



ARCADIA

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Atrial Cardiopathy and Antithrombotic Drugs In Prevention After Cryptogenic Stroke

Next Webinar: The December webinar is cancelled.
Please join us January 25, 2022 for our virtual IM (1-4p ET/12-3p CT/11-2p MT/10-1p PT)

MILESTONES

Randomized = 769 Consents = 2919
November Randomizations = 18 November Consents = 75
Active Sites U.S. = 137 sites & Canada = 10 sites

We have reached 70% of our recruitment goal.

Central Pharmacy Holiday Hours

Christmas week: 12/22/2021 will be last day of shipping study drug kits to sites until Monday 12/27/2021.

New Year's week: 12/29/2021 will be last day of shipping study drug kits to sites until Monday 1/3/2022.



CALM Lab Holiday Hours

Christmas week: You can ship blood samples Monday-Wednesday (12/20/21 to 12/22/21) The usual shipping schedule resumes Monday (12/27/2021)

New Year's week: You can ship blood samples Monday-Wednesday (12/27/21 to 12/29/21) The usual shipping schedule resumes Monday (1/3/2022)

If you obtain specimens and can't ship due to the holiday hours, please process the specimens per the CALM core lab manual to ship when the lab is open.



We wish you joy & peace this holiday season!



SPOTLIGHT ON SITES

November Top Consenting Sites

**Oregon Health & Science University Hospital
Portland, OR**

4 consents!

November Firsts - Site 1st ICF

The Queens - Honolulu, HI

Akron General - Akron, OH

November Top Randomizing Sites

Intermountain Medical Center - Murray UT

Rhode Island Hospital - Providence, RI

Methodist University Hospital - Memphis, TN

Each site had 2 randomizations!

Welcome Aboard!

**Kingston General Hospital
Kingston, ON, Canada**

Welcome Back!

UAB, Emory & Grady

Science Corner

Longer AF monitoring detects more AF but impact on clinical outcomes remains uncertain

Previous randomized trials, EMBRACE and CRYSTAL-AF, demonstrated that the detection rate for atrial fibrillation is higher using prolonged cardiac monitoring than with 24 hours of monitoring, but they left uncertain the optimal duration of monitoring, and specifically whether an implanted cardiac monitor yields a higher rate of AF detection than an external monitor. The PER DIEM trial addressed this issue [1]. Investigators at three hospitals in Alberta, Canada, randomly assigned 300 patients (median age 64 years, 40% women, 66% with stroke of undetermined etiology) within 6 months of an ischemic stroke 1:1 to prolonged electrocardiographic monitoring with either an implantable loop recorder (ILR, n = 150) or an external loop recorder for 30 days (n = 150). Patients had follow-up visits at 30 days, 6 months, and 12 months. The primary outcome was the development of definite or highly probable AF (adjudicated new AF lasting ≥ 2 minutes within 12 months of randomization). Secondary outcomes included recurrent ischemic stroke, intracerebral hemorrhage, death, and device-related serious adverse events. The primary outcome was observed in 15.3% of patients in the implantable loop recorder group and 4.7% of patients in the external loop recorder group (risk ratio 3.3, 95% CI 1.5 to 7.4). Five patients (3.3%) in the ILR group had recurrent ischemic stroke vs 8 patients (5.3%) in the external loop recorder group, but this difference was not significant, nor were differences between the groups in intracerebral hemorrhage, death, or device-related serious adverse events. The investigators concluded that among patients with ischemic stroke and no prior evidence of AF, an ILR for 12 months leads to a significantly greater proportion of patients with AF detected than external monitoring for 30 days, though it is not clear that this leads to reduced clinical outcomes, such as stroke. Limitations of the study are its use of an open label design, its use of a 2-minute threshold to define AF, the fact that almost 10% of patients did not receive the assigned monitor type, and a relatively small sample size to detect effects on clinical outcomes.

We encourage ARCADIA investigators to follow AHA/ASA guidelines for cardiac monitoring after ischemic stroke: "In patients with cryptogenic stroke who do not have a contraindication to anticoagulation, long-term rhythm monitoring with mobile cardiac outpatient telemetry, implantable loop recorder, or other approach **is reasonable** to detect intermittent AF" (Class of recommendation 2-a (moderate); Level of Evidence B-R, moderate quality evidence from randomized trials). [2] We emphasize that the level of evidence for choice of duration of monitoring remains low, and further research is needed. Patients may be randomized in ARCADIA with at least 24 hours of monitoring; further monitoring is permitted, and patients should be switched to an oral anticoagulant as indicated if AF is detected during follow-up.

