January 13, 2020 - Vol 3 Issue 1

ARCADIA

Atrial Cardiopathy and Antithrombotic Drugs In Prevention After Cryptogenic Stroke

NEXT ARCADIA WEBINAR
January 28 AT 2 PM ET/1 PM CT/12 MT/11 PM PT

MILESTONES

1500 Patients Consented

392 Patients Randomized!

Congratulations to VA Puget Sound
1st VA Facility to randomize a subject in any StrokeNet trial

Thank you to all of our sites!

BREAKING THE BLIND

Remember that breaking the blind should only be requested when knowing treatment immediately will change patient management. Generally, this will be:

- **When a patient has a recurrent ischemic stroke AND is a candidate for IV tPA**
- **When a patient has a major hemorrhage and the treating team is considering an-dexanet alpha or other reversal agent.**
- **A possible recurrent stroke alone, if there is no chance of giving tPA, should not require breaking the blind.**
- **The study PIs will ask about WHY blind needs to be broken when responding to hotline calls**
- **A diagnosis of AF does not require breaking the blind**

Call 24/7 Hotline: (833) 427-2234 If unable to reach, call (206) 535-1229

ISC PLANS

We have several exciting events happening at the ISC and look forward to seeing you there!

Unfortunately we cannot pay for anyone to attend but if you are attending please visit the ARCADIA and StrokeNet Events below!

Wednesday, February 19, 2020 @ 09:33 AM - Room 515A

ARCADIA Platform Presentation: Mitch Elkind MD - Predictors of Atrial Cardiopathy Among Patients In the ARCADIA Trial: An Analysis of the First 924 Patients

This is part of Session A4: Diagnosis of Stroke Etiology Oral Abstracts 0845 - 1015 am

There will be a number of other presentations related to ESUS and atrial cardiopathy at this session.

Wednesday, February 19, 2020 @ 8:30 - 10:30 PM - Rm. Platinum F - StrokeNet Get Together

This will be an informal gathering. Stop by for 10-15 minutes, have a drink and catch up!

Please RSVP to Pam Plummer (plummepa@ucmail.uc.edu) by January 30 if you plan on attending.

Thursday, February 20, 2020 @ 6:30 - 7:00 pm - Hall H - Ongoing Clinical Trials Posters II

Hooman Kamel MD - Atrial Cardiopathy and Antithrombotic Drugs in Prevention After Cryptogenic Stroke

We will have 2 more ARCADIA research posters as well during the meeting: details to follow!

Informed Consent Central - Coordinator Reminders

It is extremely important that informed consent be performed and documented properly!

- Failure to do so could lead to study termination.
- Please be careful and if you have any questions, reach out to Pam Plummer or Rebeca Aragon. You can always email: arcadia@ucmail.uc.edu.

Use the most current clRB approved version of the ICF when obtaining consent.

- **This version, and all approved versions, must be uploaded into the regulatory database in WebDCU™**

Consent should be obtained ONLY by staff who have been delegated this responsibility on the DoA.

Subjects who lack cognitive ability to make decisions about study participation cannot give consent.

- Have a trained site investigator assess the subject for capacity to consent and document this in the patient's EMR
- If the patient lacks the capacity to consent, a legally authorized representative (LAR) may consent on behalf of the patient
- If the subject regains the ability to consent during study participation, the consent process should be completed with the subject at that time

Do not have the LAR sign consent just because:

- Subject has trouble physically signing the ICF
- Subject is illiterate
- Subject is blind
- Subject does not speak English
- Subject prefers to have family/friend sign documents.

Double check consent document to make sure all sections have been correctly signed/dated by subject, or LAR if appropriate, and person obtaining consent.

- The participant, or LAR must personally sign and date consent.

A third party witness to informed consent must be used when there is a NON-COGNITIVE impairment that precludes the patient signing, but they are cognitively capable of consent (illiterate, blind, physically unable to sign, etc.):

- Whenever possible, participant should still "make their mark" on the signature lines of the consent form
- The full consent form should be read aloud to patients who are illiterate or blind.
- The third-party witness must be impartial
  - Do not use family members or friends
  - Do not use a member of the study team as a witness.

Before getting consent, obtain confirmation from patient's primary treating physicians, including cardiologist or others who may be treating them with antithrombotics, that the patient can be on single agent antiplatelet or apixaban

- We want to avoid having patients drop out because their other physicians want them to take open label aspiring, clopidogrel or something else

If you are evaluating a patient who may live in another city with an ARCADIA site, please do not consent them at your site, but instead contact Rebeca or Pam and we will try to arrange for the patient to be evaluated at the other site prior to consenting.

- It is difficult to transfer patients between consent and randomization

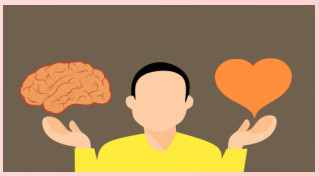
Thanks for your help in consenting properly!

An ethical ARCADIA trial is a strong ARCADIA trial!

ECHO Corner - Reminders & Tips

- Do not enter atrial volumes, size index, or other measurements into the echo form.
- WebDCU automatically calculates the index using the atrial dimension, height, and weight.
- Double check that you are entering the correct information!
- The preferred weight to use is the weight entered on the echocardiogram report (the weight measured at the time of the echo). If you think there is a more accurate weight elsewhere in the record that differs markedly from the one on the report, you can use that one. It is unlikely that a minor change in weight will affect the measures substantially.
- Please remember to send in the echos for BOTH consented AND randomized patients.

