

ARCADIA Study Coordinator Training



2017
Investigator Meeting



Learning Goals

1. The coordinator will be able to identify the 3 screening tests required to meet the atrial cardiopathy criteria for ARCADIA.
2. The coordinator will know how to collect each of the 3 atrial cardiopathy screening tests.
3. The coordinator will have knowledge about the ARCADIA Biobank.
4. The coordinator will understand how what study is provided and how it is packaged and labeled.
5. The coordinator will understand when study drug will be shipped and how it should be stored including temperature monitoring.
6. The coordinator will understand the process for how study drug is assigned and dispensed to subjects.
7. The coordinator will understand the requirements for documentation of study drug assignment, the importance of the verification code and how to document adherence.
8. The coordinator will understand the process for sites to be released to enroll (site readiness).



Screening for Atrial Cardiopathy

The definition of **atrial cardiopathy** requires that a participant have at least one of three biomarkers present:

1. $PTFV_1 > 5,000 \mu V \cdot ms$ on 12-lead ECG (**ECG criterion**).
2. Serum NT-proBNP $> 250 \text{ pg/mL}$ (**NT-proBNP criterion**).
3. Left atrial size index $\geq 3 \text{ cm/m}^2$ on echocardiogram (i.e., severe left atrial enlargement) (**ECHO criterion**).





Eligibility

- If patients meet all inclusion and non of the exclusion criteria they can be consented for the trial. They will be considered as **enrolled**.
- Among patients who provide consent for trial participation, only those who meet at least one atrial cardiopathy criterion will be **randomized**.
- Once a patient meets one of the 3 atrial cardiopathy criteria, you do not have to wait for the results of the other tests to randomize.
- If they meet the criteria based on the echo, you are still required to send the lab specimen and upload the ECG.
- An ARCADIA hotline is available to help with reviewing screening data and determining eligibility **1-833-427-2234**.



Echocardiogram Criterion

- The Echo, acquired in DICOM format by the echo lab, should be de-identified by the local echo lab prior to downloading onto the DVD.
- If your site is unable to de-identifying, DVDs can be shipped with patient information as covered in the HIPAA section of the informed consent.
- The DVD should be labelled with the patient's ARCADIA Study ID number and the date of the study.
- If there are questions you can contact: Dr. Marco Di Tullio from the Echo Lab Core md42@cumc.columbia.edu



Electrocardiogram Criterion

- The first ECG done as part of the standard stroke evaluation should be used. If this is not available, it should be noted and another ECG performed after the index stroke may be uploaded.
- A pdf copy of the ECG should be uploaded to WebDCU™
- Redact any patient identifying information before uploading
- Label the ECG with the study subject ID before uploading
- The ECG Core at Wake Forest will measure the PTFV1 and enter the quantitative value into WebDCU™ within 2 business days of receipt of the ECG.
- Sites will receive an automatic email notification when results are available in WebDCU™



NT-proBNP criterion

- To determine whether a patient meets the BNP criterion, a blood sample will be obtained after informed consent.
- The blood samples should be shipped the day they are drawn to the Lab Core at Columbia. They do not need to be centrifuged or frozen.
- The Lab core will enter the NT-proBNP measurement into WebDCU™ within 2 business days of receipt of the blood sample.
- Sites will receive an email notification when the sample results have been entered into WebDCU™



