SUMMARY OF CHANGES – PROTOCOL 2.0 – 17OCT2022

Protocol Title:
Pragmatic Randomized Clinical Trial of Early Dronedarone versus Usual Care to Change and Improve Outcomes in Persons with First-Detected Atrial Fibrillation (CHANGE AFIB)

Protocol Number: 2.0 –17OCT2022

Amendment Number: 1.0

Compound: Dronedarone

Brief Title: CHANGE AFIB

Study Phase: Post-market pragmatic clinical trial

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Regulatory Agency Identifier Number(s): NCT05130268

Authors:
This protocol was cowritten by the Duke Clinical Research Institute (DCRI) and the American Heart Association (sponsor). The outline of this template is consistent with the Guidelines for Good Pharmacoepidemiology Practices (GPP), The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist, and International Conference on Harmonisation (ICH) Guidance for Industry, E6 Good Clinical Practice (GCP): Consolidated Guidance.

1. Section 1.2: Schedule of Activities
    a. Full revision of '*Trial Visit Data Capture Requirements & Schedule*' table. See Protocol Section 1.2 for full details.
    b. This schedule of activities table reflects the collection of data that is being conducted in the course of the patient's clinical care. This is a pragmatic trial and consistent with the design, there are no diagnostic procedures or laboratory studies required by the protocol. All of the data recorded are data captured in the course of the patient's clinical care.
2. Section 5.1: Inclusion Criteria
    a. Age lowered from 60 to *21 years or older*.
    b. Definition of first-detected Atrial Fibrillation extended from diagnosis in previous 60 days to *120 days*.
    c. Acute care encounter defined as the evaluation or treatment of atrial fibrillation within 120 days.
        i. Further clarified that *patients can be enrolled from the inpatient setting during this qualifying acute care encounter or afterwards in the outpatient setting, so long as the qualifying acute care event has occurred in the past 120 days. Acute care encounters are defined as a visit to an emergency department, observation unit, or hospital admission.*
    d. Eligibility of consent by Legally Authorized Representatives.
3. Section 5.2: Exclusion Criteria
    a. Clarification on definition of chronic antiarrhythmic drug therapy (defined as *>7 days of treatment).*
    b. Clarification of prior hospitalization for AF to *explicitly not include the qualifying first-detected atrial fibrillation acute care encounter event.*
    c. Expansion of criteria #11 to *exclude patients currently breast feeding*.
    d. Clarification of criteria #12 to *defer to the opinion of the investigator on constitution of severe hepatic impairment.*
4. Section 6.2: Study Intervention Compliance
    a. Clarification on study intervention start time as follows:
        i. Participants in the intervention arm will be contacted *within 10 days of randomization* to verify that they *have filled and started taking* their prescription for dronedarone.
5. Section 6.3: Concomitant Treatment
    a. Addition of the following: *Cardioversion (pharmacologic or electrical) is not an exclusion and is permitted throughout the trial. Patients who are planned or scheduled to undergo catheter ablation during screening or at the baseline visit are not eligible. Following enrollment, if a patient experiences escalation of symptoms or refractory symptoms, escalation of rhythm control interventions, including catheter ablation, can be considered if deemed necessary by the patient's treating physician.*
    b. Antiarrhythmic Drug Therapy Definition Addition
        i. Orally administered antiarrhythmic drugs for the treatment of atrial fibrillation include Vaughan-Williams class I and III medications, including flecainide,

propafenone, sotalol, dofetilide, dronedarone, and amiodarone. Note, beta-blockers (class II) and non-dihydropyridine calcium channel blockers (class IV) are not membrane active antiarrhythmic medications.

6. Section 7: Discontinuation of Study Intervention and Participant Discontinuation/Withdrawal
    a. Additional clarification provided indicating that *patients should not be discontinued when they experience a primary endpoint event. They should continue in the trial until the end of study visit at the end of follow-up. The study intervention therapy should be continued unless deemed otherwise by the treating physician or if the patient requires initiation of a different antiarrhythmic medication.*
7. Section 8: Study Assessments and Procedures
    a. Additional clarification provided indicating that *patients can be enrolled in the inpatient setting during their qualifying acute care encounter or afterwards in the outpatient setting so long as their new-onset atrial fibrillation and acute care visit were in the prior 120 days.*
8. Section 8.1: Pregnancy
    a. Revision as follows:
        i. Women of reproductive age should use measures to prevent pregnancy during the study… Pregnancy will be recorded as an adverse event in all cases and dronedarone should be immediately discontinued.
    b. Removal of specific birth control methods, as intervention arm subjects should follow the package insert as the study medication is FDA approved.