April 15, 2021 - Vol 4, Issue 3

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 - 622 Consents - 2365

March Randomizations = 26 March Consents = 81

SITE REPORTS COMING!

Our newly designed ARCADIA site reports are on their way!

The site report reflects your enrollment, data entry and data quality metrics in ARCADIA. These reports will be generated on a quarterly basis going forward.

Your site report is shared only with your site and with the study administrative team, including the study PIs and Project Managers. The goal of the report is to provide you and your team with the information that you will need to assess, and where needed, optimize your performance in ARCADIA. The report provides a quantitative summary of several metrics for your site, and it benchmarks these against our initial optimistic targets and those being realized across all sites in the trial. These numbers thus reflect how your site is doing compared to all sites. We have also added color coding to make the report easy to follow and home in on those areas that require improvement.

Please also be sure to look at the list of **ACTION ITEMS at the top of the report, since these are things we hope you will take care of to improve your site's performance.**

We hope you will find these site reports informative and helpful. Please do not hesitate to reach out to arcadia@ucmail.uc.edu with any questions regarding the metrics or the specific numbers at your site.

See page 3 of the newsletter for an example of the report.

SPOTLIGHT ON SITES

March Top Randomizing Sites

Methodist - 3
Northwestern - 2
Hospital of the University of Pennsylvania - 2

Congratulations to this site who had their 1st Randomizations in March
New York Presbyterian, Brooklyn

March Top Consenting Sites

Rhode Island - 5
Methodist - 5
Banner - 4

Congratulations to these sites that consented their 1st subject in March
Boca Rotan, Lahey & West LA VA

141 Active Sites - U.S. 138, Canada 3

Thanks to all of our sites!

Welcome Aboard!

Sutter Medical Center
Scott & White Memorial Hospital
Sunnybrook Health Sciences

Science Corner

Patent foramen ovale, atrial fibrillation, and ESUS

Paper: Strambo D, et al. Embolic Stroke of Undetermined Source and Patent Foramen Ovale: Risk of Paradoxical Embolism Score Validation and Atrial Fibrillation Prediction. Stroke. 2021 Mar 31:STROKEAHA120032453. Epub ahead of print. PMID: 33784832.

Background: There are several potential etiologies for an embolic stroke of unknown source (ESUS). Patent foramen ovale (PFO) and intermittent atrial fibrillation (AF) are two potential etiologies. These investigators conducted an analysis of three registries analyzing patients with data on ESUS and presence or absence of a PFO. They also calculated the RoPE (Risk of Paradoxical Embolism) score, an index of whether the PFO is likely to be related to the index stroke. The research team determined the rate of AF detection over up to 10 years and analyzed results according to RoPE score. The key results are as follows:

PFO with RoPE score 7-10 3.1% rate of AF

PFO with RoPE score 0-6 20.5% rate of AF

ESUS without PFO 31.8% rate of AF

Absence of left ventricular hypertrophy, atherosclerosis, and infratentotiral stroke location were associated with PFO.

This study provides ARCADIA investigators with useful information on which patients with PFO have a higher risk for AF development. ARCADIA sites are reminded that patients with PFO are eligible for enrollment.

--Seemant Chaturvedi, Guest contributor
PI University of Maryland

FAQs

Question: A patient already randomized in ARCADIA plans to move to Europe to live full-time. Can the patient remain in ARCADIA?

Answer: We cannot ship study drug to individual patients internationally. We can send drug to our Canadian coordinating site, which then distributes drug within Canada. If a patient living in Europe is able and willing to return to the US for follow up visits to pick up study drug at their original enrolling site, or perhaps another participating site, then we can consider having them continue in the trial. Each situation would need to be evaluated individually, so please let us know if you face this situation.

Question: We have a patient who had elevated troponins at the time of stroke admission. The cardiologist thinks the patient may have had a myocardial infarction without ST elevation (NSTEMI). Her heart cath was completely normal. We want to confirm that we can enroll her at a later date – at least 4-5 weeks after this event. The protocol says: "No major-risk cardioembolic source of embolism, including intracardiac thrombus, mechanical prosthetic cardiac valve, atrial myxoma or other cardiac tumors, mitral stenosis, **myocardial infarction within the last 4 weeks**, left ventricular ejection fraction <30 percent, valvular vegetations, or infective endocarditis)." We would not consent her until after that period of time.

Answer: Unfortunately, this patient is not eligible for enrolment if there is a diagnosis of acute MI as a likely cause of the stroke. The wording in the exclusion criteria (no "myocardial infarction within the last 4 weeks") refers to the timing of the MI in relation to the stroke, not in relation to the time of enrolment. This patient's NSTEMI occurred at the time of the stroke, and could be its cause, and thus the patient does not have ESUS. It is worth confirming with the cardiologists that the patient did have an MI. As an aside, since the cardiac catheterization was negative for coronary artery disease, this patient probably had what the cardiologists call MINOCA: MI with non-obstructive coronary artery disease. Sort of like "ESUS" of the heart!