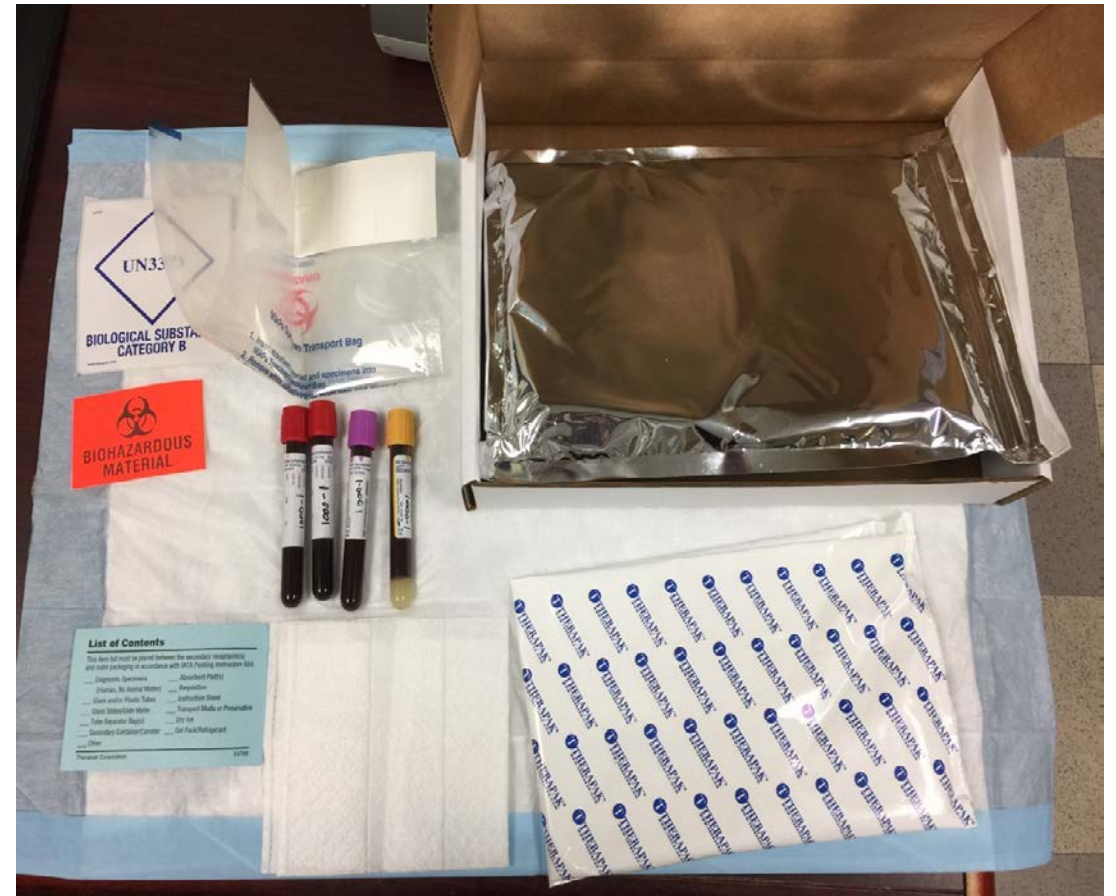
ARCADIA Biobank

- Samples collected from participants at time of screening will be used to assay NT-proBNP to determine eligibility for the study.
- Samples may also be used for other ancillary studies of stroke and cardiac disease as part of a Biobank.
- We hope that all subjects will agree to participate in the Biobank, however **subjects may decline the Biobank and still participate in ARCADIA.**
- No genetic testing will be performed without further amendment of the protocol and informed consent form.
- The Biobank repository will be kept at the Laboratory Core for the study, in the Center for Advanced Laboratory Medicine (CALM) at Columbia University Medical Center (CUMC).



Instructions for Sample collection

1. Collect 4 tubes in the following order: Gold, purple and then red tops.
2. *If the subject did not agree to participate in the Biobank portion of the study then you will only collect the Gold (serum separator tube).
3. Fill tube or tubes completely and invert 6-8 times.
4. Prepare to ship as soon as possible.
5. Do not freeze samples.



Shipping information

1. Place labels on the box as in the picture. Call Fed-Ex to arrange a pick-up.
2. Make sure that samples are only sent Sun-Thur so that they arrive at the CALM Lab from M-F.
3. Fax or email (CALM@pathology.edu) the shipment form.





- Detailed instructions for each of these Cores are included in the MOP Appendices.
- The Core Appendices and these printable forms are available in WebDCU™ under: **ARCADIA / Toolbox/Project Documents.**
- Supplies will be provided for blood sample collection these should be stored at your site at room temperature.
- Pre-paid Fed-ex labels will be provided.

Study Drug

- Apixaban, Aspirin and the matching placebo for each is being provided by Bristol Meyers Squibb company.
- The Central Pharmacy at the University of Cincinnati (NCC) will be repackaging and shipping the study drug to all sites.
- The study bottles will be packaged as kits that will contain 2 bottles. They will contain a 3 month supply.
- Sites will be initially shipped 6 kits.



Study drug kits

The **Kits** will contain either:

- Apixaban (5mg) + Aspirin placebo
- Apixaban reduced dose (2.5mg) + Aspirin placebo
- Aspirin 81mg + Apixaban (5mg) placebo
- Aspirin 81mg + Apixaban reduced dose (2.5mg) placebo



Study drug labels

- The kits will be labeled and tamper evident sealed. The tamper evident seal should not be opened until a subject is assigned that kit number. Please make sure your pharmacy staff is informed of this.
- Each bottle in the kit will also be labeled and sealed and the Subject ID should be written on each bottle as soon as they are assigned.
- If your site pharmacist/designee also creates an individualized **subject specific label** make sure the labels are affixed to the individual study **bottles**, not on the study kit box, and should not cover the pre-existing study drug bottle labels.



Study drug labels

To provide additional safeguards while packaging and for subjects:

Bottle Label numbers:

- All Apixaban bottles and their matching placebos will have a **#2 on the label**. This will help remind the subject that they should take this medication twice a day.
- All aspirin and its matching placebo will have a **#1 on the label**. This is to remind the subject that they only take this medication once a day.

Bottle Label colors:

- Apixaban 5mg and its matching placebo label will have a light yellow label.
- Apixaban 2.5mg and its matching placebo will have a light pink label.
- Aspirin and its matching placebo will have a white label.



