Safety And Effectiveness Of Multi-Site Pacing In Initial Non-responders to Conventional Cardiac Resynchronization Therapy: *SMART-MSP* Primary Results

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on Behalf of the SMART-MSP Investigators

Disclosures

Dr. Saba received research support from Abbott and Boston Scientific and provides consultation services to Boston Scientific and Medtronic

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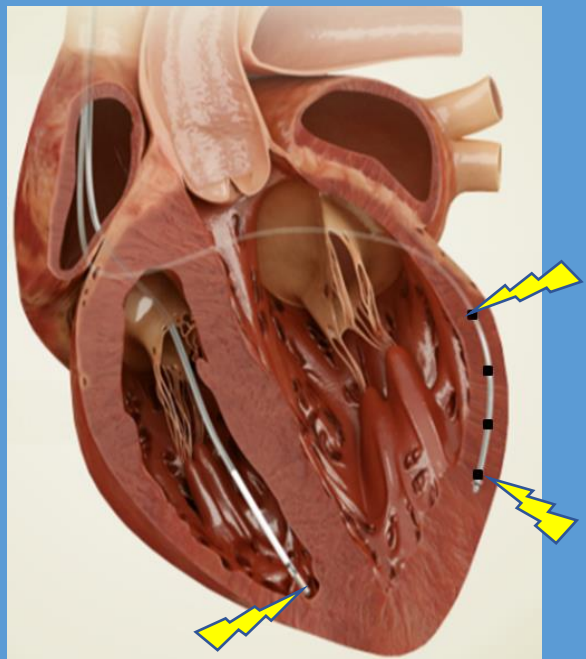
Background

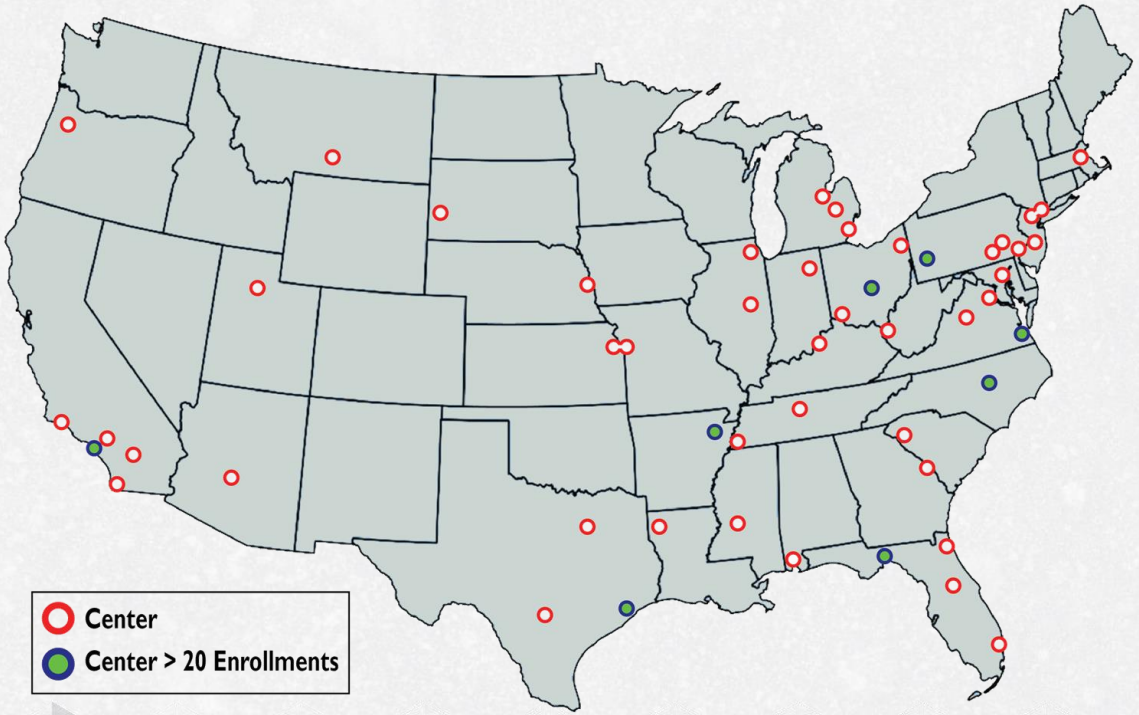
- CRT is an established HF therapy, but many patients do not respond to it
- Multi-site pacing (MSP) has shown promise in increasing CRT response rates in targeted populations
- Prior large, randomized CRT trials have failed to demonstrate superiority of multi-site over single site LV pacing
- SMART-MSP was designed to examine the safety and effectiveness of MSP in patients that are non-responsive to conventional CRT



