CHANGE AFib:

A Pragmatic Randomized Clinical Trial
of Early Dronedarone versus Usual Care to Change and Improve Outcomes in Persons with First-Detected Atrial Fibrillation

Fireside Chat – June 23, 2022

CHANGE AFib is a collaboration between the American Heart Association and the Duke Clinical Research Institute, with support from Sanofi US Services Inc.

Please Note:

- All participants will be muted upon entry.
- Meeting is being recorded and will be archived on our trial website: www.changeafib.org

Questions?

- Please hold questions until our Q&A session at the end of the call
- Feel free to submit questions in the chat throughout the call, knowing they will be addressed during the Q&A session.

If you are having issue with computer audio, please call in using the appropriate number below.

Dial by your location:

+1 (301)715-8592	(Washington DC)
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+1 (253)215-8782	(Tacoma)
+1 (346)248-7799	(Houston)
+1 (669)900-6833	(San Jose)

Meeting ID: 846 4772 3823
Passcode: 9204404820

CHANGE AFib Principal Investigator

Jonathan P. Piccini, MD, MHS, FACC, FAHA, FHRS

- Principal Investigator of the CHANGE AFib trial
- Associate Professor of Medicine with Tenure at Duke University Medical Center and the Duke Clinical Research Institute.
- Director of the Cardiac Electrophysiology section at the Duke Heart Center

JUNETEENTH 2022

The American Heart Association is committed to ensuring that our workforce, workplace and mission have a shared impact across America's diverse populations.

Thank you to the CHANGE AFib trial teams for focusing on Diversity, Equity & Inclusion as we roll the trial out!

Juneteenth National Independence Day ,also known as Jubilee Day, Emancipation Day, Freedom Day, and Black Independence Day is a federal holiday in the United States commemorating the emancipation of enslaved African-Americans. It is also often observed for celebrating African-American culture. Originating in Galveston, Texas, it has been celebrated annually on June 19 in various parts of the United States since 1865.

Agenda:

- Welcome & Introductions – 5 mins
- Overview of Trial & Progress – 10 mins
- Celebrating First Subject Enrolled! – 10 mins
- Review of Trial Updates & FAQ – 20 mins
- Q & A – 15 mins

Overview of Trial & Progress

Quick Recap - Overall Trial Design

Design: Pragmatic Randomized Trial

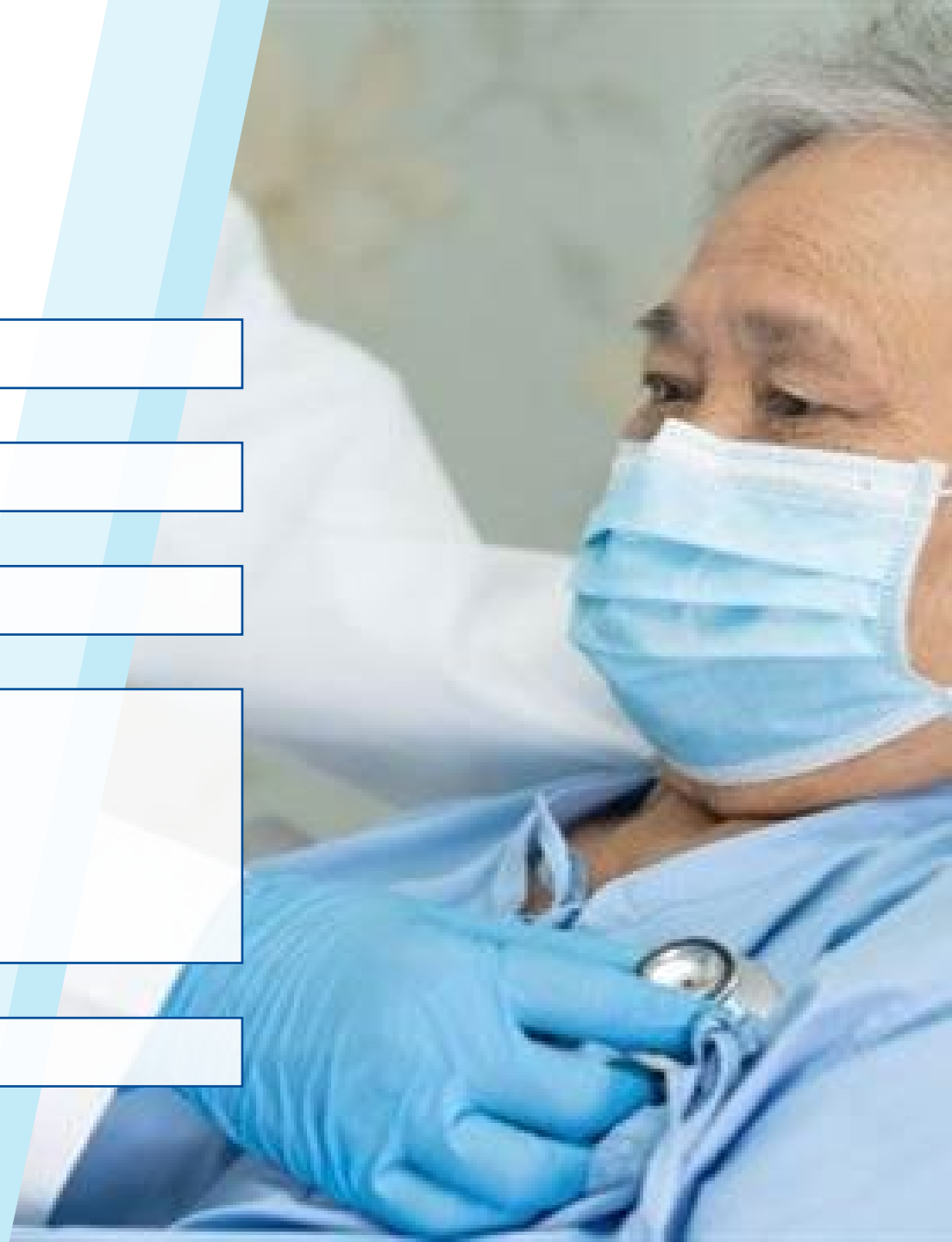
Sample Size: Approximately 3,000 patients

