



Biweekly Update 5-June 2020

StrokeNet Enrollment Update

ARCADIA	441/1100	CREST 2	1662/2480
Sleep SMART	253/3062	CREST H	141/500
TRANSPORT2	12/129	MOST	33/1200
I-ACQUIRE	22/240	ARCADIA-CSI	52/500
ASPIRE	1/700	SATURN	0/1480

StrokeNet Trial Updates



ARCADIA•CSI
Cognition & Silent Infarcts

The ARCADIA-CSI Study Team like to say thank you to all our sites for participating in the CSI study.

Amendment V2 remains at the cIRB for approval. When it is approved, we will work to submit the approvals for each individual site.

As some sites have transitioned their staff over to work on Covid 19 trials, we ask that sites update their DOA in WebDCU to reflect the changes in the study team. If there are any questions regarding this, please let the study team team know.

All sites must complete the Covid 19 Impact Assessment Form in WebDCU prior to re-opening.

Sites still pending activation:

- Update **all** regulatory documents in WebDCU
- If you need to schedule your site readiness call – do so by contacting study team members below

Sites who were open prior to the Covid-19 pause:

- Update all regulatory documents
- Upload the approved continuing review documents

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



Working towards a re-start of enrollment!

We have been able to capture one of our pending randomizations bringing us to 441 subjects randomized – thank you Stanford University team! We hope to continue to do so as per the re-start plan and as possible at all the sites with the pending subjects.

Although the cIRB has approved our site by site re-start plan, we're still waiting for permission from Columbia's IRB to have CALM lab receive our samples needed for new subject enrollments. In the meantime, we continue to re-release sites that have pending randomizations as these are not new subjects, and we will let everyone know when we can re-release sites to enroll new subjects. We hope that we will be able to begin recruiting/consenting new patients soon and we ask that you continue to complete/update the requirements for re-release of your sites. We will provide an update as soon as possible.

Key points to remember for site re-release, pending randomizations and participant engagement:

- The ARCADIA protocol Version 5 has been cIRB approved and the site-specific consent forms (ICD v7.0) are being sent to the sites as they become available. Once you have yours, you will need to upload these regulatory items onto WebDCU as soon as possible and re-consent your active participants.
 - Please let us know if you will need local IRB for acknowledgment before using these.
- Complete the COVID-19 Impact Assessment v2 including the General Comment statement where the PI agrees to follow the prescribed plan and is ready to be released (see plan for phrase).
 - Email Rebeca (ra2356@cumc.columbia.edu) when your site is ready to be considered for re-release to enroll even if only doing remote screening, enrollments and follow ups.
- The randomization window is now 180 days from the subject's stroke, please do not close out subjects that are below this threshold so that we may randomize them once the pause is lifted at your site. However, please closeout those subjects beyond 180 days after their index stroke.
- 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 regarding new emails sent to the sites.

We're awaiting the official approval of the request for additional financial support to address the Baseline increase and shipping support for our sites. More information to come once these are approved. The Schedule of Payments link on your CTA will be corrected once we have the official approval to avoid any re-signing of changes and the shipments will be via a FedEx account to be provided.

We are looking forward to resuming our trial enrollment while 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 June 28th 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>).



SATURN is very excited to reopen enrollment!

We recently amended the study protocol to allow for obtaining remote consent from potential subjects or their surrogates to minimize in-person exposure. Protocol and ICF v4 were distributed to all sites.

Procedures for reopening SATURN enrollment were distributed to all sites.

In order to restart enrollments for sites that were previously released to enroll:

- Site must be approved on Protocol v4, Informed Consent Form v4.
- Indicate on the COVID Impact Assessment in WebDCU that your institution allows subject enrollment.
- Notification will be sent when site enrollment suspension is lifted in WebDCU

Sites that have not yet been released to enroll should follow the steps outlined above once they have been activated. This requires reconciling all regulatory documents in WebDCU. The COVID Impact Assessment will only be accessible to the sites that have been activated.

SATURN hosted a PI/Coordinator webinar on Thursday May 28th. You can view the recording here: <https://www.nihstroke.net.org/saturn-trial/webinars>

Please continue to update the COVID Impact Assessment with information on anticipated timelines for resuming research activities.

MGH has resumed shipping lab kits out to sites who have completed a readiness call. Please remember to confirm receipt of the lab kits in WebDCU once you are able to do so.

