Medtronic News

# FDA Advisory Panel Recommends Expanded Indication for Medtronic Cardiac Resynchronization Therapy with Defibrillator (CRT-D) Devices

*Medtronic CRT-D Devices Demonstrate Survival Benefits for Mildly Symptomatic Heart Failure Patients in Two Pivotal Clinical Trials*

MINNEAPOLIS--(BUSINESS WIRE)--Dec. 7, 2011-- Medtronic, Inc. (NYSE: MDT) today announced that the U.S. Food and Drug Administration's (FDA) Circulatory Systems Devices Advisory Panel determined that the overall clinical benefits of Medtronic cardiac resynchronization therapy with implantable cardioverter defibrillator (CRT-D) devices outweigh the risks in treating certain mildly symptomatic heart failure patients. The recommendation, which was based on data from the landmark RAFT (Resynchronization/Defibrillation in Ambulatory Heart Failure Trial) and REVERSE (REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction) clinical trials, pave the way for a potential expanded labeling approval for these devices. While Medtronic's CRT-Ds are currently approved for patients with moderate-to-severe heart failure, these pivotal studies show their use can benefit mildly symptomatic heart failure patients by reducing mortality and heart failure hospitalization rates.

Specifically, the Advisory Panel voted in favor of the CRT-D devices' strong safety (Yes: 5 votes, No: 0 votes) and efficacy (Yes: 3 votes, No: 2 votes) profile in treating a mildly symptomatic patient population. The panel voted in favor of the overall risk-benefit profile (Yes: 3 votes and No: 2 votes) The FDA will consider the Panel's feedback as it reviews Medtronic's request to expand its CRT-D indication to include New York Heart Association (NYHA) Class II heart failure patients with a left ventricular ejection fraction (LVEF) of less than or equal to 30 percent, left bundle branch block (LBBB), and a QRS duration greater than or equal to 120 milliseconds.

"Today's favorable Panel vote brings us one step closer to providing more heart failure patients with advanced treatment options that are proven safe and effective and can significantly improve survival and quality of life," said Pat Mackin, president of the Cardiac Rhythm Disease Management business and senior vice president at Medtronic. "We look forward to working closely with the FDA during the regulatory process so that we may expand the use of our innovative portfolio of CRT-D devices in an effort to enhance patient outcomes in a broader heart failure population."

While certain NYHA Class II patients are already indicated for an implantable cardioverter defibrillator (ICD) to protect them from sudden cardiac arrest, they are still vulnerable to experiencing an exacerbation of their heart failure. However, a growing body of clinical evidence suggests that earlier intervention with CRT-D can decrease the risk of morbidity and mortality in this mildly symptomatic patient population. CRT-D therapy works by resynchronizing the contractions of both ventricles by sending tiny electrical impulses to the heart muscles, which improves the heart's blood-pumping ability. The device also has defibrillation capability, allowing for termination of life-threatening ventricular arrhythmias.

"As was seen in the RAFT and REVERSE trials, clinical evidence demonstrates that CRT-D prevents hospitalization and can save lives in mildly symptomatic patients," said Michael R. Gold, M.D., Ph.D., REVERSE study investigator and steering committee member, Michael E. Assay professor of medicine and director of cardiology at the Medical University of South Carolina. "Utilizing this lifesaving therapy earlier in a milder heart failure population would allow us to treat these patients before their symptoms exacerbate, ultimately enabling us to better address this serious, often debilitating and costly disease."

*RAFT Clinical Trial*

Findings from the landmark RAFT clinical trial, published in the *New England Journal of Medicine*, showed that CRT-D significantly reduced mortality for mildly symptomatic heart failure patients (NYHA Class II) by 29 percent when compared to patients treated with guideline-recommended implantable ICDs and medical therapy (p=0.006; HR=0.71). The study also demonstrated a significant reduction (27 percent) in combined mortality and heart failure hospitalizations for this population (p=0.001; HR=0.73), consistent with previously published studies. All patients were followed for at least 18 months, and had an average follow-up of 40 months, making it the longest follow-up and largest patient months-of-experience of any study of CRT therapy.

*REVERSE Clinical Trial*

With 610 patients studied, REVERSE was the first large-scale, global, randomized, double-blind trial to demonstrate the impact of CRT in mild heart failure patients or asymptomatic patients who previously had heart failure symptoms. All of the randomized subjects received a Clinical Composite Response at 12 months. The Clinical Investigation Plan pre-specified that a comparison would be made between subjects with CRT and those without. The results showed that 21 percent of subjects without CRT worsened, compared with 16 percent with CRT (p=0.10).

In a post-hoc analysis, more patients in the trial improved with CRT than without (54 percent vs. 40 percent, respectively). The Clinical Composite Response measure for heart failure consists of several different endpoints, including death, hospitalization for heart failure, crossover to the opposite arm due to worsening heart failure, a progression to a worsened NYHA class, or a moderate or marked worsening of the patient's self-assessment (administered by the blinded clinician). Furthermore, the analysis of secondary endpoints in the REVERSE trial showed that CRT leads to improvement in both cardiac structure and function as measured by echocardiography, meaning the heart size improves and beats more effectively. In an additional analysis, REVERSE also demonstrated that CRT delayed the time to first heart failure hospitalization in this patient group and reduced hospitalization or death by 51 percent.

The use of Medtronic CRT-D devices for mildly symptomatic heart failure patients (NYHA Class II) is investigational and not an approved use in the United States. Medtronic has supported seven major heart failure trials evaluating CRT that have contributed to the continued development and broadening of treatment guidelines.

About Medtronic

Medtronic, Inc. (www.medtronic.com), headquartered in Minneapolis, is the global leader in medical technology – alleviating pain, restoring health, and extending life for millions of people around the world.

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