Targeted Number of Participating Sites: 200

Patient Eligibility

- Age ≥ 60 years
- First-detected Atrial Fibrillation
- Estimated life expectancy of at least 1-year
- Capable of giving signed informed consent

Duration of Follow Up: 12 months



CHANGE AFib

Patient Population: Inclusion & Exclusion Criteria

Enrollment Settings: Hospital Encounter or Outpatient Clinics (More on this later!)

INCLUSION CRITERIA

- Adults aged **≥60 years**
- First-detected AFib (AFib diagnosed in the previous 60 days)
- ECG documentation of AFib
- Estimated life expectancy of **≥1 year**

EXCLUSION CRITERIA

- Prior or planned treatment with **rhythm control***
- Planned cardiothoracic surgery

- Prior hospitalization for AFib
- Permanent AFib
- Pregnancy
- Severe hepatic impairment

- PR interval **>280 msec**, or 2nd / 3rd degree AV block without a permanent pacemaker/cardiac implanted electronic device
- Corrected QT interval **≥500 msec**

- NYHA class III/IV HF or hospitalization for HF in the last **4 weeks**
- Reduced ejection fraction (LVEF ≤ 40%)
- Bradycardia (resting heart rate <50 bpm)
- Ineligible for OAC, unless CHA_2DS_2-VASc <3 (women) or <2 (men)

*Either catheter ablation or antiarrhythmic drug therapy.

