CHANGE AFib

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

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

Featured Presenter:
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- Principal Investigator of CHANGE AFib
- 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

Agenda

- Quick Overview
- Frequently asked questions
- Discussion

WHAT IS CHANGE AFIB?

- Pragmatic randomized clinical trial
- Investigating whether the early use of dronedarone can improve outcomes in patients with first-detected atrial fibrillation (AFib)

Trial Design Overview

Design: Pragmatic Randomized Trial

Sample Size: Approximately 3,000 patients

Targeted Number of Participating Sites: 200

Patient Eligibility

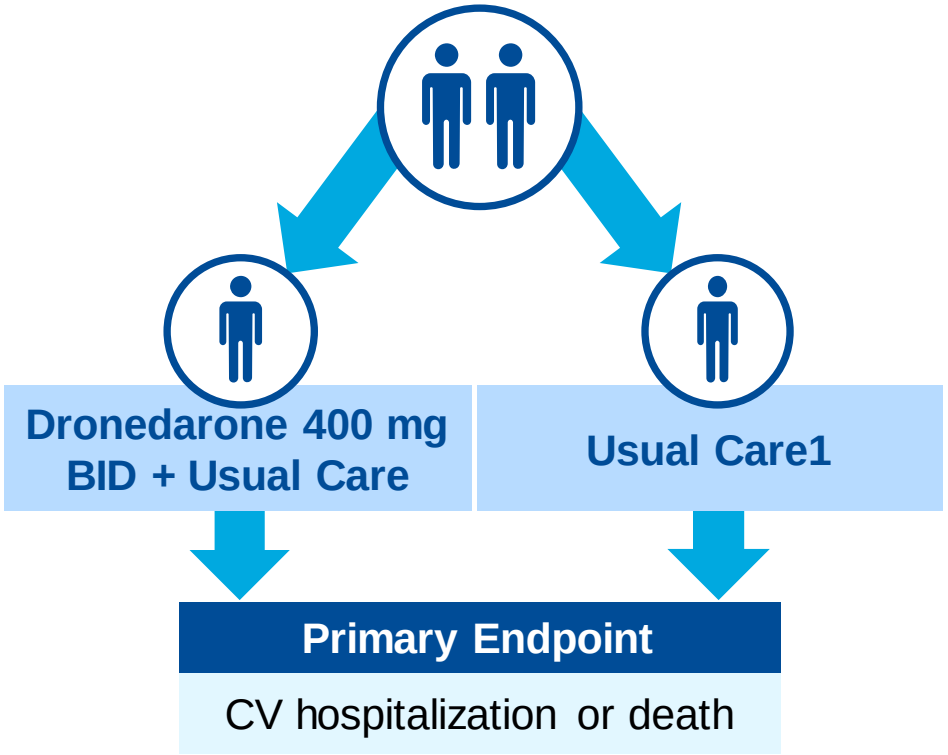
- Age ≥ 60 years
- First-detected Atrial Fibrillation
- Estimated life expectancy of at least 1-year
- Capable of giving signed informed consent

Duration of Follow Up: 12 months

CHANGE AFib /

Designed as an open-label pragmatic clinical trial nested within the GWTG®-AFib registry

STUDY DESIGN



- Conducted within **200 hospitals** participating in the GWTG® - AFib Program[1]
- Will enroll **3,000 patients**
- Follow-up will be conducted **6-months** and **12-months**

1 Hospitals need to be research ready, have established systems for obtaining IRB approval, and be willing to enroll in the GWTG-AFib program

WHY DRONEDARONE?

- Well-tolerated
- Effective at preventing recurrent AFib
- Reduces CV hospitalization
- Safe
- Post-hoc analyses suggest it performs well in persons with early AFib

1. Hohnloser SH, et al. N Engl J Med. 2009;360(7):668–678. 2. Singh BN, et al. N Engl J Med. 2007;357(10):987–999. 3. Davy J-M, et al. Am Heart J. 2008;156(3):527.e1–9. 4. Touboul P, et al. Eur Heart J. 2003;24:1481–1487. 5. Multaq (dronedarone hydrochloride) Prescribing Information. Sanofi-Aventis U.S. LLC: Bridgewater, NJ.