1. Buck BH, et al. Effect of Implantable vs Prolonged External Electrocardiographic Monitoring on Atrial Fibrillation Detection in Patients With Ischemic Stroke: The PER DIEM Randomized Clinical Trial. *JAMA*. 2021;325(21):2160-2168.
2. Kleindorfer DO, et al. 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline From the American Heart Association/American Stroke Association. *Stroke*. 2021 Jul;52(7):e364-e467.

FAQ

Question: Our site is screening a patient that had multiple infarcts in the parietal lobe based on the MRI, possibly in a watershed distribution. The stroke symptoms lasted less than 24 hours. Is the patient eligible?

Answer: As long as the treating team is calling the stroke subtype ESUS, and the patient meets all inclusion criteria and no exclusion criteria, then having multiple strokes or a watershed stroke pattern, does not disqualify the patient. We generally think that watershed infarcts imply an atherosclerotic stenosis in the vessel feeding that territory, but it doesn't have to be the case. Cardioembolic infarcts can also have a watershed appearance. This is why it is important to exclude both intracranial *and* extracranial stenosis $>50\%$ of the vessels in all patients. If negative, then they are eligible.

PROJECT MANAGER STUDY REMINDERS

While pandemic challenges continue, let's remember that we have **remote processes** to overcome some of those issues:

- ▲ Consenting
 - eConsent
 - remote consents by using other methods: mailing, emailing, or faxing potential participants the consent forms and then conducting the informed consent process over the telephone or other approved tele-health methods permitted at your site
- ▲ Randomizations can be done remotely as long as you reconfirm eligibility with the participant and then ship them their study drug and study documents via FedEx so that they can start taking the study drug within 48 hours.
- ▲ Follow-up visits should almost NEVER be done out of window since you can start these by doing a chart review of inpatient and outpatient medical records at your site. You can later revise the follow-up form once you reach the participant a few days later. Nonetheless, please keep trying to reach subjects for their follow-up visits. Sometimes the subject will need the visit done early and we understand, but all out of window visits must be reported as a UAE/PD.

In order to enroll, you must check your lab kit components and make sure they have not expired and no items are missing.

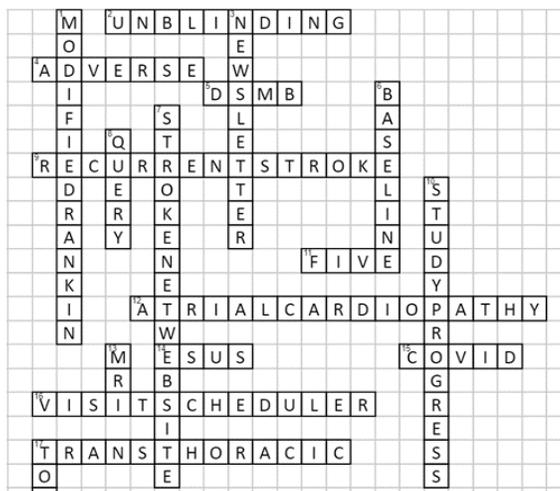
- ▲ Use the Lab Kit Accountability Log in the toolbox to keep your inventory complete & current.
- ▲ Order any expired/missing items with some lead time to make sure you always have full kits when you need them.
- ▲ Don't forget to follow the holiday shipping schedule for the CALM lab in December to make sure samples are not lost.

Checking WebDCU for Subject Eligibility

If you have not received your WebDCU email regarding your subject's randomization eligibility you can check using the subject status tab in WebDCU.

- 1) First check to make sure that you have completed F101, Inclusion/Exclusion Criteria CRF. If this form is not completed the subject will appear as "not eligible" whether they are or not.
- 2) Click on the "Study Progress" tab
- 3) Click on the "Subject Status" tab
- 4) Find your subject using their subject ID
- 5) The form will tell you if F101 criterion was met, if the 3 cardiopathy criterion were met, and if your subject is eligible for randomization.

