



# ARCADIA



**Atrial Cardiopathy and Antithrombotic Drugs In Prevention After Cryptogenic Stroke**

**Webinar: November 24th at 2p EST/ 1p CST/ 12n MT/ 11a PT**  
**Next Month: December's Webinar has been cancelled**

## Happy Thanksgiving!

**We are so thankful for all of your help with ARCADIA this past year! Enjoy your holiday!**

### MILESTONES

**Randomized - 533    October Randomizations = 18**

**Consents—2024    October Consents = 85**

**Let's get to our halfway point of 550 before Christmas!**

### Hot off the Press!

A virtual Investigator Meeting for all ARCADIA study teams is being planned for January 2021.  
Date, time and agenda will be announced later.

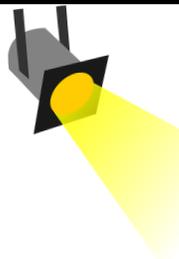
### Pharmacy Update

**Study Drug is expiring November 30, 2020 & March 31, 2021**

Study Drug will expire 11/30/2020. The sites have been restocked. Please make sure this is removed from your inventory in WebDCU and destroy per your institutional pharmacy policy.

Study Drug will expire 3/31/2021. Do not dispense date is 12/31/20. Study drug kit restock will be taking place November 17<sup>th</sup>, 2020 through December 22<sup>nd</sup>, 2020.

### SPOTLIGHT ON SITES



#### October Top Consenting Sites

**Methodist University Hospital, Memphis TN**

**OU Medical Center, Oklahoma City, OK**

**Yale New Haven Hospital, New Haven CT**

**4 Consents each site!**

#### October Top Randomizing Sites

**Tufts Medical Center, Boston**

**2 randomizations!**

#### Welcome Aboard

**St. John's Hospital, Springfield, IL**

**Hamilton General Hospital,  
Ontario, Canada**

**Both released in October 2020**

#### 127 Sites Released Post COVID Pause

**Thanks to all of our sites that have worked so hard to be released after our pause. You rock!**

## SCIENCE CORNER

### Cerebral microbleeds and recurrent stroke in NAVIGATE

It is well known that with appropriate MRI sequences, cerebral microbleeds (CMBs) can be detected in 10-30% of patients with ischemic stroke. CMBs represent advanced small vessel disease and are thought to be a harbinger of increased risk for intracerebral hemorrhage (ICH). Given the concern for ICH in the presence of CMBs, the impact of anticoagulation in patients with CMBs is of great interest.

In this secondary analysis of the NAVIGATE ESUS trial<sup>1</sup>, the authors used baseline MRI data from this randomized trial that compared rivaroxaban 15 mg per day with aspirin 100 mg per day in patients with embolic stroke of unknown source. There was information on CMBs at baseline among 3699 patients (51% of the trial population). Overall, among patients with at least one CMB, mean age was 69.5 years and 61% were men; 11% of the cohort had the presence of at least one CMB, with 68% having 1-2, 27% having 3-10, and 5% having >10 CMBs. Regarding location, 55% of CMBs were deep only, strictly lobar in 26%, and mixed in 19%. During follow-up, the majority of recurrent strokes were ischemic, with only 12 ICH events. Regardless of treatment with anticoagulation or aspirin, patients with CMBs had an increased risk of ischemic stroke, ICH, and mortality. With rivaroxaban, there was an increase in ICH risk regardless of the presence or absence of CMBs, but confidence intervals were very wide.

Comment: This study reinforces the notion that patients with CMBs are at heightened risk for both ischemic and hemorrhage stroke, as well as mortality. This analysis did not show increased harm from using an anticoagulant relative to aspirin in the presence of CMBs but the number ICH events was small. Data from other trials that use DOACs in patients with CMBs will be important in the future.

- Contribution from Seemant Chaturvedi, MD, ARCADIA Co-investigator

<sup>1</sup>Shoamanesh A et al. Microbleeds and the Effect of Anticoagulation in Patients With Embolic Stroke of Undetermined Source: An Exploratory Analysis of the NAVIGATE ESUS Randomized Clinical Trial. *JAMA Neurol.* 2020 Oct 19: e203836. doi: 10.1001/jamaneurol.2020.3836. Epub ahead of print. PMID: 33074284; PMCID: PMC 7573796.

### UAE Reporting

Any Unanticipated Events (UAEs) and Protocol Deviations (PDs) need to be reported in real time using the UAE/PD form located in WebDCU. You can find this form under the Project Management tab.

In most cases, if the event was an AE or SAE, an additional UAE report is not needed.

Please complete the form in its entirety and submit. A Project Manager will review the form and may contact you for more information or to amend the document.

Please remember that any event that includes a risk to the subject needs to be reported promptly. Most ICF issues will also need to be reported promptly.

If you should need any assistance please reach out to Rebeca or Pam. They are happy to assist you in getting the form completed and submitted.

### We need your help enrolling patients into the ARCADIA-CSI Substudy!

We have created form 515 to make screening a breeze. When a patient is randomized in ARCADIA, form 515 is posted in the patient's ARCADIA binder in WebDCU. This form serves as the ARCADIA-CSI screening form and as a reminder to reach out to the patient to ask if (s)he would like to join ARCADIA-CSI. We currently have 128 forms pending completion.