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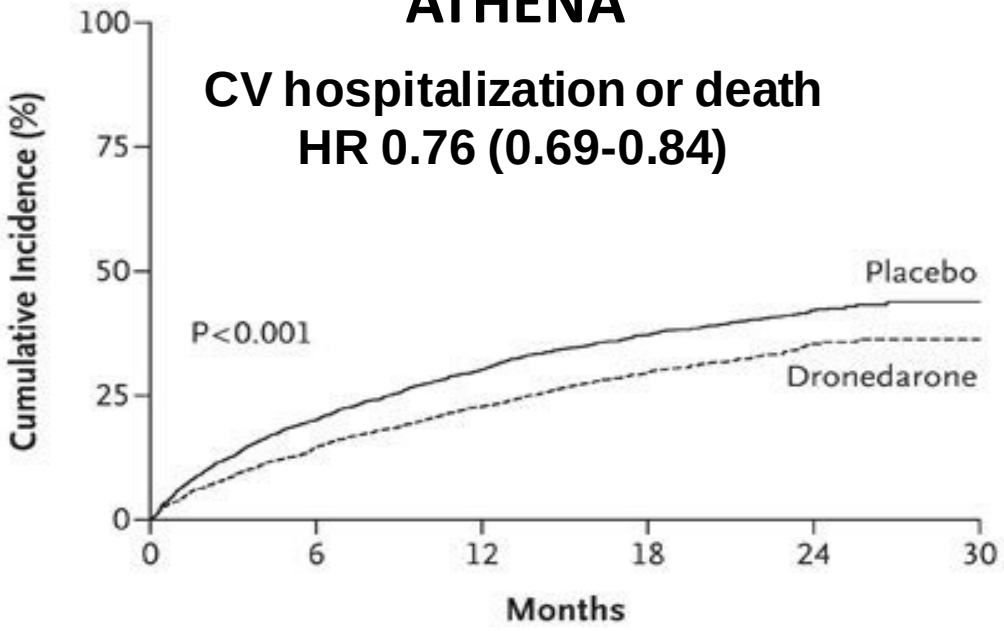
Rhythm control improves outcomes in patients with atrial fibrillation

ATHENA

CV hospitalization or death
HR 0.76 (0.69-0.84)

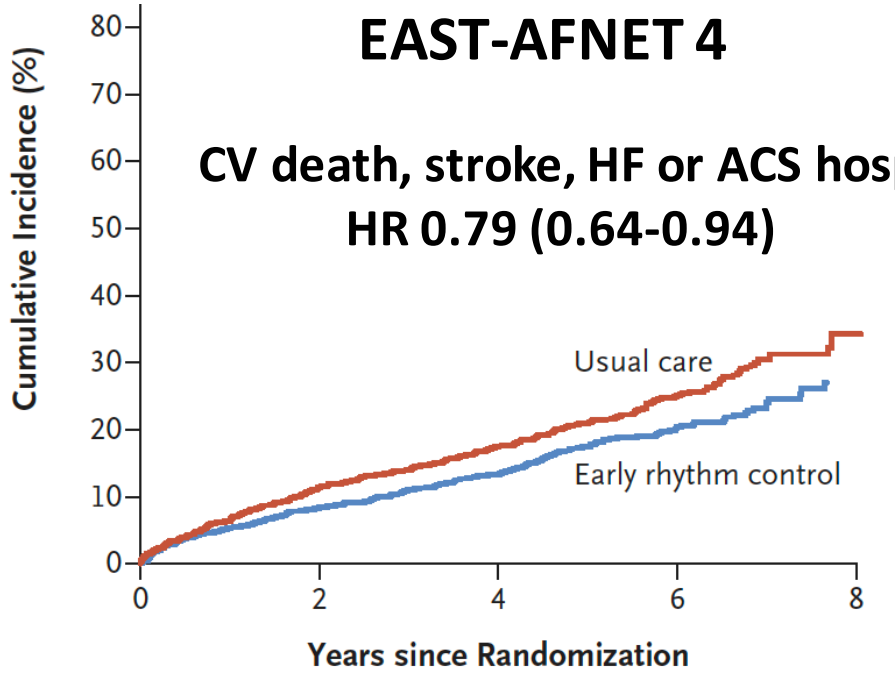


No. at Risk						
Placebo	2327	1858	1625	1072	385	3
Dronedarone	2301	1963	1776	1177	403	2

Hohnloser SH. *N Engl J Med* 2009;360:668-678.