November Crossword Puzzle Solution



Calendar of Events

- December 16 - SC Open Conference Call
- December 20 - January 2—NCC is closed
- December 22 - last day to ship specimens to the CALM lab until after Christmas; last day the central pharmacy will ship study drug until after Christmas.
- December 25 - Merry Christmas
- January 1 - Happy New Year
- January 25 - Virtual Investigator Meeting
(1-4p ET / 12-3p CT / 11-2p MT / 10-1p PT)

Just For Fun!

Celebrating the cultural diversity of the Holiday season, below are trivia questions about Kwanzaa, Hanukkah & Christmas

1. What traditional Christmas decoration is actually a parasitic plant? _____
2. In what modern-day country was Saint Nicholas born? _____
3. According to the English lyrics of "The Dreidel Song" which children sing at Chanukah (Hanukkah), out of what material is a dreidel made? _____
4. The holiday of Kwanzaa was introduced in what year? _____
5. When was the 1st Christmas card sent? _____
6. What well-know Christmas carol became the 1st song ever broadcast from space in 1965? _____
7. One of the most related items to Hanukkah are candles, since on each night of the holiday, one is lit to remember the miracle of oil that happened many years ago. Because of this, Hanukkah is often known as the festival of what? _____
8. How many days are in the Kwanzaa holiday? _____
9. How many gifts in total were given in the "Twelve Days of Christmas" song? _____
10. To celebrate the "miracle of oil", fried potato pancakes are eaten in Hanukkah. What are these called? _____
11. Which country has a tradition of a witch dropping gifts for children through the chimney at Christmas? _____
12. Canada, the U.K. and most other Commonwealth countries officially celebrate the day after Christmas as what holiday? _____
13. When children play with the dreidel in Hanukkah, they also gamble! Of course, they don't do this with real money, but with gelt, made of what? _____
14. What is the object called that holds the candles for Kwanzaa? _____
15. What does the Christmas wreath represent? _____
16. What does the Statue of Liberty have to do with Christmas? _____
17. Oil is an essential part of Hanukkah, this because it's actually what is celebrated. The Talmud says that when the temple was rededicated, very little oil was left to light the menorah, a candelabrum which was supposed to be lit every night. It appeared that it would only burn for one night, however, how long did the oil last? _____
18. Which U.S state was the 1st to declare Christmas an official holiday? _____
19. What day of the year does Kwanzaa start? _____
20. According to the folklore of Austria and other countries, what figure punishes naughty children at Christmas? _____
21. Which U.S. President objected to a Christmas tree in the White House because he felt it was wrong to cut down trees for decorations? _____
22. Why are Christmas candy canes red and white in color? _____
23. How many players are needed to play a game of dreidel? _____
24. Which country started the tradition of putting up a Christmas tree? _____
25. A little bit of history is needed to understand Hanukkah. Which Greek king, known for almost conquering Egypt, oppressed Jews, leading them to revolt and start the history of this holiday? _____
26. What is the meaning behind Kwanzaa? _____

ARCADIA Contacts

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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

With the holidays fast approaching, we thought it time to remember Euphrosyne, the Greek goddess of good cheer, joy and mirth. Her name is the female version of the Greek word *euphrosynos*, which means "merriment". Euphrosyne was one of the Charities, goddesses created to fill the world with pleasant moments and good will. In art, Euphrosyne is usually depicted with her sisters dancing.

L'Allegro, a pastoral poem by John Milton circa 1645, describes the idyllic joys of a day in the countryside and references Euphrosyne. Here are a few lines, which evoke a sense of Arcadia. (*L'Allegro* means "the happy man" in Italian.)

In Heav'n yclept Euphrosyne,
And by men, heart-easing Mirth,
Whom lovely Venus at a birth
With two sister Graces more
To ivy-crowned Bacchus bore.

Jest and youthful Jollity,
Quips and Cranks, and wanton Wiles,
Nods, and Becks, and wreathed Smiles,

Whilst the landscape round it measures,
Russet lawns, and fallows grey,
Where the nibbling flocks do stray

Meadows trim with daisies pied,
Shallow brooks, and rivers wide.

These delights, if thou canst give,
Mirth with thee, I mean to live.



The Three Graces (sculpture at the Hermitage, Saint Petersburg).
Euphrosyne (left) is depicted with her sisters Thalia and Aglaea.