July 26, 2021 - Vol 4, Issue 5

ARCADIA

ARCADIA

Atrial Cardiopathy and Antithrombotic Drugs In Prevention After Cryptogenic Stroke

Next Webinar: July 27, 2021 AT 2 PM ET/1 PM CT/12 MT/11 AM PT

Mark you calendar for next month's webinar! August 24, 2021

MILESTONES

Who is going to randomize the 700th subject?

Randomized - 697 **Consents = 2595**

June Randomizations = 27 **June Consents = 73**

146 Active Sites - U.S. = 140 & Canada = 6

Webinar Tuesday July 27th

Please join us tomorrow for our July webinar. The following topics will be discussed:

Please let us know if there are topics you would like to discuss.

- Enrollment updates
- Causative Classification of Stroke - explained
- Science Article Discussed
- Updates to site start up, eConsent, CR
- Confirming Eligibility
- Maintaining Lab kits and much more!

ARCADIA SC Hero's

Vasiliki Patsiogiannis!

Massachusetts General

She reached out to weeks in advance to discuss a logistically difficult case. She managed to organize the patient/family/LAR, the facility medical staff and the study team to make sure the subject could be randomized safely into ARCADIA. She prepared a comprehensive research binder for the staff at the SNF to include in her medical chart just in case of any eventualities and she obtained the medical staff's willingness to work a bit more so that this patient could participate in ARCADIA. Her diligence also prevented the subject from being given the study drug while on aspirin. Thank you for your dedication to your participant & ARCADIA Vasiliki.
Your commitment has not gone unnoticed!

SPOTLIGHT ON SITES

June Top Randomizing Site

Methodist - 4 randomizations!

Hospital of the University of Pennsylvania - 2 randomizations!

June Top Consenting Site

Methodist & University of Alberta- 4 consents each!

UH Cleveland - 3 consents!

Sites with First Randomizations for June

Rush University Medical Center

Neurologic Research Centre

Welcome Aboard!

No new sites were released in June but we have several U.S and Canadian sites in start up that we are anxious to get started soon!

Science Corner

Apixaban was associated with lower rates of cardiovascular events than warfarin among Medicare patients with AF of all levels of frailty, while other DOACs were associated with benefits only among the non-frail.

Investigators conducted a propensity score-matched analysis of Medicare data (2010-2017) among beneficiaries with atrial fibrillation taking either warfarin, apixaban, rivaroxaban, or dabigatran. The primary composite outcome comprised death, ischemic stroke, or major bleeding. Stratified analyses were conducted across three levels of frailty (non-frail, pre-frail, and frail). Among the 218,738 patients on apixaban compared to warfarin, and followed for a median of 84 days, the event rate was 60.1 per 1000 person-years for apixaban initiators versus 92.3 per 1000 person-years for warfarin initiators (Hazard ratio (HR) 0.68, 95% CI 0.65 - 0.72). The hazard ratios were similar across the three different levels of frailty (for non-frail, HR 0.61, 95% CI, 0.52 - 0.71; for pre-frail HR 0.66, 95% CI 0.61-0.70; and for frail HR 0.73, 95% CI 0.67 - 0.80). Neither rivaroxaban nor dabigatran was associated with a reduction in event rates compared to warfarin (for rivaroxaban, HR 0.88 CI, 0.77 to 0.99; for dabigatran, HR 0.98, 95% CI 0.92-1.05). Both rivaroxaban nor dabigatran were associated with a modest benefit among the non-frail, but neither was associated with a benefit among the pre-frail or frail. The rates of death, stroke, and major bleeding were each lower in the apixaban-treated patients compared to the warfarin-treated patients. Secondary outcomes were not all lowered consistently for the other DOACs.

Although direct comparison across the three DOACs is not possible due to the study design, these results suggest that apixaban is a particularly good choice of agent among elderly, frail patients with atrial fibrillation. These data may be of use when discussing participation in ARCADIA with prospective patients.

Reference:
Kim DH et al. Ann Intern Med 2021;doi: 10.7326/M20-7141. Epub ahead of print. PMID: 34280330.

Left atrial appendage occlusion during heart surgery in patients with atrial fibrillation prevents strokes

The LAAOS (Left Atrial Appendage Occlusion Study III) was a multicenter, randomized trial to test the hypothesis that occlusion of the left atrial appendage, the site of most thrombi from AF, would reduce stroke risk. Investigators included patients who had atrial fibrillation and a CHA_2DS_2-VASc score of at least 2, who were scheduled to undergo cardiac surgery for another reason. Patients were randomized to having their left atrial appendage occluded or not during surgery, and otherwise underwent usual care. The primary outcome was occurrence of ischemic stroke or systemic embolism. There were 2379 patients in the occlusion group and 2391 in the no-occlusion group. The overall mean age was 71 years and the mean CHA_2DS_2-VASc score 4.2. Over a mean 3.8 years of follow up, 4.8% (n=114) patients in the occlusion group and 7.0% (n=168) patients in the no occlusion group met the primary outcome (hazard ratio with surgery 0.67, 95% CI 0.53-0.85). Complications did not differ between groups. The majority (77%) of patients continued anticoagulant therapy.