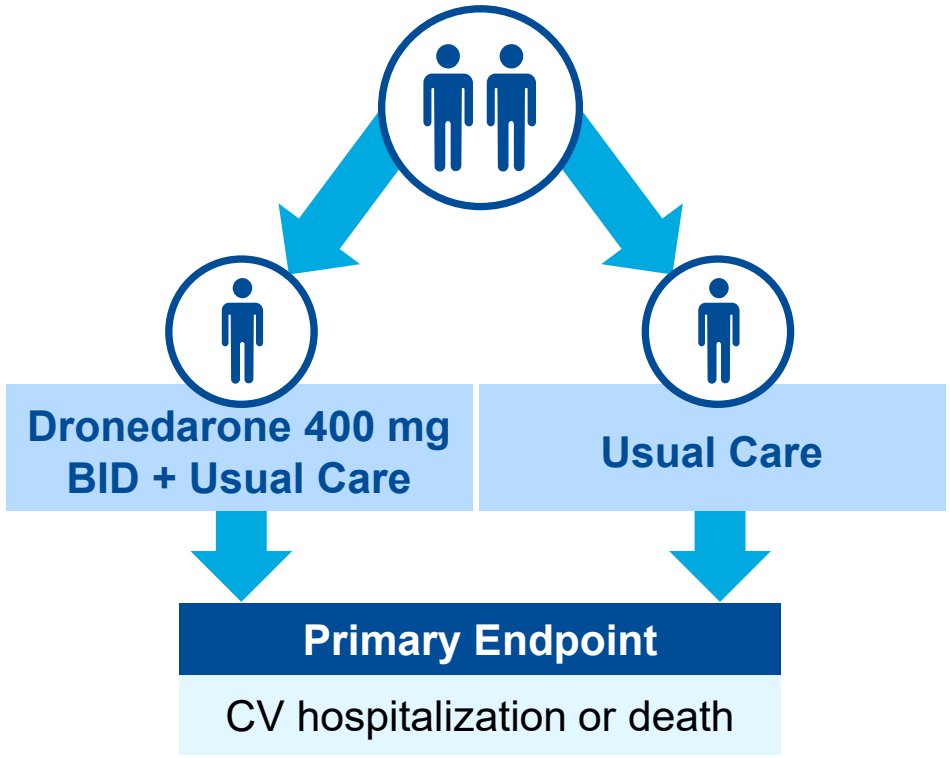
AFib: atrial fibrillation; AV: atrioventricular; bpm: beats per minute; ECG: electrocardiogram; HF: heart failure; LVEF: left ventricular ejection fraction; OAC: oral anticoagulation; NYHA: New York Heart Association.

CHANGE AFib: Objective

Determine if early treatment with the antiarrhythmic drug dronedarone improves cardiovascular and long-term outcomes in patients presenting to the hospital with first-detected AFib.

First-Detected AFib:

- ECG evidence of atrial fibrillation
- Diagnosed in the previous 60 days



Patients who present to the hospital (acute care encounter) for the initial diagnosis of AFib

OR

Patients who present to an outpatient clinic for follow-up from an AFib acute care encounter within 60days of initial diagnosis will be enrolled and randomized to the study intervention.

- The study intervention group will receive dronedarone 400 mg orally twice daily in addition to usual care.
- The study control group will receive usual care alone (where patient treatment will be at the discretion of the care team per routine clinical practice).

An acute care encounter is defined as an encounter and discharge from an ER, Observation Unit or Inpatient Admission.

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Recap of Schedule of Activities

Assessments/ Procedures	Baseline	6 months	12 months/End of Study
Informed consent & release of medical records	X		
Patient randomization	X		
Demographics	X		
Medical history	X		
Echocardiographic data	X		
Atrial fibrillation history	X		
Vital signs	X	X	X
Laboratory Data	X	X	X
Pharmacotherapy (Drug Log)	X	X	X
Adverse & Safety Events	X	X	X
Quality of Life Instruments (AFEQT & MAFSI)	X		X
Drug Discontinuation		X	X
Outcomes (Primary, Secondary, & Tertiary)		X	X
Document cardiac procedures		X	X

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Recap of Electronic Data Collection (EDC) Systems:

Participant Data Collection

Patient Consent & Randomization

REDCap®[1]