SCIENCE CORNER



Atrial cardiopathy and ipsilateral arterial plaque appear to be common and independent causes of stroke in patients with ESUS, despite a confluence of risk factors

(Paper: Kamel H et al. Atrial Cardiopathy and Nonstenosing Large Artery Plaque in Patients With Embolic Stroke of Undetermined Source. Stroke 2020; PMID: 31893985 [Epub ahead of print].)

In an interesting secondary analysis of the NAVIGATE ESUS trial, Dr. Kamel and colleagues tested the hypothesis that the presence of atrial cardiopathy is inversely associated with the presence of large artery plaque among patients with ESUS. In other words, they wanted to see whether only one or the other of these two common mechanisms for stroke would be present in an individual patient, implying—indirectly--that that the specific mechanism present (i.e., atrial cardiopathy or plaque) is more likely to be causal. Among nearly 4000 eligible patients, about a quarter had ipsilateral plaque, another quarter had left atrial enlargement (a marker of atrial cardiopathy), and 9% had both of these. While risk factors for both atrial enlargement and plaque were male sex, white race, hypertension, tobacco use, and coronary artery disease, the presence of increasing left atrial size was not significantly associated with presence of ipsilateral plaque after adjustment for covariates. This finding implies that these two potential stroke mechanisms are independent of each other. The authors concluded that atrial cardiopathy and atherosclerotic plaque could be separable, nonoverlapping causes of stroke among ESUS patients. Limitations of the study include the fact that other markers of atrial cardiopathy (like NT-proBNP and P wave abnormalities) were not studied, and that assessment of carotid plaque and atrial cardiopathy were not standardized or collected systematically in all patients. Nonetheless, the findings support the ARCADIA hypothesis that a substantial proportion of patients with ESUS have a specific cause--atrial cardiopathy. Furthermore, the results suggest that our pre-study estimate of the proportion of patients with atrial cardiopathy is correct: 25%. In fact, in ARCADIA, ~26% of ESUS patients have atrial cardiopathy and get randomized.

Table. Potential stroke mechanisms in patients with ESUS (NAVIGATE ESUS)

Potential stroke mechanism	N (Total 3983)	%
Substenotic arterial plaque ONLY	673	16.9%
Left trial enlargement (“atrial cardiopathy”) ONLY	942	23.6%
Both plaque and atrial enlargement	360	9.0%
Neither plaque nor atrial enlargement	2008	50.4%

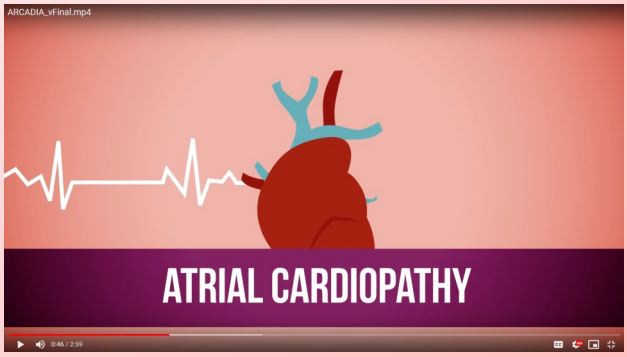
The ARCADIA Recruitment Video is here!

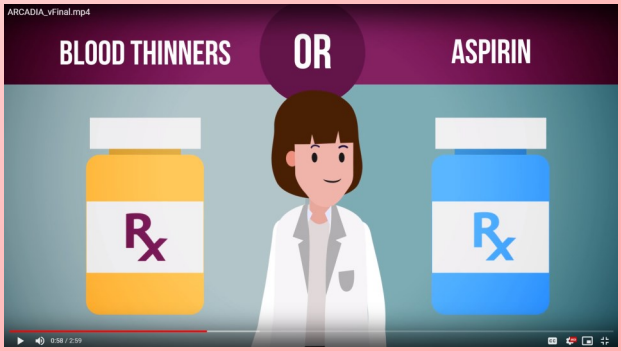
We have created an animated video that explains to potential patients ESUS, atrial cardiopathy, and what participation in ARCADIA is all about.

The video has been approved by the CIRB as an educational tool for sharing with patients in the process of recruitment. We are developing other means to publicize it and will keep you posted!

You can access the video by hitting Control and clinking on this link: ARCADIA_vFinal.mp4

Here are some screen shots from the ARCADIA recruitment animated video:





ARCADIA Contacts

ARCADIA@ucmail.uc.edu

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

Principal Investigators

Mitchell Elkind, MD, MS, Columbia University; mse13@columbia.edu
Hooman Kamel, MD, Weill Cornell Medicine; hok9010@med.cornell.edu
Will Longstreth, MD, MPH, University of Washington; wl@uw.edu
David L. Tirschwell, MD, MSc, University of Washington; tirsch@uw.edu

Project Manager	Pam Plummer	plummepa@ucmail.uc.edu	513-558-3941
Project Manager	Rebeca Aragon	ra2356@cumc.columbia.edu	212-342-0102
Pharmacy Core	Lindsay Vandergriff	strokenetcpharm@ucmail.uc.edu	513-584-3166
Pharmacy Core	Elizabeth Costea	strokenetcpharm@ucmail.uc.edu	513-584-3166
Pharmacy Core	Eric Muller	strokenetcpharm@ucmail.uc.edu	513-584-3166
WebDCU	Faria Khattak	khattak@musc.edu	984-221-0266
Lab Core	Jane Netterwald	jn355@cumc.columbia.edu	212-305-4837
ECG Core	Sayed Soliman	esoliman@wakehealth.edu	
ECHO Core	Marco Di Tullio, MD	md42@cumc.columbia.edu	212-305-9875
ECHO Core	Rui Lui	rl483@cumc.columbia.edu	212-305-2820