EAST-AFNET 4

CV death, stroke, HF or ACS hosp
HR 0.79 (0.64-0.94)

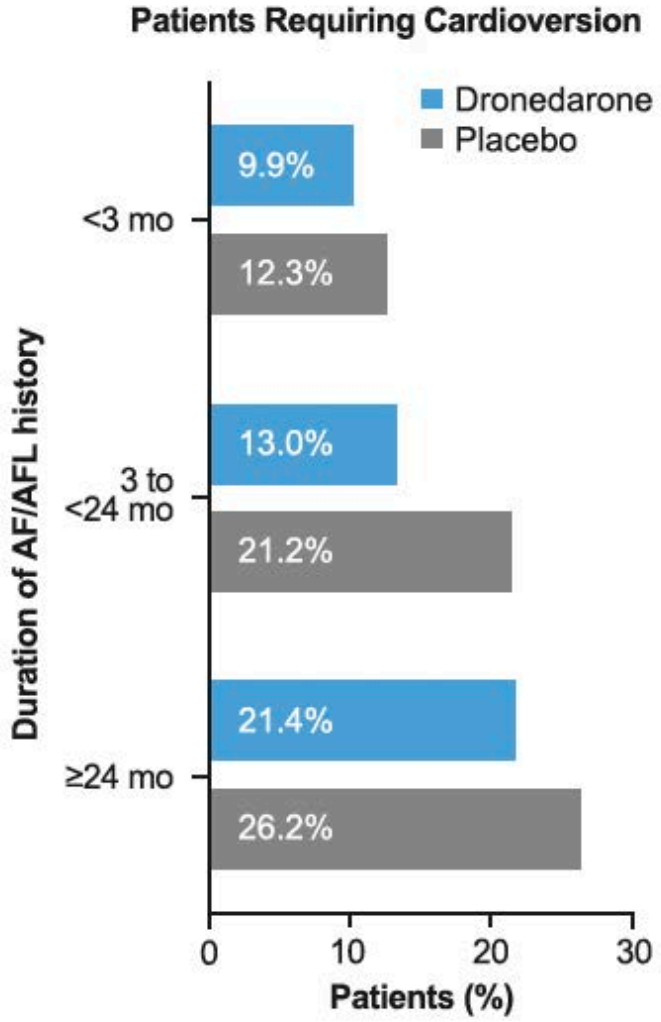


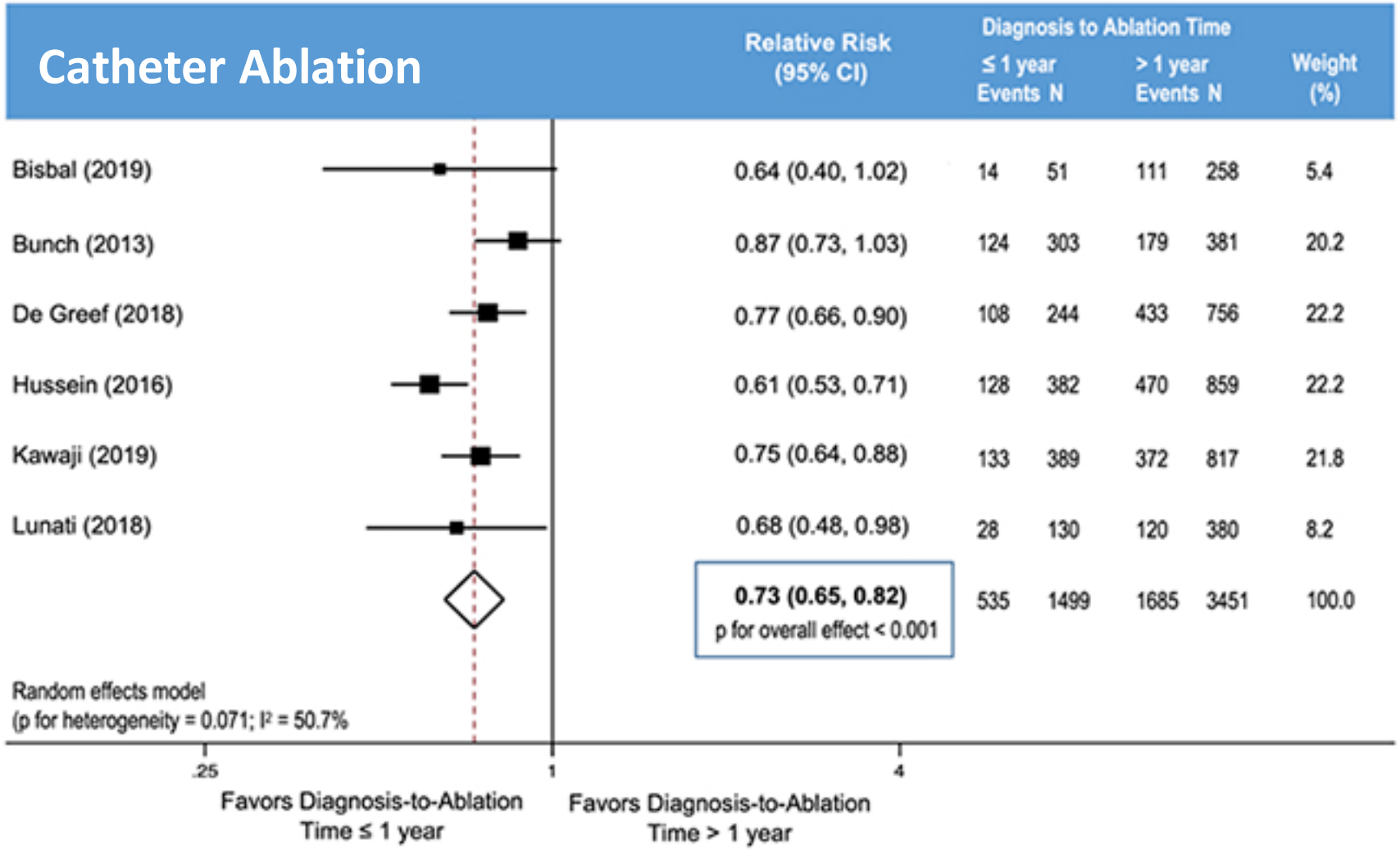
No. at Risk						
Usual care	1394	1169	888	405	34	
Early rhythm control	1395	1193	913	404	26	