Baseline & Follow Up Visit Data

American Heart Association®
Get With The Guidelines®
AFib

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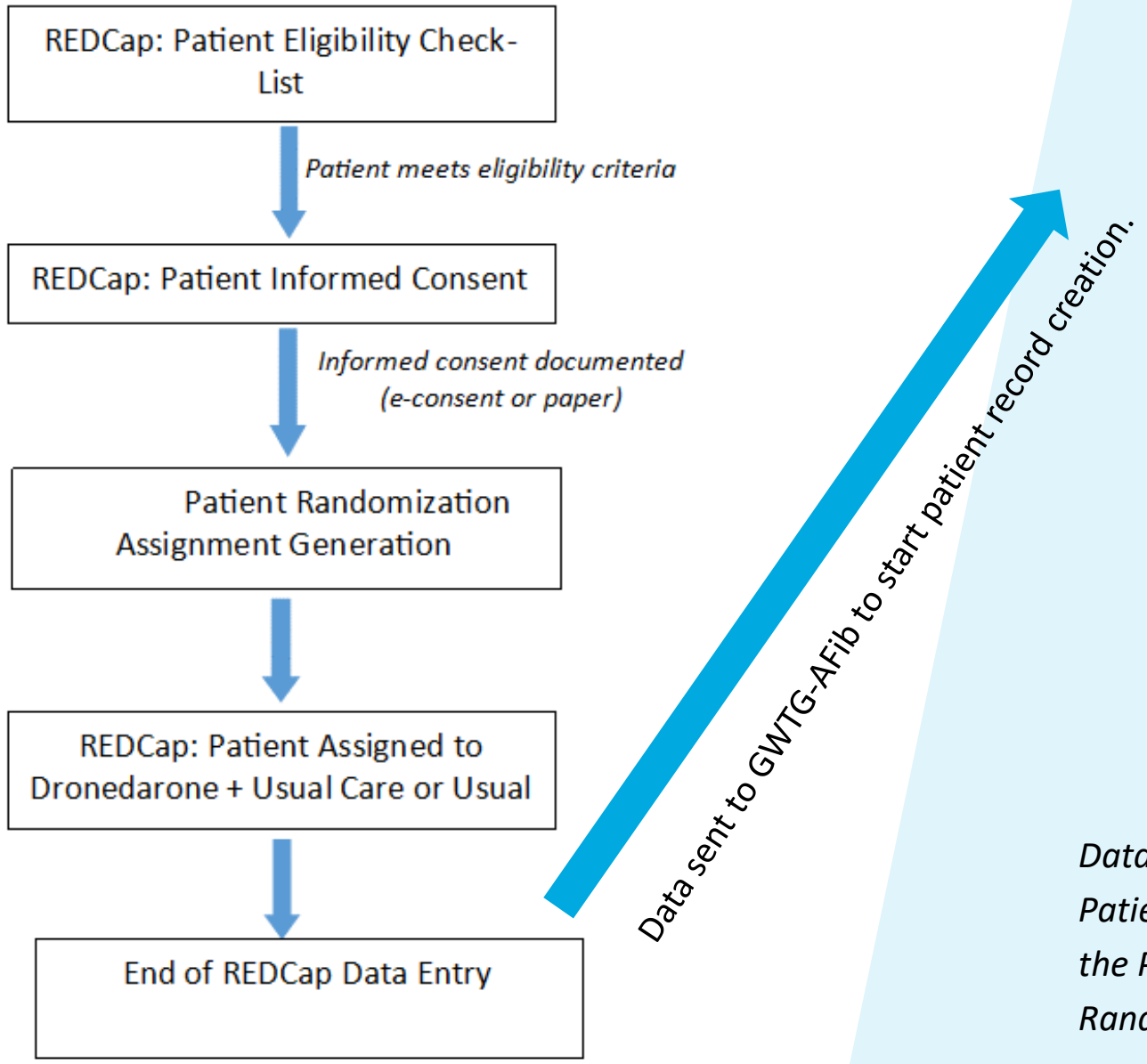
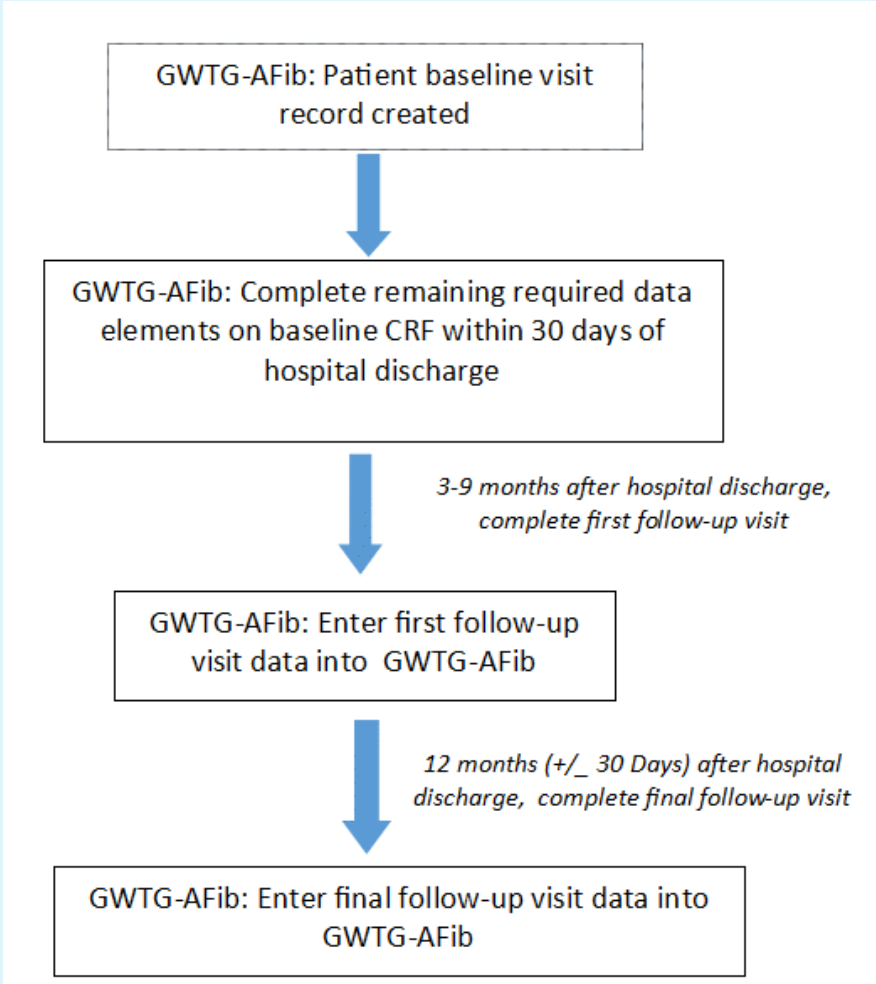
Research data will be collected in both REDCap and GWTG-AFib EDC systems. Research staff will need access to both

