requirement for the NIH StrokeNet RCC Coordinators/Managers

The next webinar is scheduled for Wednesday, 27-May, at 1:30pm ET. Topic and presenter(s) TBA.

Steering Committee Call

Steering Committee Calls are a requirement for all NIH StrokeNet RCCs
(one representative per RCC required)

The next Steering Committee call is scheduled for **Wednesday, 13-May, 2020, 12 noon ET.** Dial in: 513-621-0220; 1-877-621-0220; Passcode 434578.

Trial Presentations: TEACH2 – Dr. Babak Benjamin Navi 12:00 – 12:30

INSPIRE – Dr. Neeraj Badjatia 12:30 – 1:00

To join the meeting: **https://nihstrokenet.adobeconnect.com/steering/**

Please enter as a guest, then your first and last name or your email address.

To take part in the audio you **MUST** dial in: Dial-In Number: **(877) 621-0220** Passcode Number: **434578**

Professional Development Webinar

Professional Development Webinars are a requirement for the NIH StrokeNet Trainees

Monday, May 11, 2020

Presenters:

1:00 **Tamra I J Ranasinghe, MD** UCSD
The Role of Ejection Fraction in 90-day Functional Outcome in Acute Ischemic Infarction Patents Receiving Acute Stroke Therapy

1:30 **Amir Shaban, MD** University of Iowa
Acute Ischemic Stroke Following Herpes Zoster Infection

2:00 **Ossama Khazaal, MD** University of Pennsylvania
Prognosis of Acute Symptomatic Carotid Artery Occlusion

2:30 **Nicholas Joseph Reish, MD, PhD** Northwestern University
Monocyte Biomarkers as Predictors of Infection After Intracerebral Hemorrhage

Moderator: **TBA**

To join the meeting: *https://nihstrokenet.adobeconnect.com/pdw/.* Please enter as a guest, then your email address or your first and last name.

To take part in the conversation you MUST dial-in. (877) 621-0220 Passcode: 190825

Grand Rounds

Grand Rounds are a requirement for the NIH StrokeNet Trainees, however all are welcome to participate.

Thursday, May 28, 2020

Topic: Anticoagulation Reversal in ICH

Presenter: **Holly Hinson, MD, MCR** OHSU

Moderator: **Cemal Sozener, MD**

To join the meeting: *https://nihstrokenet.adobeconnect.com/grandrounds/*. Please enter as a guest, then your email address or your first and last name.

To take part in the conversation you MUST dial-in. (877) 621-0220 Passcode: 190825

NIH StrokeNet Employment Opportunities

YALE SCHOOL OF MEDICINE - DEPARTMENT OF NEUROLOGY

POSTDOCTORAL JOB DESCRIPTION

GENERAL SUMMARY/ OVERVIEW STATEMENT:

This is an opportunity for a highly motivated individual with a background in biological or data sciences to perform cutting-edge research utilizing clinical, physiological, genetic and imaging data assembled from human subjects with stroke or acute brain injury. There are also opportunities to design or analyze trial data. Receiving general direction from one of the Division of Neurocritical Care & Emergency Neurology faculty members, and working in close collaboration with several investigators from across Yale and other institutions in the US, the incumbent will advance research work focused on acute stroke, brain injury, both ischemic and hemorrhagic, with focus on clinical trial design and execution, physiological monitoring, neuroimaging analyses and population genetics.

Visa sponsorship for non-US applicants is possible

PRINCIPAL DUTIES AND RESPONSIBILITIES:

The postdoc will be responsible for project management, preparation of presentation materials, writing of manuscripts and grant applications, supervision of technologists and coordinators, presentations at local, national and international conferences. With broad support from Faculty members, the post-doctoral fellow will design and implement studies on the topics mentioned above, will analyze relevant data and lead the process of manuscript and grant writing. We are committed to tailor the training experience to the trainee's goals and career stage, providing the necessary background and tools to prepare the her/him for competitive faculty or residency/fellowship positions.

QUALIFICATIONS:

- MD, PhD, ScD, DrPH, MPH or MSc (required)
- Proven experience in multi-tasking various assigned scientific/research projects (required)
- Training in Epidemiology and/or Biostatistics (preferred)

SKILLS / ABILITIES / COMPETENCIES REQUIRED:

- Time Management: Exceptional organizational skills and ability to organize time and priorities effectively, asking for direction when appropriate. Flexibility to handle multiple tasks and deadline pressures.
- Analytical Skills: Ability to conceptualize and conduct complex analysis of research data
- Capacity for independent work
- Critical Thinking/Decision Making: Ability to appropriately evaluate all aspects of a situation and to independently make appropriate and timely decisions.
- Interpersonal/communication: Excellent interpersonal/communications skills and a good command of English language, including medical and scientific terminology.
- Information Systems/Technology Skills: Exceptional computer skills (including operating systems, word processing, database, electronic mail, Internet, and spreadsheets).
- Experience with statistical and programing software (R, MatLab, SQL, Stata), preferred.

Please send CV and 3 professional references to:

Kevin N. Sheth, MD
15 York Street | LLCI Room 1003C
New Haven, CT 06520
kevin.sheth@yale.edu

University of Cincinnati Vascular Neurologist

The Department of Neurology and Physical Medicine and Rehabilitation at the University of Cincinnati has new, exciting opportunities for **Vascular Neurologists** at Assistant, Associate, or Professor levels on both clinical and research career tracks.

The candidate will join an internationally renowned stroke program that includes:

- A highly collaborative, multidisciplinary team of 9 Vascular Neurologists, 7 Emergency Medicine Stroke Specialists, 9 Neurocritical Care Intensivists, 3 Interventionalists from Neurosurgery and Neurology, 2 Cerebrovascular Neurosurgeons, 6 Neuroradiologists, a large cohort of extremely experienced Research Coordinators, among others
- A JCAHO-Certified Comprehensive Stroke Center, including a 20-bed Neuroscience Intensive Care Unit and 10-bed variable acuity unit
- Multicenter, high-volume approach to acute stroke treatment and trial enrollment (550+ treated with reperfusion therapies in 2019), including a newly activated Mobile Stroke Unit
- A large, NIH-funded stroke research program, ranging from clinical trials in treatment, prevention, and rehabilitation/recovery, to epidemiology studies in health disparities and brain health, to molecular genetics
- A home to the National Coordinating Center (NCC) and a Regional Coordinating Center (RCC) of the NIH StrokeNet

The clinical practice would consist of a personally tailored combination of inpatient service, acute stroke call (including telemedicine), outpatient clinic, and teaching of residents and fellows from several different disciplines.

Exciting collaborative research opportunities are available for participation and growth, but not required.

MINIMUM QUALIFICATIONS: Must have an MD or DO, completed an ACGME-approved Vascular Neurology fellowship program, and be BE/BC.

HOW TO APPLY: Contact Pooja Khatri, MD, Director of the Vascular Neurology Division: pooja.khatri@uc.edu

The University of Cincinnati, as a multi-national and culturally diverse university, is committed to providing an inclusive, equitable and diverse place of learning and employment.

For more information about StrokeNet employment opportunities, please visit
http://nihstrokenet.org/education/employment-opportunities
Contact: Jamey Frasure, PhD, RN, Director · NIH StrokeNet Coordinating Center · frasurjs@ucmail.uc.edu · 513-558 1742
https://www.nihstrokenet.org