Kirchhof P. *N Engl J Med*. DOI: 10.1056/NEJMoa2019422.

Impact of Duration of AF/AFL History

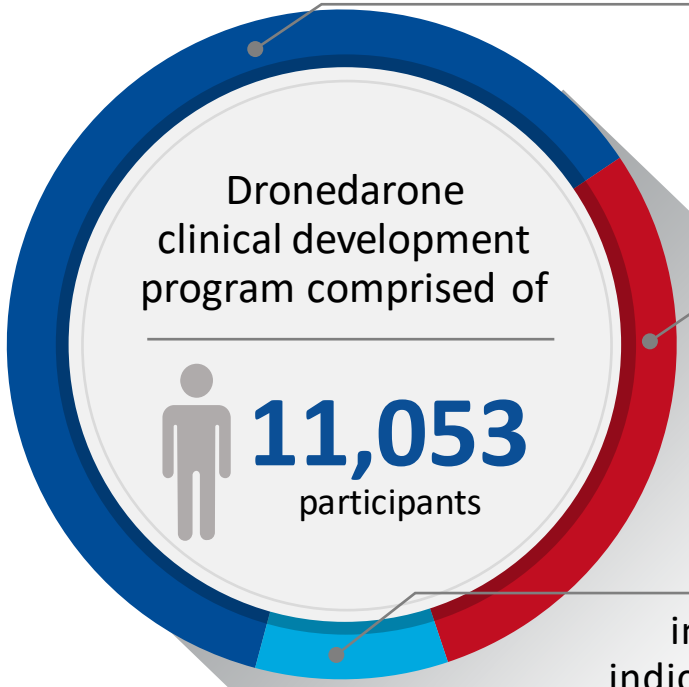
Drug Therapy





Chew DS. *Circ Arrhythm Electrophysiol*. 2020; 13: e008128.
Blomstrom-Lundqvist C. *Clin Cardiol*. 2020;43:1469–1477.