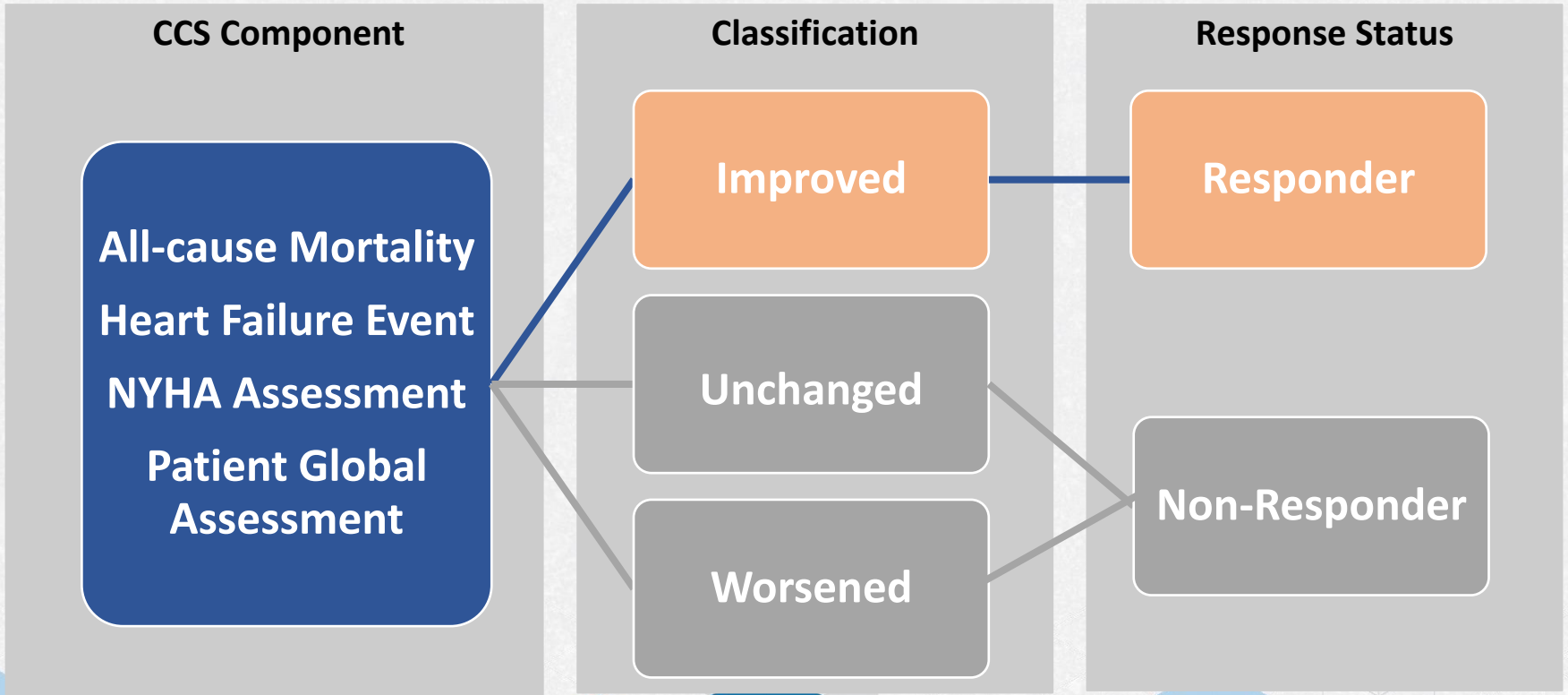
SMART MSP: *Study Design*

SMART MSP Trial is a prospective, observational study that enrolled 584 CRT recipients at 52 US sites

CRT recipients were assessed at 6 months follow-up using the clinical composite score (CCS). Non-responders had the LV MSP feature turned on and were followed till 12 months