If you have any questions regarding SATURN and reopening enrollment at your site please contact:

Kimberlee Bernstein NCC Project Manager gammk@ucmail.uc.edu

Sarah Marchina Prime Project Manager (BIDMC) smarchin@bidmc.harvard.edu



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

AMENDMENT: Amendment v5.0 changes to your site-specific ICD were in most cases already made by the NCC, and submitted to the CIRB on your behalf. A good number have already been approved. 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.

RE-OPENING: On May 15, 2020, the CIRB approved our request to end the study-wide hold on in-person interactions, including enrollment, in Sleep SMART. Please report this to your local IRB, if appropriate. In WebDCU, please update the COVID Impact Assessment survey to reflect the current status of research at your institution and, if you are ready to re-start enrollments, to indicate confirmation (in 'general comments') of the statements in the memo dated May 15, 2020. Email Joelle to let her know when your local IRB has acknowledged the recent amendment. Pending NDMC queries may delay our ability to release you, so please catch up on these. You will not be released to enroll until you receive official permission through a WebDCU email.

Sites not yet released to enroll:

If your site is not yet released to enroll, please work toward site activation:

- 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. As a reminder, please ask subjects to answer PROMIS questions as they are written (do not provide specific instructions to attempt to eliminate the influence of COVID).
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.



Site Startup and Enrollment Updates: sites: **54**; enrollments: **141**

WE ARE BACK IN BUSINESS! The CIRB has approved unpausing CREST-H enrollment, and those centers who have been approved to enroll may now do so. Many thanks to Mayo Rochester who hit the ground running with 2 patients in the last week, bringing our total to 141, **40%** of our target. We have 6 additional sites in the onboarding pipeline.

Please also continue to be vigilant about cognitive visits. Because the 1-year cognitive test is the primary outcome in CREST-H, it is critical to obtain the **1-year telephone cognitive test** for CREST-H patients. The Survey Research Unit at University of Alabama Birmingham has resumed operations. PI's and coordinators, please make sure the cognitive exams – as part of the CREST-2 protocol -- are done for the 1-year time point.

Also, due to **restrictions on research imaging** at some medical centers are still on hold at the moment, so **1-year CREST-H perfusion scans** may be delayed. We have gotten approval to delay the 1-year scans until after your site reopens its scanners to research. You will have up to 3 months from that point to complete the scan.

We are still recruiting additional sites. Contact Randy Marshall rsm2@columbia.edu, Ron Lazar rlazar@uabmc.edu, Jaya Vijayan vijayan.jaya@mayo.edu, or Kevin Slane KJS4@columbia.edu with any questions.



- Thank you to **Forsyth Medical Center** for completing their Site Readiness Call!
- Congratulations to **Sarasota Memorial, Tampa General** and **Akron General Hospital** who have been released to enroll!
- Congratulations to **UF Health Shands Hospital** and **Vanderbilt University Hospital** who have been released to receive study drug in preparation for release to enroll!
- **Wake Forest, Kaiser Permanente LA Medical Center, SUNY Upstate Medical Center** and **WVU** have restarted subject recruitment at their sites. There are now **58** sites that have been released to enroll, **19** of which are actively recruiting!

Please join us for the **MOST June Investigator Call on Monday, June 8 at 2:00pm ET**. The webinar invitation along with Adobe Connect and teleconference information has been sent. Let us know if you did not receive the invitation.

- **Reminders**
 - For sites that are released to enroll please continue to complete screening logs in WebDCU™.
 - For sites that have not been reactivated, please continue to update the COVID Impact Assessment in WebDCU™ with information on anticipated timelines for resuming research activities.

Thank you all for your efforts!

The PI hotline is available 24/7 for any questions: 1-833-229-MOST

From the CREST-2 Clinical Coordinating Center:



	CREST-2	CREST-2 StrokeNet
CEA	875	382 (44% of total)
CAS	787	134 (17% of total)
Total	1662	516 (31% of total)

ATTENTION

Milestone. Thursday at 2:24pm EST, Inova Fairfax randomized patient number 1662 into CREST-2 – this ties ACAS for most enrollments of any asymptomatic trial in North America.

Reminder that CREST-2 is re-initiating enrollment! Currently, **17 of 57** StrokeNet sites have communicated to their respective site managers that they have completed the steps to re-initiate CREST-2 enrollment at their institution. We encourage you to reach out to the Clinical Coordinating Center to let us know the status of your institution opening up research operations and specifically CREST-2. **Starting June 1st, we will need to enroll a minimum of 15 patients per month through October 2020, 25 patients per month through May of 2021, and 30 patients per month until target completion of 2480 patients in December of 2022. We need the expertise of the CREST-2 teams at all StrokeNet sites to help our trial succeed!**

The risk factor mitigation program has entered phase 2, providing blood pressure cuffs to patients so that measurements can be made during virtual follow-up visits. Thanks Dr. Tanya Turan and her team at MUSC!



