



Biweekly Update 22-May 2020

StrokeNet Enrollment Update

ARCADIA	441/1100	CREST 2	1654/2480
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



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.

The amendment has been submitted to the cIRB and we expect to get the approval back sometime this week or next. Site submissions will follow Prime level cIRB approval.

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.

We also want to remind sites to complete the Covid 19 Impact Assessment Form in WebDCU. This is important to re-opening our sites.

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.



- 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 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



Site Startup and Enrollment Updates: sites: **54**; enrollments: **139**

We are at **139** patients, **40%** of our target. We have 6 additional sites in the onboarding pipeline!

CIRB approval to restart CREST-H was approved this week. This means whenever a CREST-2 site is ready to resume recruitment, CREST-H can be restarted as well. CREST-2 follow ups can be done by telephone. 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.



Due to the upcoming Memorial Day Holiday, our next PI and Coordinator call will be on **Tuesday, May 26th at 11am ET**. If anyone has topics they would like to discuss during the call, please send them to Julia Gonzalez, (Julia.jackson@duke.edu).

The Reactivation Risk Mitigation Plan for reopening Transport2 at sites has been approved by the Central IRB. This letter was distributed to sites from Dr. Feng on Friday, May 15th, 2020. This document must be submitted to sites local IRB's for approval prior to restarting any study activities. Additionally, sites will need to complete the **COVID-19 Impact Assessment** in WebDCU under the **Project Management** tab. Upon completion of this assessment, sites will be reactivated within WebDCU for study enrollment. 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.

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.

From the CREST-2 Clinical Coordinating Center:



	CREST-2	CREST-2 StrokeNet
CEA	870	381 (44% of total)
CAS	784	134 (17% of total)
Total	1654	515 (31% of total)

ATTENTION

CREST-2 Has Been Approved to Re-Initiate Enrollment! The Clinical Coordinating Center has received approval by the CIRB to re-initiate enrollment into the trial! This is great news as we are incredibly excited to begin CREST-2 enrollment again. **We ask that you please notify your site manager when your site is ready to begin enrollment prior to re-initiating and follow the guidelines the CIRB provided:**

- Sites will minimize participant and study staff COVID-19 exposure, transmission, and infection. These procedures address:
 - Screening individuals for COVID-19 symptoms and exposure prior to study visits.
 - Potential transmission by asymptomatic infected individuals.
 - Any other study-specific precautions for research visits.
 - Remote study visit feasibility

If you have any questions, please feel free to reach out to the Clinical Coordinating Center. With that, we want to stress the **importance of recruitment into CREST-2**. While COVID-19 restrictions may create barriers for your institution in regards to research, we want to emphasize to those who are able to enroll that it is essential we prioritize recruitment. As you can see, StrokeNet is accounted for only **31%** of randomizations in the trial. With only **826** randomizations left in the trial, we have put in place a strict enrollment procedure of **at least 15 patients per month until October 2020, at least 25 patients per month until May of 2021, and 30 per month until enrollment is completed in December of 2022**. We know that with your help we can achieve success. We would like to recognize the **VA Ann Arbor** and **Mayo Clinic Florida** as StrokeNet sites that already have patients interested in CREST-2! We look forward to additional sites re-initiating enrollment!

Sleep SMART

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 of the statements in the memo dated May 15, 2020.

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 check "Alerts" in WebDCU to find unresolved queries.
5. Visit our website: www.nihstrokenet.org/sleep-smart-trial/research-team to review helpful materials.
6. 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)
7. 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.
8. 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.

- Thank you to the following three sites that completed Site Readiness Calls!
 - **Tampa General Hospital, Tampa, FL** - David Rose and Andrea Bozeman
 - **University of Kansas, Kansas Hospital, Kansas City, KS** - Dr. Laith Maali and Alissa Poitras
 - **Sarasota Memorial Hospital, Sarasota, FL** - Mauricio Concha and Jeanette Wilson
- Congratulations to the following teams that have reactivated subject recruitment!
 - **Greenville Hospital**
 - **St. John Tulsa**
 - **University of Virginia**
 - **Memorial Hermann**
 - **Mayo Clinic Jacksonville**
 - **University of Michigan**
 - **Houston Methodist**
 - **Yale New Haven Hospital**
 - **University of New Mexico**
- Congratulations to the following team that has received study drug in preparation for release to enroll!
 - **University of Chicago**
- **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



SATURN is very excited to begin 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.

PLEASE JOIN US! SATURN is hosting the first PI/Coordinator webinar on **Thursday May 28th 12:30pm**. Calendar invitations went out.

To join the meeting: <https://nihstrokenet.adobeconnect.com/trials/> - Enter as a guest, then your first and last name. To take part in the conversation you **MUST** dial in. 1 (877) 621-0220 Pass Code: 745694. We will be discussing more about reopening study enrollment.

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

If you have any questions regarding start-up please reach out to these contacts at the NCC:

Kimberlee Bernstein Project Manager gammk@ucmail.uc.edu

Wren Hanson Contracts hansonwm@ucmail.uc.edu

Emily Stinson Regulatory stinsoey@ucmail.uc.edu

Jen Golan Regulatory golanjl@ucmail.uc.edu



Looking forward to a safe and productive re-start of enrollment!

Now that our re-start plan has been cIRB approved and it has been emailed to all site PIs/PSCs on May 13th, we're poised to start releasing sites to enroll as soon as it's feasible at each site. The focus 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 depending on your site's restrictions and whether the CALM lab will be able to work on ARCADIA samples. We will provide an update as soon as possible.

Key points to remember:

- 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.
 - 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.
- 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. However, please closeout those subjects that have exceeded 180 days after their index stroke.
- 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 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 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>).

NIH News

All About Contracts Podcast

The latest “All About Grants” podcast series introduced us to the world of contracts at the NIH, what they are, how they differ from grants, where to find them, what types of research are solicited, tidbits to focus on when developing a proposal, and more. The transcript from the 11-May podcast can be viewed at [https://grants.nih.gov/podcasts/All About Grants/episodes/All-About-Contracts.htm](https://grants.nih.gov/podcasts/All%20About%20Grants/episodes/All-About-Contracts.htm). Subscribe via iTunes or visit <https://grants.nih.gov/news/virtual-learning/podcasts.htm> for more information.

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 on or after May 25, 2020 and FORMS-E for due dates on or before May 24, 2020. 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/>.

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.

Coordinator Webinar

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

Wednesday, May 27, 1:30pm ET

Topic: On-going Trial Updates

Presenter: Study Project Managers

Moderator: Dave Haney, Case Western Reserve University

To join the meeting: <https://nihstrokenet.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.

In case you missed it, the TEACH2 and INSPIRE webinar presentations can be viewed at <https://www.nihstrokenet.org/intranet/minutes/trial-proposal-presentations>, after login.

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

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, Director · NIH StrokeNet Coordinating Center · frasurjs@ucmail.uc.edu · 513-558 1742
<https://www.nihstrokenet.org>