Study drug shipments

- Automated WebDCU™ study drug shipment requests will alert the Central Pharmacy when sites are released to enroll, subjects are randomized, refills are needed, or study drug is damaged/expired.
- When kits are received at your site they must be accepted in the WebDCU™ system. This notifies the system that the kits are available and can be assigned to a subject.
- The amount of study drug kits sent in subsequent shipments will depend upon the expected number of refills required and enrollment rates at your site.



Verification of study drug

- WebDCU™ will assign the study kit to be dispensed to the subject. When the randomization form is completed.
- Print out the randomization form listing the Kit number and the bottle numbers
- The site pharmacist/designee should pull the study kit from inventory matching the kit number assigned.
- On the study kit there will be a **3-digit Verification Code**.
- The site coordinator should enter the **3-digit verification code** listed on the study drug kit label onto **The Study Drug Kit Dispensing Form 513 in WebDCU™** as an additional safeguard to ensure the correct medication was dispensed.



Study drug adherence

- Study drug adherence will be assessed using pill counts by the study coordinator at each study visit on **Form 209** in WebDCU “**Study Drug Usage and Adherence**”.
- For subjects who have intentionally stopped study drug, the reason for discontinuation or temporary interruption should be reported using a set of coded choices (e.g., elective procedure, new contraindication to treatment, etc).



Documentation at follow-up visits

When a subject comes in for a F/U visit or when a phone F/U is performed, the coordinator will enter Form 513 (Study Drug Dispensing CRF)

Information collected includes:

- Confirm subject is still taking study medication
- Subject's weight (if known)
- Subject's creatinine (if known)

If the subject meets the criteria for the adjusted dose of apixaban 2.5 mg (≥ 2 of the following: age ≥ 80 years, body weight ≤ 60 kg, or known serum creatinine ≥ 1.5 mg/dL.), a kit with the adjusted dosage will be dispensed. Otherwise, the kit dispensed will correspond to the normal 5mg dose.



Study drug re-supply

- Kits will contain a 3 month supply of medication (+10/20 extra tablets)
- Subjects will have in person F/U visits **Q3 months** until 1 year
- After 1 year **in person** F/U visits are required **Q6 months**
- However, because the study drug supply is only for 3 months, you must do a study drug resupply visit Q3 months as long as the subject is active on study medication.
- These **drug resupply visits** can be done over the phone (if you have a way to get the medication to the patient) in the clinic, or at the patient's residence.



Study drug destruction

- Log all dispensed/expired/damaged/replaced study drug in WebDCU.™
- Once all prescribed study drug is accounted for, it is not necessary to save returned, damaged, or expired bottles.
- Expired/unused study drug can be destroyed at the clinical site per local procedures.
- If a site is unable to destroy study drug, it may be returned to Central Pharmacy. A Study Drug Return Form must be completed and returned with the drug. This form will be available in WebDCU™. Additional Instructions are listed in the Site Pharmacy Manual.



Study drug accountability

- Each clinical site will be required to maintain drug accountability records via the WebDCU™ system.
- Additional internal recordkeeping detailing the receipt and distribution of study medication may be required per local institutional policy.
- Sample templates of study drug dispensing and accountability logs are provided in the Site Pharmacy manual, available under Project documents in WebDCU™



Study drug temperature monitoring

- The study drug must be stored at room temperature between **15-25 °C** or (59-77 ° F).
- It should be protected from excessive exposure to light.
- Storage areas should be monitored for temperature variations.
- Any known temperature excursions should be reported to the Project Manager irene.ewing@uc.edu.
- Sample logs for temperature monitoring and temperature excursions are included in the Site Pharmacy Manual appendix 26.1 of the MOP.



Sample Temperature Tracking Log

SITE ADDRESS:				SITE:		
				PI:		
Instructions: Under the appropriate date record time of the temperature reading, the current temperature, minimum temperature, maximum temperature, conformation of resetting of the thermometer if applicable and initials. Report any excursions promptly to study sponsors.						
MONTH:			YEAR:			
Date	Time of Reading (24 hour clock)	Current Temp (°C)	Minimum Temp (°C)	Maximum Temp (°C)	Confirmation of Reset of Reading	Reader's Initials
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						



Site Readiness

- Study drug will not be shipped until the site completes a readiness call with the ARCADIA team.
- A copy of the Readiness Checklist is posted under the toolbox/project documents in WebDCU. It will also be emailed to sites in advance of the call
- A study coordinator and study team physician must be on the call. Ideally it should be the primary site coordinator and Primary site PI.
- Because we will not be doing site initiation visits, the purpose of this call is to ensure everything is in place at your site, all team members are listed and trained and to address any questions before your site is released to enroll.
- Irene Ewing, Project Manager or Daniel Velez, Columbia Coordinator will arrange the readiness calls.



Key Readiness checklist items

- Protocol Trial Agreement signed
- DOA complete and up to date in WebDCU™
- All Personnel have appropriate training, forms uploaded, WebDCU™ access
- Site CIRB approval/ICF approval
- Plan for screening and recruitment at your site
- Current address for drug shipment and plan for drug storage
- Lab supplies at site