Dronedarone: A highly studied antiarrhythmic drug for the treatment of AFib



6,813
in 6 trials* in AFib/atrial flutter[1-5]

3,236
in phase 3 trial in permanent AFib[6]

1,028
in 13 studies in non-AFib indications and 37 studies in healthy volunteers[7]

1.8 million patient-years
estimated cumulative dronedarone treatment time worldwide†[7]

*In the following clinical trials until 2011: ADONIS, ATHENA, DAFNE, DIONYSOS, ERATO, and EURIDIS. †From July 1, 2009 through July 31, 2021. AFib: atrial fibrillation.

1. Davy JM, et al. *Am Heart J*. 2008;156:527.e1-9. **2**. Hohnloser SH, et al. *N Engl J Med*. 2009;360:668-678. **3**. Le Heuzey JY, et al. *J Cardiovasc Electrophysiol*. 2010;21:597-605. **4**. Singh BN, et al. *N Engl J Med*. 2007;357:987-999. **5**. Touboul P, et al. *Eur Heart J*. 2003;24:1481-1487. **6**. Connolly SJ, et al. *New Engl J Med*. 2011;365:2268-2276. **7**. Sanofi. Data on file.

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IS DRONEDARONE BEING PROVIDED BY THE STUDY?

- No
  - Dronedarone is not being supplied

CHANGE AFib

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

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

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

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

Patient Population: Inclusion & Exclusion Criteria

Patients presenting to the hospital

INCLUSION CRITERIA

- Adults aged **≥60 years**
- First-detected AFib
- ECG documentation of AFib
- Estimated life expectancy **≥1 yr.**

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.

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 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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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

ARE THERE SPECIFIC TESTS THAT NEED TO BE DONE ON PATIENTS IN THE DRONEDARONE ARM DURING FOLLOW-UP?

If so, who would prescribe these?

No, the trial protocol does not mandate phlebotomy or lab draws beyond those conducted for usual clinical care.

WHAT DOES THE BUDGET LOOK LIKE?

Site Incentive Payments

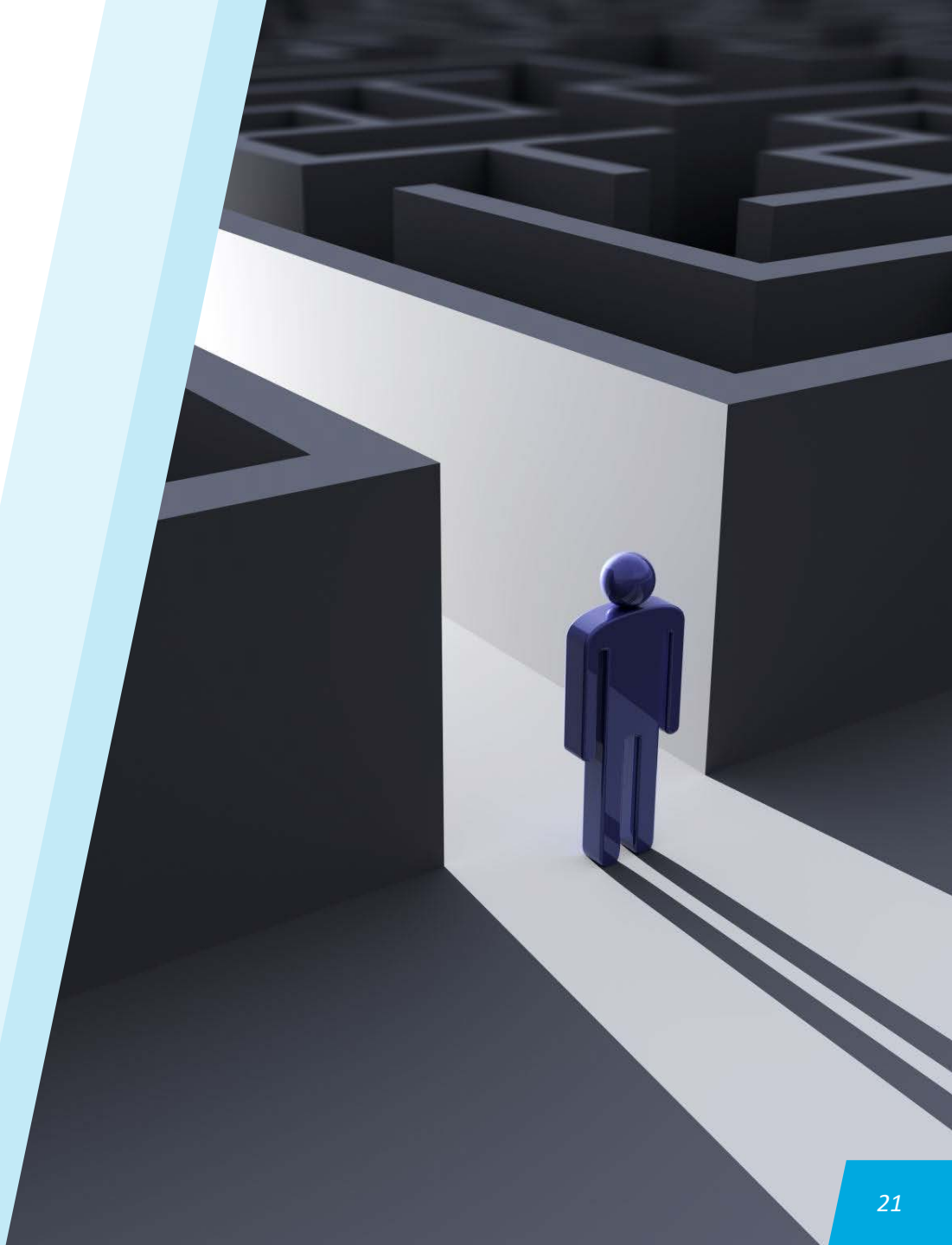
- $5,500 start-up payment
- $5,500 participation incentive Years 2 & 3
  - must enroll and collect data within GWTG-AFib for at least one patient
- $6,000 payment per participant, contingent upon data entry
  - $2,000 for patient randomization & baseline data
  - $2,000 for first (3-9 month) follow-up visit & data
  - $2,000 for the second (12-month) follow-up visit & data