Site Report Example

Site Name & Location
ARCADIA Monitoring Report Card
Date of Report Card

Basic Stats	N
# Subjects Randomized	
# Subjects Enrolled	
# Screen Failures	
# Unanticipated Events Reported	
# Protocol Violations: Eligibility	
# Protocol Violations: Visits Out of Window	
ACTION ITEMS	
# Not Eligible, Need to Move to End of Study	
# Regulatory Documents Outstanding	
# ECHOs Pending Shipment	
# CRFs Past Due	
# Open Rule Violations	
# Open Data Queries	
# Subjects with Follow Up Visits Past Due	

Performance Dashboard	Target	Trial-Wide	Site
Recruitment			
Current Rate of Consent (# Subjects Consented/Number Months Open)	1.33	0.62	
Current Rate of Randomization (# Subjects Randomized/Number Months Open)	0.33	0.16	
*Percent of Enrolled Subjects Randomized^*	*25.0*	*21.38*	
# Randomized Subjects with an Eligibility Violation on F101	0.0	0.11	
Percent of Biomarker Positive Subjects who were Not Randomized	0.0	26.44	
Percent of Randomized Subjects who Withdrew Consent	0.0	10.00	
Percent of Randomized Subjects who are Lost to Follow-Up	0.0	1.51	
Data Quality			
Percent of CRFs First Submitted in Window	100	78.14	
Median Days until Query Response	5.0*	12.00	
Median # of Queries per Subject	N/A	2.00	
Data Entry Error Rate (Queries where an Error was Corrected or a Missing Item/CRF was Added Divided by the Total Number of Data Points)	0.02	0.41	
Visit Quality			
Percent of Subjects Off Study Medication (Excluding SAE, Clinical Outcome Event, or AE of Special Interest)	0.0	12.20	
Percent of Subjects ±20% Compliant with Both Pills (Taken/Subjects on Medication)	100.0	74.97	
*Percent of Visits via Chart Review if Visit Type is Reported^*	*N/A*	*3.75*	
Percent of Subjects with Follow Up Visits Out of Window	0.0	41.82	

*AE Forms are expected to be reported within 24 hrs of first awareness
^italicized these metrics are not driven by site performance
Color code: Green = On target, continue the good work; Yellow = Caution,your performance on this metric is below average performance of sites in this trial and actions should be taken to bring this back on target;Red = Danger, your performance on this metric is significantly below average compared to the other sites and action is immediately required.

Updates/Reminders/Tips

From our Project Managers

- The EMR review is meant to obtain subject data if you are unable to reach the subject and to maintain the study visit within window. Please do not forgo talking with yours subject, whether in-person or remotely, when they are available.
- UAE/PDs for OOW visits are not being reported as instructed. If you have received an email about OOW visits that have occurred at your site, please report them as soon as possible.
- The visit scheduler, located in the WebDCU toolbox will help you keep your subjects within their visit windows.
- If you have not returned your completed Implementation Form please do so immediately. The study needs to know if you are using remote consent processes and if you want to participate in the eConsent process.
- If you have difficulty obtaining a kit for randomization or follow up please remember there is a Hotline number you can call for assistance. 1-866-450-2016
- Upon collection of the Baseline blood sample, please do not forget to enter F503 Biosample Collection Shipping in WebDCU, print it and send it in with sample shipment.
- Don't forget to send us your TTE DVD for each subject and enter the Date Shipped in F505 Echocardiogram Collection in WebDCU.
- If you haven't uploaded your v5.1 protocol approval letter and/or the v5.1 protocol signature page signed by your PI, please do so immediately.
- Please make sure you have lab kits in inventory and if needed order early to avoid delays in receiving replacement kits.

From our WebDCU Team

- Please welcome Jennifer Sherillo, Data Manager, to the WebDCU Team! She will be working on the ARCADIA study as well as other StrokeNet studies. She can be reached by email, Sherillo@musc.edu
- Please check for queries and rule violations frequently. An open query or rule violation may hold up a visit payment.
- All baseline CRFs should be completed immediately. Your subject may show that they are not eligible for randomization even though they meet cardiopathy criteria if your I/E CRF, F101, has not been completed.
- Please do not access WebDCU using multiple browsers, windows, or tabs. This can cause data issues in the study database.

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

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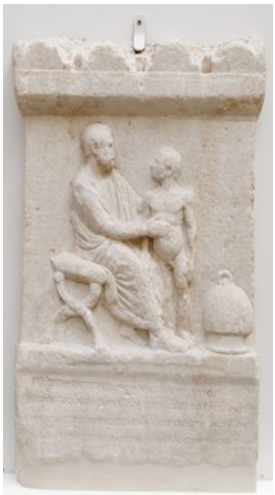
Greek Culture corner

What did the ancient Greeks think about the heart?

Aristotle (*circa* 350 BC) considered the heart the most important organ of the body. This was in part due to his observation that it was the first to form, based on his observations of the development of chick embryos. He thought the heart must be the seat of intelligence, motion, and sensation – all abilities we now consider brain functions, of course. The heart, which he thought had three chambers, was also considered the source of heat and vitality in the body; many other organs surrounding it, including the brain and lungs, were though to exist solely to cool the heart.



In the second century AD, Galen, in his *On the Usefulness of the Parts of the Body*, reaffirmed this notion of the heart as the body's heat source and the organ most closely related to the soul. He also appreciated how hard the heart worked throughout life, and considered it a tough organ, writing: "The heart is a hard flesh, not easily injured. In hardness, tension, general strength, and resistance to injury, the fibers of the heart far surpass all others, for no other instrument performs such continuous, hard work as the heart." Nonetheless, Galen thought the heart secondary in importance to the liver, the site of production of the humors. These ideas predominated until the seventeenth century, when the English physician William Harvey explained the heart's role in the circulatory system in *On the Circulation of the Blood* (1628).

Precordial palpation is an ancient and simple useful art of physical examination, continuing to be an integral part of cardiac evaluation. This relief from the Athenaean funerary stele of Jason (~100 AD, British Museum) shows the physician Jason of Acharnai seated and examining a patient by palpation of the epigastrium.