1 REDCap: Research Electronic Data Capture .

CHANGE AFib Data Capture



Data sent to GWTG-AFib to start patient record creation.



Data Elements Populated in GWTG-AFib include: *Patient ID, CHANGE AFib Patient ID (will be the same as the Patient ID), Date Informed Consent Obtained, Randomization assignment, Arrival Date, DOB*

Trial Progress – as of June 23, 2022

Site Status	Current Status	Trial GOAL!
Subject Enrollments	**1**	**3000**
Activated Sites	10	**200**
Sites in Onboarding	36	**-**
Sites Assessing Feasibility	78	**-**

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Participating Site Incentive Program – Newly Launched

Item	Requirement	Amount	Unit	Total
Contract Submission	Completed within 4weeks of receipt	$2,500	One-time	**$2,500**
IRB Submission – Local	Completed Submission w/in 4weeks of materials receipt	$2,500	One-time	**$2,500**
IRB Submission – Central	Completed Submission w/in 2weeks of materials receipt	$2,500	One-time	**$2,500**
Subject Enrollment	Per subject enrolled w/in the 1st month of trial site activation	$500	Per Subject, up-to 10 subjects during the 1st month of trial site activation	**$5,000**
Subject Screening Log	Completed Submission of weekly Subject Screening Logs submitted by end-of-day weekly on Fridays	$100	Monthly, up-to 9months post trial-site activation	**$900**

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Celebrating First Subject Enrolled!

First Subject Enrolled

Workflow & Best Practices

- **Screening Process**
  - Review of daily AFib census report created by Information Services Team
    - This report lists all patients in the hospital with a charted medical diagnosis of atrial fibrillation or nursing documentation of atrial fibrillation rhythm from telemetry
  - Coordinators review list, perform chart review for screening, discuss potential trial subject opportunities with PI daily
- **Enrollment Workflow**
  - Patient questions during the consent process
    - Medication interactions and risk assessment
    - Insurance coverage
    - Discuss trial with family/spouse confirm addressing all questions
  - Insurance Review
    - Case Management collaboration
    - Insurance verification after prescription is written
    - Prepared financial resources
- **Best Practices**
  - Daily screening first thing in the morning
  - Screening ED patients
  - Adding team member from Dr. Ofori's office for ED follow up patients

Wooster Community Hospital
HEALTH SYSTEM

Location: Wooster, OH
PI: Dr. Cyril Ofori
Study Coordinator: Erica Stahl, MSN, RN, APRN-AGCNS-BC

Review of Trial Updates

Does A Patient Have To Be Admitted To The Hospital To Be Eligible For Change AFib?

- A patient must have had an acute care encounter at the hospital for first-detected Atrial Fibrillation.

- For eligibility, this is defined as presenting to the hospital as:
  - An Inpatient Admission,
  - Evaluation/Treatment/Discharge from the Emergency Room or Observation Unit.

Can We Enroll Patients in the Outpatient Setting?

- YES. If you encounter a patient who meets fits eligibility criteria and has been diagnosed with first-detected AFib in the past 60 days, they **can be enrolled & randomized** from the outpatient setting.