*Sites will need to invoice AHA on a pre-defined basis to receive incentive payments

WHAT HAPPENS IF A PARTICIPANT DIES, WITHDRAWS CONSENT, OR IS LOST TO FOLLOW-UP?

How will payments to my site be impacted?

- Death (initial follow-up visit):
  - Complete follow-up form indicating that the patient has died.
  - Site receives $2,000 payment for completion of the follow-up form.
  - Do not complete a second follow-up form.
    - Sites will only receive one payment for patients that are deceased at the time of the initial follow-up visit.



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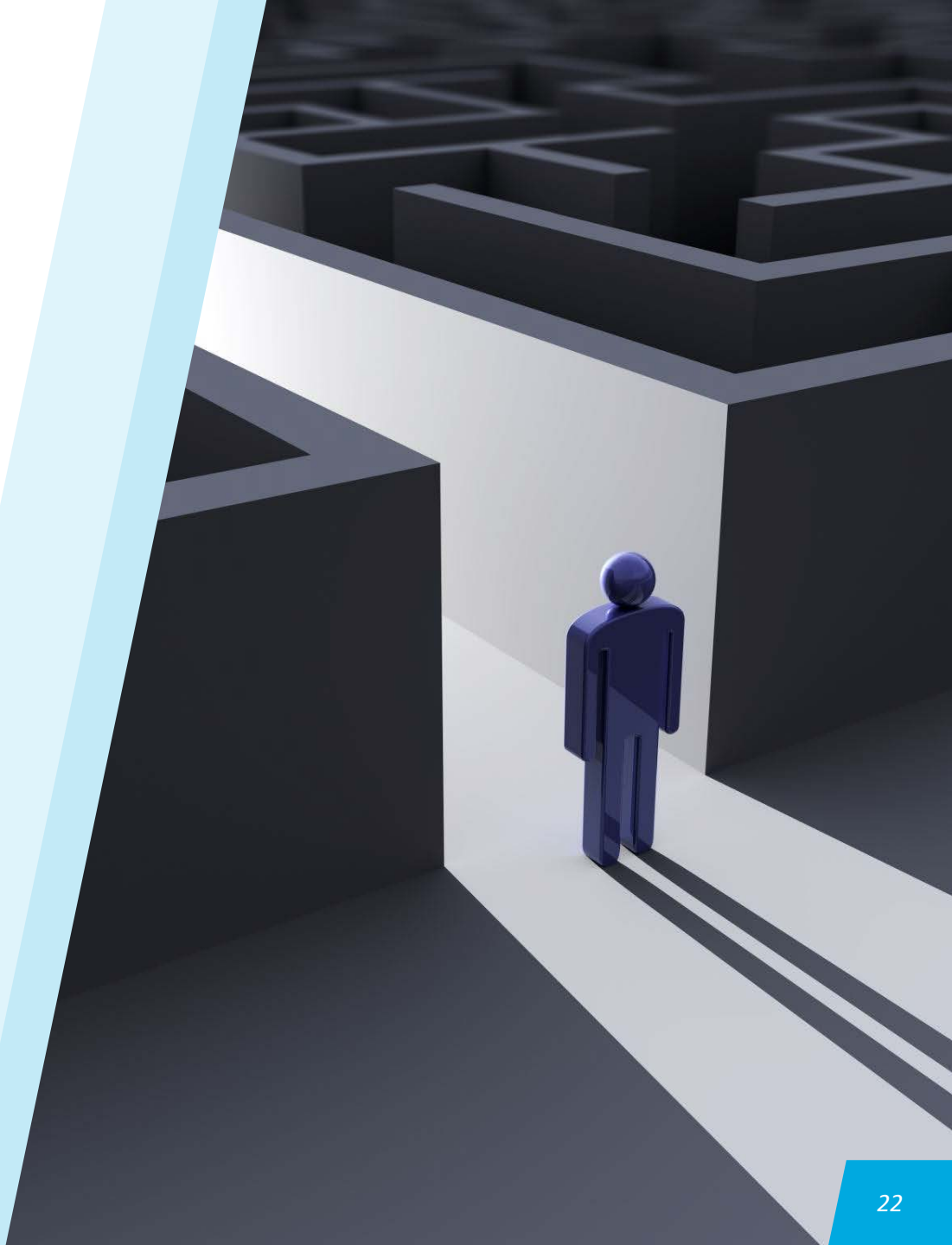
WHAT HAPPENS IF A PARTICIPANT DIES, WITHDRAWS CONSENT, OR IS LOST TO FOLLOW-UP?