In summary, among those with AF/ CHA_2DS_2-VASc score $\geq$2 who undergo heart surgery, left atrial appendage occlusion surgery reduces risk of stroke by about a third.

Relevance to ARCADIA

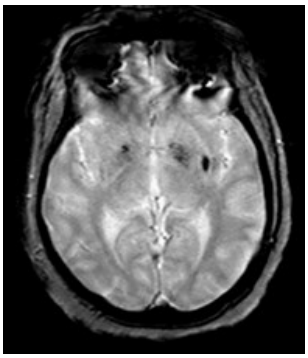
If ARCADIA demonstrates a benefit to anticoagulation among patients with atrial cardiopathy, demonstrating that biomarker defined atrial cardiopathy is a clinical entity that can be therapeutically targeted, future studies might consider the role of surgical occlusion of the LAA to prevent stroke as well.

Reference: Whitlock RP et al. Left atrial appendage occlusion during cardiac surgery to prevent stroke. N Engl J Med. 2021;384:2081-2091.

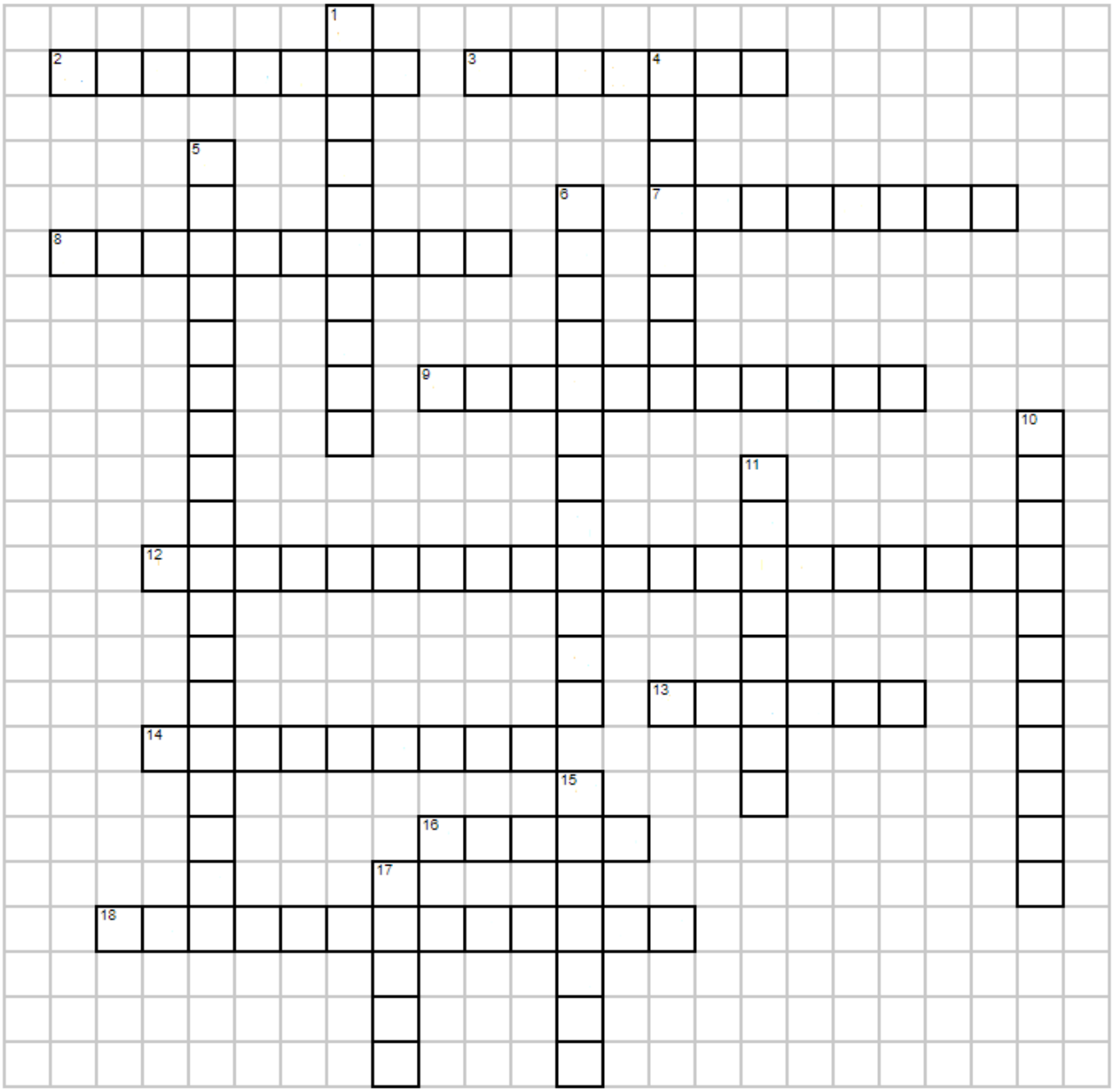
FAQ

Question: This patient has a subclinical chronic hemorrhage that the PI considers more than just a microhemorrhage. There is no history of intracerebral hemorrhage. Are they eligible for ARCADIA?