- Congratulations to **Mayo Clinic, Jacksonville, FL** for enrolling ASPIRE's first patient on Tuesday, May 26, 2020!
- On May 12, 2020, the cIRB approved out plan to **re-open the trial to enrollment** and procedures for remote consent, randomization, and participant follow-up.
 - Suspended sites have been contacted to enquire if they are able to resume enrollment.
 - Before being re-released to enroll, the site PI must attest that resumption can take place safely, in conformity with local restrictions, and without contributing to shortage of resources needed for care of COVID-19 patients.
 - All sites must complete a Remote Informed Consent Implementation form to be submitted to the cIRB via the ASPIRE NCC Project Manager.
 - The cIRB approved **ASPIRE Remote Study Procedures** and **Remote Informed Consent Implementation form** are posted in WebDCU > ASPIRE Toolbox and will be reviewed in detail during the ASPIRE Webinar on May 27, 2020
- Screening activities are continuing as permitted by local institutional policies.
- Please remember to update the **COVID-19 Impact Assessment v2** in WebDCU to alert us to any changes in local restrictions on screening or enrollment.
- For sites still pending activation, please:
 - Upload/waive pending regulatory documents.
 - Enter addresses for study drug and lab kit shipments.
 - If CTA and cIRB approval in place, schedule readiness call.
- ASPIRE next Webinar is June 24, 2020 3:00p-4:00p EDT <https://nihstrokenet.adobeconnect.com/trials/>
To take part in the conversation dial 1 (877) 621-0220 Passcode: 745694

StrokeNet eConsent Process

Thank you to those who joined the **StrokeNet CIRB eConsent Webinar** on Monday, 1-June. The recording can be found at <https://nihstrokenet.org/education/nih-strokenet-webinars-and-meetings>. A pdf of the slide set is available there, as well.

Mentioned in the webinar was a StrokeNet SOP that describes the central process for utilizing an electronic platform for obtaining informed consent: SOP ADM 24 Central Electronic Informed Consent Process will soon be able to be found at https://nihstrokenet.org/sop_gcp.

REMINDER: TEACH2 and INSPIRE Feasibility Surveys

Just a reminder, the TEACH2 feasibility survey was due to be sent to the NDMC on 3-June. The INSPIRE feasibility survey is due to the NDMC on **15-June**.

NIH News

***NEW* Grant Application Forms**

Attention June 5 cycle applicants!! NIH is transitioning to an updated set of application forms we refer to as FORMS-F. Use FORMS-F forms for grant application due dates. For more information about navigating this transition, visit <https://nexus.od.nih.gov/all/2020/05/12/working-on-an-nih-grant-application-make-sure-you-are-using-the-right-forms/>.

Coordinator Webinar

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

Wednesday, 24-June, 1:30pm ET

Topic: RCC Manager Survey Summary

Presenter: RCC Managers Planning Group

Moderator: Dave Haney, Case Western Reserve University

To join the meeting: <https://nihstroketnet.adobeconnect.com/coordinator/>

To take part in the conversation you **MUST** dial in. 1 (877) 621-0220 Pass Code: 434578

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, 10-June, 2020, 12 noon ET**. Dial in: 513-621-0220; 1-877-621-0220; Passcode 434578. Agenda to follow.

NOTE: Please review the attached StrokeNet Start Up Site Communication Process Flowchart before the call.

Grand Rounds

Grand Rounds are a requirement for the NIH StrokeNet Trainees, however all are welcome to participate. Information for the next Grand Rounds will be available later this summer. Stay tuned.

Professional Development Webinar

Professional Development Webinars are a requirement for the NIH StrokeNet Trainees

Information for the next PDW will be available later this summer. Stay tuned.

NIH StrokeNet Employment Opportunities

*For more information about StrokeNet employment opportunities, please visit
<http://nihstrokenet.org/education/employment-opportunities>*

Please share this update with your satellites and study teams!

*Contact: Jamey Frasure, PhD, RN, Administrative Director · frasurjs@ucmail.uc.edu · 513-558 1742
<https://www.nihstrokenet.org>*