Please contact Tashia Harris, [herndotl@ucmail.uc.edu](mailto:herndotl@ucmail.uc.edu) or Stephanie Kemp, [skemp@stanford.edu](mailto:skemp@stanford.edu) with any questions.

## Updates/Reminders/Tips

- ◆ Please make sure you are checking your site's regulatory & people documents in WebDCU. Many sites have items that have expired and need renewed. If your team member has an expired assessment certificate, i.e. NIHSS certificate, then they will not be able to complete these assessments for a research subject until updated.
- ◆ When adding new team members to your site's DoA, you must upload their documents immediately and completely so that they will be able to participate.
- ◆ The study needs your subjects' ECHO discs! Please remember you can ship the ECHO discs when shipping your specimens to the CALM lab. The lab will make sure your ECHOs make it to the ECHO lab. You also need to add your shipping date to the subject's CRF in WebDCU.
- ◆ As the pandemic continues to ramp up in all areas of the country, please make sure your COVID-19 Impact Assessment v2 form in WebDCU is completed and updated as things change at your institution. Also please make sure to let the Project Managers know if team members and enrollment is being impacted at your site.
- ◆ Remember that you have to save AND submit the CRFs, don't just save the CRFs.
- ◆ We still have sites that have not been re-released since the COVID pause. Please let us know your site's plan in restarting.
- ◆ We are planning on moving forward with eConsent. This will take some time as we must receive cIRB approval for the study to do this. After approval is received, we will reach out to each site individually to see if your site is interested in the eConsent process.

## Clarifying the mRS

For study inclusion the mRS score must be 4 or less. This assessment measures the degree of disability or dependence in the daily activities of people who have suffered a stroke.

**mRS 4:** The patient has moderately severe disability. They are unable to attend to own bodily needs without assistance, and unable to walk unassisted.

- The patient requires someone else to help with some daily tasks, whether walking, dressing, toileting, or eating. This patient will be visited at least once and usually twice or more times daily, or must live in proximity to a care giver.

**mRS 5:** The patient has severe disability. They require constant nursing care and attention and are bed-ridden and incontinent.

- Someone will always need to be available during the day and at times during the night, though not necessarily a trained nurse.

## 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

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### FAQ

**Question:** During our monitoring visit, the monitor saw a consultation note from prior to randomization that stated, "On tele monitoring, the patient was noted to have brief episodes of atrial fibrillation as well as frequent premature atrial beats." Later in the record, there is progress note amendment from the cardiologist stating that: "There was one documented brief run of atrial arrhythmia lasting for seven beats... No other documented episodes of atrial arrhythmia or atrial fibrillation noted in review of the chart. As such, I do not believe that the patient has enough evidence to label her as having paroxysmal atrial fibrillation so far." Was the patient incorrectly enrolled? Was this a protocol violation?

**Answer:** No. There are many types of atrial arrhythmia. It is not clear in this case that the patient had atrial fibrillation, though they may be at risk of developing AF. The cardiologist's note makes clear that the patient does not have definite AF, and so the patient is eligible. In such circumstances, it is ideal to have a cardiology colleague document their interpretation clearly, as was done here.

### Culture corner

#### Ancient Mythology: The Celtic God Esus

This month we take a detour away from Greek history and mythology to consider Celtic mythology. The Celts were an Iron Age people of Western Europe; their time period spanned roughly from 500 BCE through 500 CE. Much of their religious belief is lost to time, but they did believe in a deity named **Esus**. Esus, which means "Lord" or "Master" in Celtic, was one of three powerful deities in the Celtic pantheon mentioned by Roman poets. According to later commentators, people who were sacrificed to Esus were ritually stabbed and hung from trees.

A relief from the Cathedral of Notre-Dame in Paris portrays Esus as a woodman cutting a branch from a willow tree. Another relief in Germany associates Esus with the sacred bull and its accompanying cranes or egrets. Some, such as Miranda Green, have suggested that the willow-tree symbolizes "the Tree of Life [...] with its associations of destruction and death in winter and rebirth in the spring". [Miranda Green (1992). *Symbol & Image in Celtic Religious Art*. London: Routledge. pp. 103–104.] She also writes that the cranes represent "the flight of the soul (perhaps the soul of the tree)."

Esus may have had medical powers. The Gallic medical writer Marcellus of Bordeaux may refer to Esus in his *De medicamentis*, a compendium of pharmacological preparations written in Latin in the early 5th century. The work contains a magico-medical charm which appears to invoke the aid of Esus in curing throat ailments.

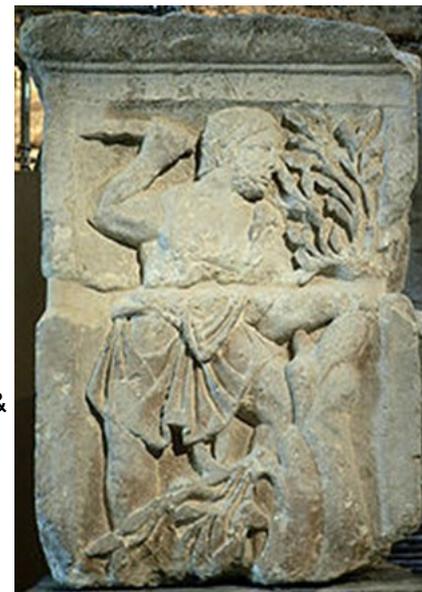


Image of Esus cutting the branches of a willow tree on the Gallo-Roman Pillar of the Boatmen, first century CE.