Answer: The patient has chronic left basal ganglia hemosiderin deposition consistent with a small, asymptomatic chronic hemorrhage. This should not exclude them from ARCADIA.



Just For Fun!



ACROSS

2. What is the password to view the study slides on the StrokeNet website?
3. What should you review at each visit to prevent prohibited medications? (2 words abbreviated)
7. What lab test is one of the 3 cardiopathy criteria?
8. What do you need to do to study drug, until cleared for use, if a temperature excursion occurs?
9. What should you do if your subject is not responding for a visit? (3 words)
12. What is open label aspirin considered if subject is taking study drug? (2 words)
13. Where do you upload all of your site and people documents?
14. How do you report an out of window visit in Web-DCU? (2 words)
16. What is the maximum number of years a subject can participate?
18. What date are study visits based from?

DOWN

1. What does your subject need to carry on them at all times? (2 words)
4. What is REDCap used for?
5. What irregular heart rhythm is an exclusion for participation? (2 words)
6. Who can you call for study assistance? (3 words)
10. What needs to be uploaded if a subject has an SAE? (2 words)
11. What drug is being compared to aspirin?
15. What's important to attend monthly to get up to date study information?
17. What is the required format for the ECHO CD? (abbreviation)

***See solution in the next issue*.**

ARCADIA Contacts

ARCADIA@ucmail.uc.edu

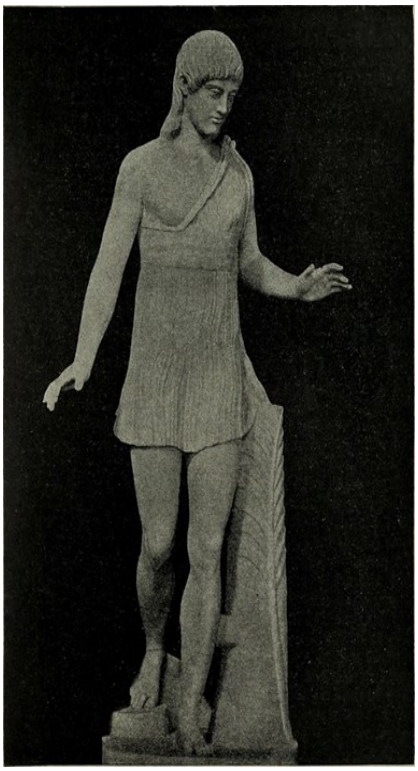
24/7 Hotline: (833) 427-2234 if unable to reach please call (206) 535-1229
For an emergency that requires knowing whether patient is taking apixaban (Eliquis) or aspirin

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
Canadian Project Manager	Angie Djuric	Angie.Djuric@phri.ca	905-521-2100 x40545
StrokeNet Pharmacy Core	Lindsay Vandergriff	strokenetcpharm@ucmail.uc.edu	513-584-3166
StrokeNet Pharmacy Core	Brittany Gebelt	strokenetcpharm@ucmail.uc.edu	513-584-3166
StrokeNet Pharmacist	Noor Sabagha	Noor.sabagha@uchealth.com	513-584-3166
WebDCU	Faria Khattak	khattak@musc.edu	984-221-0266
WebDCU	Patty Hutto	huttoja@musc.edu	843-876-0904
Monitoring Manager	Aaron Perlmutter	perlmutt@musc.edu	843-792-2784
Lab Core	Erin Popavich	ep2681@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

Greek Culture corner - The Heraean Games



Most people are aware that the Olympics began in ancient Greece, but they are not aware that there were separate games for women: the Heraean Games, named for the Greek goddess Hera, Queen of the gods. Women were not allowed to participate in the Olympics, so the Heraean games were their only alternative. Like the Olympics, the Heraean Games took place every four years at Olympia. The only event was a foot race called the *stadi-on*, which was one sixth shorter than the men's foot race. There were three different age categories. Only unmarried women were allowed to participate. The winners were awarded a crown of olive leaves and part of a cow which was sacrificed to Hera. They also dedicated statues inscribed with their name to Hera.

A running girl at the Heraen Games. The short *chiton* she wears, exposing her right breast, and her loose hair, are distinctive characteristics of the competitors in the Heraean Games. This marble statue is likely a Roman copy of a Greek original, from c. 460 BC. (from Wikipedia)