- Keep in mind the following when enrolling outpatients:
  - As defined in the protocol, patients must have a new diagnosis within 60 days of randomization.
  - If a patient is randomized to the intervention (dronedarone) arm they must be contacted within 10 days of the randomization to confirm start of dronedarone prescription.
  - Their baseline case report form needs to be filled out completely with information from their index hospitalization.
  - The redcap database will need to be completed to allow randomization and treatment assignment.

What is Considered ‘Usual Care’?

- Usual care is defined as best-practice, guideline-directed therapy of AFib, including but not limited to
  - stroke prevention therapy,
  - rate-control, and
  - treatment of risk factors.
- More specifically, oral anticoagulation in those with a CHA2DS-2VASc $\geq$ 2 in men or $\geq$3 in women, rate control, and treatment of concomitant cardiovascular conditions (e.g., CAD or HF).

What Is Considered ‘Prior Antiarrhythmic Drug Therapy’?

And How Does This Relate To Exclusion Criteria #1?

- Antiarrhythmic drug therapy means chronic outpatient therapy (>7 days)

- One time dosing of an antiarrhythmic drug or pharmacologic cardioversion are not considered “prior AAD therapy”

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How Should Patients With A Contingency Plan For Ablation Be Handled?

- Patients with planned ablation at the time of enrollment, or those patients where ablation is highly anticipated are **NOT** candidates for CHANGE AFib.
- Recurrent AFib requiring escalation of rhythm control (including ablation) is
  - expected
  - not counted as an unplanned cardiovascular hospitalization event
- Patients may continue dronedarone after AFib ablation

At What Point Is a Cardioversion Allowed After Randomization?

- A cardioversion is allowed at any time during the conduct of the trial (in either arm).

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What Is The Timeframe For The Bradycardia, Pr Interval, & Corrected Qt Interval Exclusions?

What if a patient has a single instance of bradycardia?

- Providers should evaluate the patient's most recent ECG(s), likely from the hospital admission.

- For a single episode of bradycardia, the PI's judgment can be used.
  - If there is a transient bradycardia that was reversible, then that would not necessarily exclude participation.

ECG: electrocardiogram; PI: Principal Investigator

Do Patients Need To Be Symptomatic To Be Enrolled?

- There is no requirement as it relates to symptoms.

- Eligible patients are those with first-detected AFib
  - Diagnosis within 60 days
  - No prior hospitalization for AFib

Do Patients Need To Have Paroxysmal AFib?

Are patients with persistent AFib excluded?

- Patients with both paroxysmal and persistent AFib are eligible for participation.

- Based on the inclusion criteria, it is expected that most of the cohort will be patients with paroxysmal AFib.

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Does The PI Need To Prescribe Dronedarone For The Entire 12 Months?