How will payments to my site be impacted?

- Withdrawal of consent (initial follow-up visit):
  - Complete follow-up form indicating that the patient has withdrawn consent
  - Site receives $2,000 payment for completion of the follow-up form
  - Do not complete a second follow-up form
    - Sites only receive one payment for participants that withdraw consent at the time of the initial follow-up visit

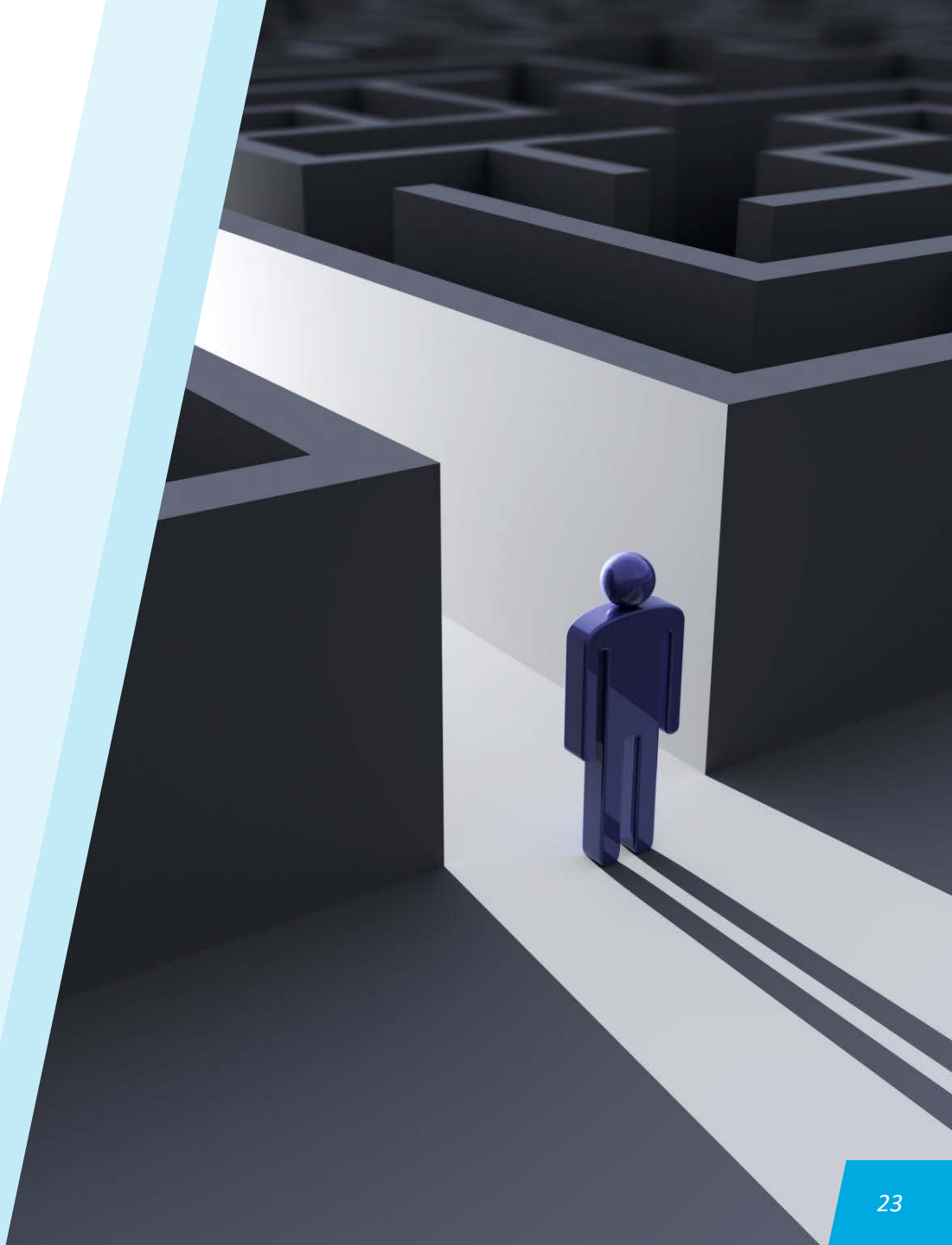


WHAT HAPPENS IF A PARTICIPANT DIES, WITHDRAWS CONSENT, OR IS LOST TO FOLLOW-UP?

How will payments to my site be impacted?

- Lost to follow-up (initial follow-up visit)
  - Complete the follow-up form and indicate the patient has been lost to follow-up
  - Site receives the $2,000 payment for completion of the initial follow-up form

- You should attempt to reach the patient again for the final follow-up visit at 12 months
  - If attempt is made, complete the second (end of study) follow-up form
  - Site receives the final $2,000 payment for completed form



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IS IRB APPROVAL REQUIRED?

Central or Local IRB Approval is permitted

Yes, IRB approval is required.

- If a site does not require use of their own or local IRB, AHA will facilitate the use of a central commercial IRB (Advarra).
- Institutional IRBs have the right to sign a waiver of oversight (rather than bring it up for review), which defers to the decision made by the central IRB.
- Either approach is acceptable, so long as one or the other is on record with each site.

- Each site is responsible for maintaining a copy of their IRB and copies must also be sent to the AHA.

