Supplementary Online Content

Singh JP, Solomon SD, Fradley MG, et al; MADIT-CHIC Investigators. Association of cardiac resynchronization therapy with change in left ventricular ejection fraction in patients with chemotherapy-induced cardiomyopathy. *JAMA*. doi:10.1001/jama.2019.16658

Box 1. Clinical Inclusion Criteria
Box 2. Clinical Exclusion Criteria

This supplementary material has been provided by the authors to give readers additional information about their work.

BOX 1: Clinical Inclusion Criteria

- Subject is age 18 (or of legal age to give informed consent specific to state and national law) up to 80 years of age
- Male or female
- Subject who was without clinical heart failure at initiation of chemotherapy/radiation - induced treatment for an underlying malignancy but developed clinical heart failure (cardiomyopathy: reduced LVEF with a LBBB-type of conduction disturbance; see next inclusion item) 6 months or more after initiation of the chemotherapy without other evident cause of the cardiomyopathy.
- Subject eligible for implantation of a CRT-D device according to one of the following options in currently available guidelines:

  Class I:
  - *LVEF ≤ 35% AND*
  - *Sinus Rhythm*
  - *LBBB with a QRS duration ≥ 150 ms AND*
  - *NYHA class II, III or ambulatory IV symptoms on guideline-directed medical therapy*

  Class IIa1:
  - *LVEF ≤ 35% AND*
  - *Sinus Rhythm*
  - *LBBB with a QRS duration 120-149 ms AND*
  - *NYHA class II, III or ambulatory IV symptoms on guideline-directed medical therapy*

  Class IIa2:
  - *LVEF ≤ 35% AND*
  - *Sinus Rhythm*
  - *Non-LBBB with a QRS duration ≥150 ms AND*
  - *NYHA class II, III or ambulatory IV symptoms on guideline-directed medical therapy*

- Patient on stable* optimal pharmacologic therapy for the cardiac condition that is guideline-based and may include one or more of the following medications: Loop diuretics (e.g., furosemide, bumetanide, torsemide) unless the subject is not indicated, is contraindicated, or is intolerant of loop diuretics; Angiotensin converting enzyme (ACE) inhibitors and/or angiotensin receptor blocker (ARB) unless the subject failed, is not indicated, or is contraindicated for these therapies; Aldosterone antagonists unless the subject is not indicated, or is intolerant of aldosterone antagonists; Beta-blockers unless the subject is not indicated, contraindicated, or is intolerant of beta-blockers. The choice of selective or non-selective beta-blockers use is left to the Investigator's discretion

  * For purposes of the study, "stable" is defined as patient prescribed set medication doses for at least one month prior to study registration, unless contraindicated or not tolerated. Medications may be prescribed and adjusted as required for cardiac condition during the study.

Box 2: Clinical Exclusion Criteria

- Currently implanted pacemaker or ICD device
- Previous implant with a CRT/CRT-D device
- Cardiac condition not presumed to be caused by chemotherapy
- Documented symptomatic or hemodynamically unstable ventricular tachyarrhythmia
- Patients on active chemotherapy (must be at least 6 calendar months after last chemotherapy treatment)
- Permanent or chronic AF, or cardioversion for AF within the past 3 calendar months before consent date
- Structural heart disease such as congenital heart disease, valvular heart disease, e.g., rheumatic valvular heart disease, amyloid heart disease, etc.
- Coronary artery bypass graft surgery or percutaneous coronary intervention within the past 3 calendar months before consent date
- Enzyme positive myocardial infarction within the past 3 calendar months prior to consent date
- Unstable angina needing a diagnostic work up and intervention with hospitalization within the past 3 months prior to consent date
- Angiographic evidence of coronary disease who are candidates for coronary revascularization and are likely to undergo coronary artery bypass graft surgery or percutaneous coronary intervention in the foreseeable future
- Class IV heart failure and patient expected to undergo transplant within study duration
- Current or previous drug addiction or abuse that caused cardiomyopathy
- Patient who is pregnant or plans to become pregnant during the course of the trial. Note: Women of childbearing potential must have a negative pregnancy test within 7 days prior to consent date
- Recent CVA or TIA within the previous 3 months prior to consent date.
- Presence of any disease, other than the subject's cardiac disease, associated with a reduced likelihood of survival for the duration of the trial, e.g., cancer, uremia, liver failure, etc.
- Patient participating in any other clinical trial
- Patient unwilling or unable to cooperate with the protocol
- Inability to complete the QOL questionnaire
- Patient who lives at such a distance from the clinic that travel for follow-up visits would be unusually difficult
- Patient who does not anticipate being a resident of the area for the scheduled duration of the trial
- Unwilling to sign the consent for participation
- Physician does not allow participation

Abbreviations: AF = atrial fibrillation;