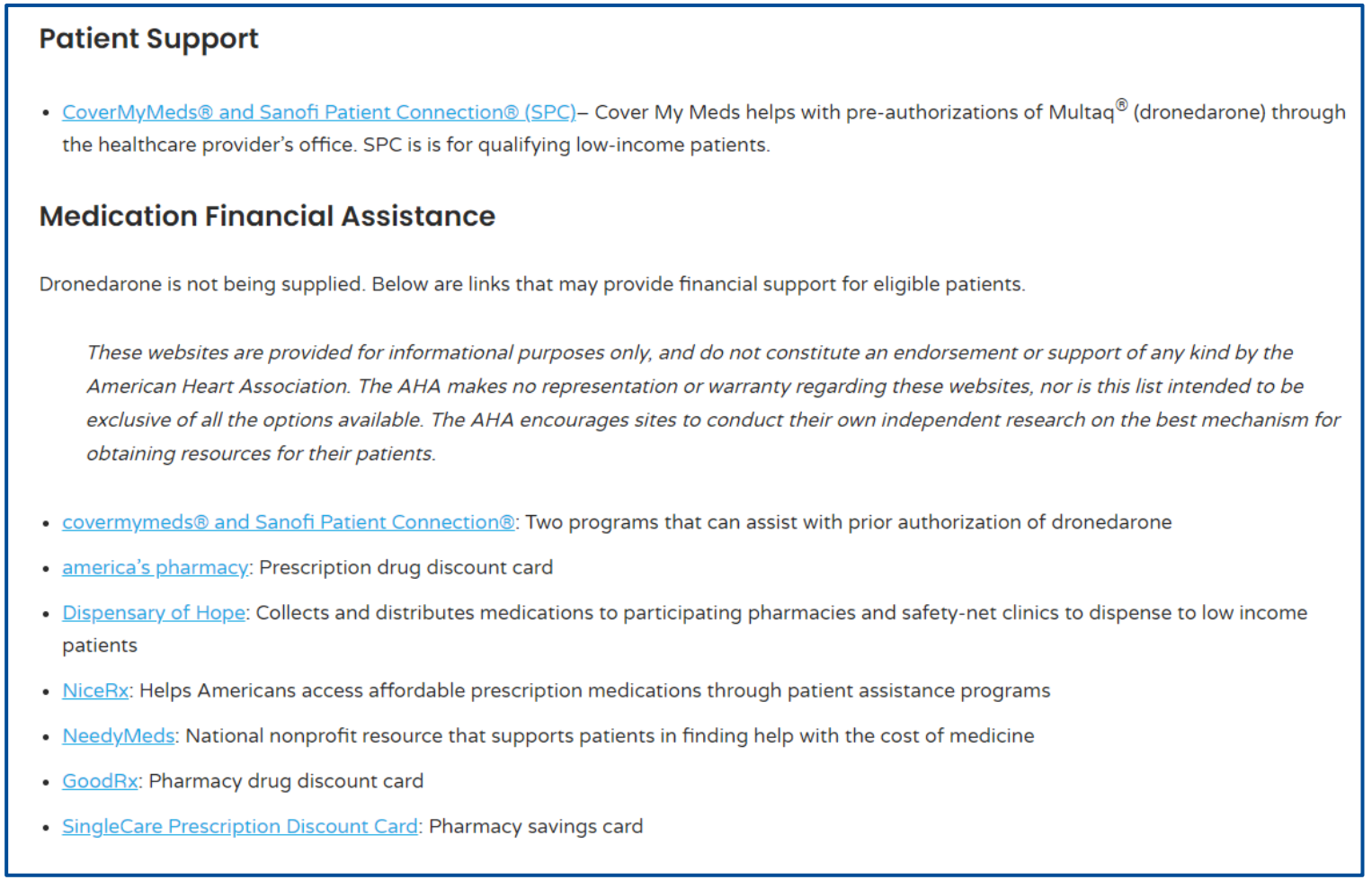
- No, another trial team member may prescribe the drug.

- The PI should assume responsibility for the patient, their participation, and for protocol adherence.

PI: Principal Investigator

Is Dronedarone Being Provided By The Study?

- No. Dronedarone is not being supplied.
- Please visit the ***'Patient Support' & 'Medication Financial Assistance'*** section of the **Resources** page of the trial website.



Patient Support

- CoverMyMeds® and Sanofi Patient Connection® (SPC)– Cover My Meds helps with pre-authorizations of Multaq® (dronedarone) through the healthcare provider's office. SPC is is for qualifying low-income patients.

Medication Financial Assistance

Dronedarone is not being supplied. Below are links that may provide financial support for eligible patients.

These websites are provided for informational purposes only, and do not constitute an endorsement or support of any kind by the American Heart Association. The AHA makes no representation or warranty regarding these websites, nor is this list intended to be exclusive of all the options available. The AHA encourages sites to conduct their own independent research on the best mechanism for obtaining resources for their patients.

- covermymeds® and Sanofi Patient Connection®: Two programs that can assist with prior authorization of dronedarone
- america's pharmacy: Prescription drug discount card
- Dispensary of Hope: Collects and distributes medications to participating pharmacies and safety-net clinics to dispense to low income patients
- NiceRx: Helps Americans access affordable prescription medications through patient assistance programs
- NeedyMeds: National nonprofit resource that supports patients in finding help with the cost of medicine
- GoodRx: Pharmacy drug discount card
- SingleCare Prescription Discount Card: Pharmacy savings card

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How Do We Handle Insurance Delays?

Many of patients have a very short hospital stay

- Electronic medical record systems may identify medications approved by insurance
  - If unclear at discharge, dronedarone can be prescribed as soon as possible after discharge

- Patients in the intervention arm are contacted after discharge to confirm they filled their dronedarone prescription.

Questions

Connect With Us!

How to reach the CHANGE AFib Team

Enrollment Site Managers:

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Mariel Dronson@heart.org

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Resources to Remember

For important trial information and today's meeting recording, go to the **Resources** page at **www.changeafib.org**