Clinical trial guidance for Mount Sinai Nursing

Study sponsor: InCarda
Study acronym: RESTORE-1
Study title: A phase 3, randomized, double-blind, placebo-controlled trial of flecainide acetate inhalation solution for cardioversion of recent-onset, symptomatic atrial fibrillation to sinus rhythm (RESTORE-1)
Study arms: FlecIH-103 (flecainide inhalation solution) vs placebo (randomized 3:1)
Approvals: IRB, ED medical/nursing leadership, Pharmacy.

For study-related questions/issues, please contact:

- *Clinical Trials Research Coordinator*: 646-960-1911 (weekday daytime)
- *Clinical Trials Manager*: 201-423-3585 (weekday daytime)
- *Site Principal Investigator*: Jonathan Schimmel, MD, via Epic Secure Chat or 646-818-9502 (**24/7**)

Study summary

- Placebo-controlled, double-blind, randomized, study on efficacy/safety of nebulized flecainide to convert AFib to sinus rhythm.
- Flecainide is an approved antidysrhythmic drug, but it is not yet approved by an inhaled route.
- This trial examines if nebulized flecainide is effective in converting AFib to sinus rhythm.
  - Subjects can get a beta blocker, calcium channel blocker, digoxin, magnesium, and adenosine.
  - Subjects *cannot* get a different antidysrhythmic drug (eg amiodarone or procainamide).
  - Many subjects are on a home anticoagulant. If not, we evaluate CHADS-VASc score for stroke risk.
- *Trial rationale*: Expected to have faster onset and shorter duration (safer) vs. oral flecainide.
- Subjects get a monetary stipend for participation.

Eligibility

- Research Coordinators determine eligibility and obtain consent.
- Adults (18-85) with recent onset of symptomatic newly diagnosed or paroxysmal AF.
  - Excluded if RR > 22, QRS ≥ 120 msec, hypokalemia or hypomagnesemia, decompensated heart failure, or ≥3 consecutive measurements of SBP <100 or ≥160, DBP ≥95 mmHg, ventricular HR: <80 or >160 bpm

Assessments

- This trial collects a research-only lab test at 3 time points (flecainide concentration), not ordered in Epic.
  - Research Coordinators will attempt blood draws, but may need assistance. They will tell you what time windows to anticipate for phlebotomy, based on when drug is given.
- Assessment (screening)
  - Height/weight and vitals (Research Coordinator assists)
  - Possible echo in ED
- **Observation period** = time from randomization to 90 min after starting drug.
- **T_0** = time of drug administration
- Measure vitals: HR, BP, SpO2, and supplemental oxygen details
  - At 45 min (±2 min) pre-T_0 in semi-recumbent position, *with temperature*.
  - At 30 min (±2 min) pre-T_0 in semi-recumbent position, then place in seated upright position
  - At 15 min (±2 min) pre-T_0 in seated upright position.
    Note: Semi-recumbent means HOB ~45°. Patient should be in the required body position ≥5 min before collecting vitals. Repeat abnormal vitals if suspected from technical/machine error.
- Patient should be upright from 15 min pre-T_0 until the end of dosing.

- **Start drug (T_0)**
    - Instill drug into nebulizer and turn on wall air at 5 LPM (Research Coordinator assists).
    - Nebulizer device: green ball on top can switch from breath-actuated to continuous, ensure it's set as breath-actuated. Nebulizer should be inserted past the teeth, but bottom lip should not cover the exhale valve. Apply nose clips.
- **During Dosing**:
    - Patient inhales drug until AFib converts to sinus rhythm (SR) and SR lasts ≥1 min, or until full dose is administered, whichever occurs first.
    - Dosing consists of 2 separate 3.5 minute inhalation periods, separated by a 1 minute break.
- **After Dosing**:
    - Patient should return to semi-recumbent position.

Drug

- Epic order: "GCO#21-1670 flecainide/placebo ampules inhalation"
- Research Coordinators bring the drug from pharmacy to RN (not via tube station).
    - Drug/placebo look identical.
- Administration instructions
    - Research Coordinator will provide nebulizer instructions.
    - Scan the patient wristband and drug barcode before administration

Risks

- VTach, hypotension, bradycardia, sinus pause post-conversion of AFib to SR, or AFlutter with RVR.
- Notify the provider/study team immediately for new signs, symptoms, or vital sign changes.

Monitoring

- Patients should be in the ED Resuscitation zone and on telemetry.
- Record times precisely (vitals, drug administration, blood draws).
- Record vitals accurately (eg respiratory rate, well-fitting BP cuff).