GWTG Contracting

What does my site need to do to join CHANGE AFib?

- If not already contracted, contract for GWTG-AFib
  - Brand NEW GWTG Customers need to sign a GWTG-AFib Unified Participation Agreement (UPA)
  - Existing GWTG customers, new to GWTG-AFib
    - Sign an amendment

- All sites must sign a separate CHANGE AFib site agreement

Brand new GWTG customers: sites that do not participate in any GWTG module
Exiting GWTG customers: already participate in at least one GWTG module (e.g., GWTG-Stroke, GWTG-HF, GWTG-CAD, GWTG-Resus)

ARE SATELLITE SITES PERMITTED FOR THE TRIAL?

We are part of a large healthcare system and would like to have several campuses involved under one PI

- Yes, within a single healthcare system, one PI is permitted to oversee multiple sites.
  - It is highly recommended that each individual site has their own “CHANGE AFIB Champion” to raise awareness and promote patient education and enrollment into the trial.

- Contracting:
  - Each site requires a unique GWTG-AFib registry instance to track the patients enrolled at their location.
  - Contact us for specific questions related to healthcare systems.

Connect With Us!

How to reach the CHANGE AFib Team

Visit **changeafib.org** to learn more and complete the contact us form

Reach out to your local AHA contact or email **changeafib@heart.org**

Resources to GET STARTED

For information on how to get started, including a listing of all essential documents for trial activation, go to the **resources** page at **changeafib.org**

DISCUSSION

Thank you for joining us!