March 27, 2021 - Vol 4, Issue 2

ARCADIA

Atrial Cardiopathy and Antithrombotic Drugs In Prevention After Cryptogenic Stroke

Next Webinar: April 27 AT 2 PM ET/1 PM CT/12 MT/11 PM PT

MILESTONES

Randomized - 609

Consents - 2314

February Randomizations = 14

February Consents = 64

Congratulations to McLaren Macomb for randomizing our 600th subject!

Utilizing "Teach back" in Research

After reading the consent form and giving the patient ample time to review, narrow it down to four or more teaching point.

The "must haves" or "vital few" for the patient to know prior to signing the consent form.

Suggestions for opening script to the teach back questions. You want to ask in a non-shaming way for the patients to explain in his/her own words what was understood:

- I just gave you a lot of information, maybe you could explain to me…
- I sometimes talk fast and maybe go over information too quickly. Let's talk about what you would do if…
- I want to be sure I explained everything to you clearly. Could you explain to me in your own words…

Find the rest of the Teach Back information in the March 23rd Investigator-Coordinator Webinar at https://www.nihstrokenet.org/arcadia/webinars

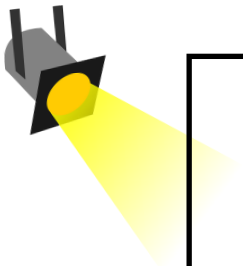
ARCADIA SC Hero

Jennifer Powers, PSC
University of Cincinnati

Jennifer works around her participants schedule and not her own. She calls them after their work hours to avoid interrupting them. Recently, to stay engaged with one of her subjects, she attended a grueling Jazzercise class on the weekend. She goes above and beyond research work and shows her participants that she truly cares and supports them. These extra efforts are why the UC site has 100% retention.

Thank you Jennifer for all of your hard work! You definitely are an ARCADIA Hero!

SPOTLIGHT ON SITES



February Top Randomizing Site

Memorial Hermann

2 randomizations!

Congratulations to these site who had their 1st Randomizations in January 2021

Sanford Medical & St. John's Hospital

February Top Consenting Site

Rhode Island Hospital

4 Consents!

141 Active Sites - U.S. 139, Canada 2

Thanks to all of our sites!

Welcome Aboard!

Memorial Hermann The Woodlands

Boca Raton Regional Hospital

UPMC Altoona

Thomas Jefferson University

Science Corner

Hot Off the ISC 2021 Press: STROKE AF results

ARCADIA is testing the concept that atrial cardiopathy without atrial fibrillation is a common cause of Embolic Stroke of Undetermined Source (ESUS), and that the risk of recurrent stroke will be reduced by anticoagulation in patients with ESUS and atrial cardiopathy, just as it is in those with AF. Undergirding these hypotheses is the notion that atrial cardiopathy is particularly associated with ESUS, and not with other ischemic stroke etiological subtypes, like lacunar and atherosclerotic stroke. The same has been assumed to be true of AF: i.e., that AF is a risk factor for embolic strokes, and not other types of strokes. The corollary to this is that AF is expected to be discovered more frequently in patients with ESUS than in patients with other stroke subtypes.

Data presented at the recent virtual International Stroke Conference, however, suggest that ESUS does not have a privileged connection to AF, and that AF is in fact found at similar rates after all stroke subtypes. Dr. Lee Schwamm presented the STROKE AF (Atrial Fibrillation in Non-Cardioembolic Stroke of Presumed Known Origin) trial results on Thursday March 18 in the Main Event session. ARCADIA PI Hooman Kamel was one of the lead investigators in STROKE AF, as well. In STROKE AF, investigators randomized 496 patients with recent small vessel or atherosclerotic stroke at 33 sites to an implanted cardiac monitor vs a control arm in which sites followed standard of care for identifying AF after stroke. Patients with cryptogenic stroke or definite cardioembolism were excluded. AF was defined as at least 30 seconds of AF. At 12 months, the incidence rate for detection of AF was 12.1% among those with the implanted monitor versus 1.8% among those in the standard of care arm (hazard ratio for detection of AF 7.41, 95% CI 2.60-21.28, p<0.001). Rates of detection were similar to those of patients in the CRYSTAL-AF trial, which focused on patients with cryptogenic stroke. Of note, patients with small vessel occlusion (12.6%) and large artery atherosclerosis (11.7%) had similar rates of AF detection at 12 months. Incidence rates of recurrent stroke were lower in the implanted monitor arm, although these results were not statistically significant. Follow-up is continuing on the cohorts.

The implications of the STROKE AF trial are that: (1) detection of AF among patients with small vessel and atherosclerotic strokes is higher with an implanted monitor than with standard of care monitoring; (2) stroke patients of multiple types have an increased risk of AF, not just those with ESUS; and (3) the detection of AF after stroke of multiple causes is rather high: ~1% per month, cumulatively. These results, however, may not be all that surprising looked at in the context of other recent studies of detection of AF in populations at high vascular risk. In the REVEAL AF study, for example, a non-randomized study of AF detection using an implanted monitor in those without AF, among 385 participants with CHADS2 score ≥3 (or 2 with at least 1 additional risk factor), the incidence of AF (at least 6 minutes) at 12 months was 27.1%. All these studies, perhaps, suggest then that AF is very prevalent among patients with cardiovascular disease, including stroke, and not only those with ESUS. The same could be true of atrial cardiopathy, although further research would be needed to determine whether this is true, and what the therapeutic implications are. If ARCADIA proves its primary hypothesis, future trials could test the role of anticoagulation among patients with non-ESUS stroke subtypes who also meet biomarker criteria for atrial cardiopathy.

[1] **Sanna T et al. Cryptogenic stroke and underlying atrial fibrillation. N Engl J Med. 2014;370(26):2478-86.**

[2] **Reiffel JA et al. Incidence of Previously Undiagnosed Atrial Fibrillation Using Insertable Cardiac Monitors in a High-Risk Population: The REVEAL AF Study. JAMA Cardiol. 2017;2(10):1120-1127.**

FAQs

Question: Do patients with a history of gastric bypass surgery have any issues with absorption with the ARCADIA study drug?

Answer: Changes to absorption kinetics of drugs after bariatric surgery have high variability among individuals. No single algorithm or practice tool can accurately predict these changes for all patients. For apixaban, limited evidence suggests that apixaban does not require dose adjustment after bariatric surgery. If absorption issues are suspected, patients can crush apixaban tablets and mix them with water, or apple juice.

Question: Can a patient with a kidney transplant participate in the study?

Answer: Yes they can participate if their creatinine is <2.5 mg/dL. But as we always suggest, a conversation with their nephrologist, & care team, prior to consenting, is the best practice.

Updates/Reminders/Tips

From our Project Managers

- Don't be caught with expired lab tubes. Please QA your lab kits monthly. Send in your resupply order early so you can get the tubes when you need them. The lab resupply order is located in the Lab Core Manual in the WebDCU toolbox.
- ARCADIA Site Report Cards will be emailed to the sites approximately 4/6/2021. These will be emailed quarterly.
- The ARCADIA webinars, Power Point slices and payment schedule, located in the ARCADIA StrokeNet website, are now password protected. Select the resource you would like to view and type in "Arcadian" when prompted to open the document. This password is for sites participating in ARCADIA only.
- Out of window visits are being tracked weekly. If you have received an email to record an OOW visit in the UAE/PD report in WebDCU and have not completed one, please do so immediately. These records are reported non-prompt to the clRB unless the subject was at risk, i.e. ran out of study drug.
- We are missing a large number of ECHO discs. Please remember you can sent them in with your lab shipments or batch them and send every 3 months.
- When shipping study drug to your subjects, please let Rebeca know the tracking number as she needs to reconcile the invoices for payment.
- Don't forget about the documents in the Toolbox. There are many to assist you in enrolling and educating your patients.
- PRIME eConsent has been approved by the clRB. Watch your email for the Implementation Form. This is to be completed and returned to let us know if your are interested in using eConsent.
- If your subject was eligible for randomization but wasn't randomized, please enter the reason in the general comments section of the EOS CRF.

From our WebDCU Team

- If your site uses a site-specific standalone HIPAA and/or Bill of Rights document, these should be appended to the signed ICF and uploaded as a single document into WebDCU upon randomization.
- The "Alerts" tab in WebDCU will give you a snapshot of any outstanding items that need to be addressed, such as missing, expired or rejected regulatory documents, open rule violations and open DCRs.
- WebDCU will have a data freeze on 4/15/2021.
- Do not open WebDCU in multiple browsers, windows, or tables. This can cause data issues in the study database.

ARCADIA Contacts

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24/7 Hotline: (833) 427-2234 if unable to reach please call (206) 535-1229
For an emergency that requires knowing whether patient is taking apixaban (Eliquis) or aspirin

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Greek Culture corner

Daughter of Demeter and Zeus, Persephone is the beautiful goddess of spring. She is called Kore: Beautiful Maiden, Her story is one of abduction, love, grief, and celebration.

Persephone was a young goddess that lived apart from the others and delighted in picking flowers in the woods. She was honored as Kore, meaning "Beautiful Maiden." She was Demeter's daughter, and Demeter loved her truly.

Hades, the God of the Underworld wanted Persephone to become his bride. One story points a finger at Aphrodite, who fearing that Persephone would remain a virgin, instructed her son Eros (Cupid) to shoot his sharpest arrow through Hades' heart.

Afraid that Demeter would not allow her to depart to the Underworld with him, Hades abducted Persephone while she was picking flowers. Again, some stories say that her father, Zeus was mixed up in the abduction. Some accounts say that seeing that Hades loved her, and knowing Demeter's temper, Zeus suggested the abduction to Hades. We shall never know.

Demeter, upset that her daughter was gone, went out to the ends of the Earth to find her child. Demeter soon learned that Zeus allowed Hades to marry Persephone. Grief and fury overwhelmed Demeter when she heard the news. Demeter halted all plants from flowering and ripening. She created winter for the first time. Zeus couldn't let the Earth die so he allowed for Persephone to return home if she had not tasted food in the Underworld. Unfortunately Persephone had eaten a number of pomegranate seeds that bound her to the Underworld, one month per year for each seed.

Each year when Persephone returns to the world from the Underworld, the earth again is alive with new growth. There is dancing and singing, and celebrations of the new life and the return of Persephone. In the late fall, when she has to go back to the Underworld, the world gets quiet, cold, and forbidding. Winter is when she is gone. For when she is in the Underworld, Demeter takes away the gifts of grain and harvest until she returns.

Courtesy of https://www.theoi.com