Clinical Composite Score



SMART MSP: *Patient Selection and Endpoints*

Patient Selection

Inclusion Criteria

1. Recipients of *de novo* BSC Resonate CRT-D with Acuity LV quadripolar lead
2. Presence of RA and RV leads
3. Subjects who are willing and capable of providing informed consent

Exclusion Criteria

1. Subjects with prior LV pacing
2. Subjects with documented history of permanent AF or AV block

Endpoints

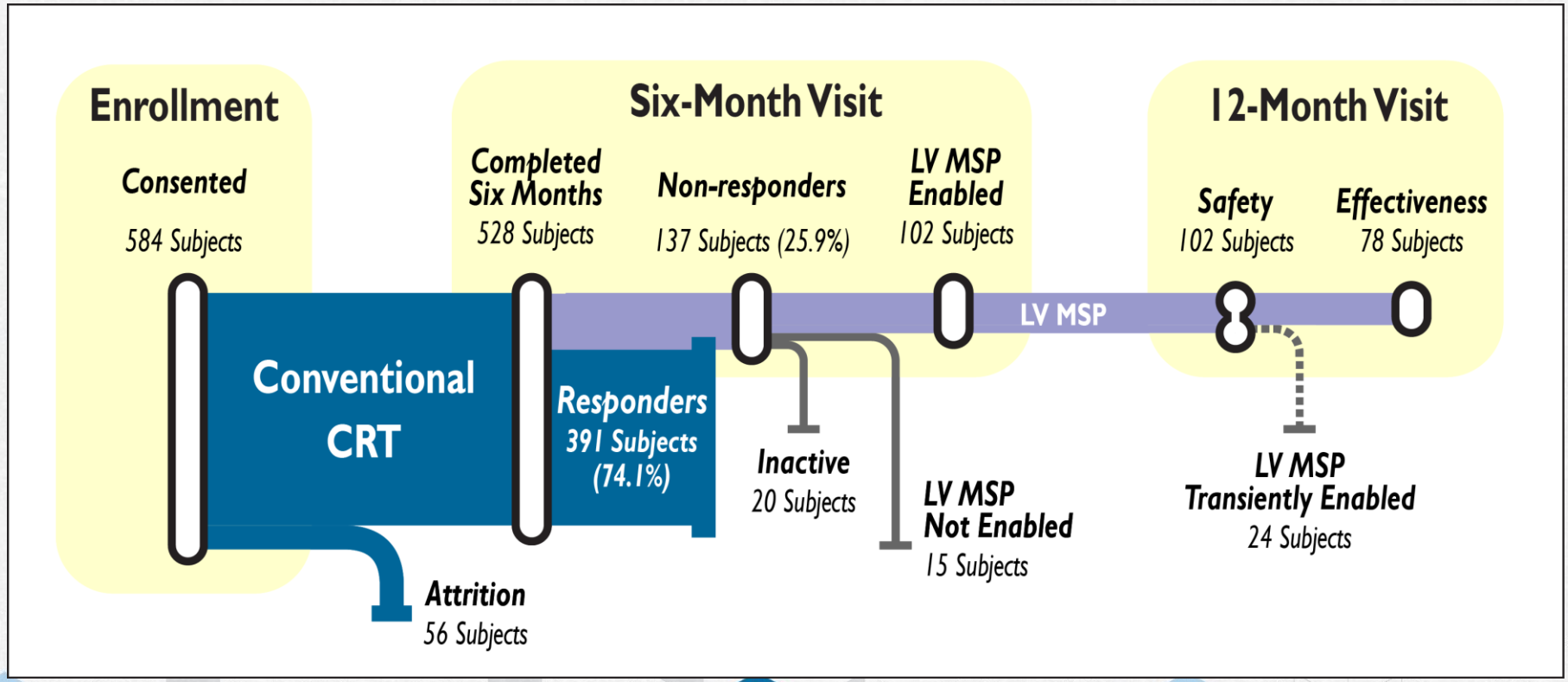
Primary Safety Endpoint

- Complication free rate of LV MSP feature between the 6-month and 12-month visit, compared to a performance goal of 90%
- Complications defined as 'related' or 'possibly related' to the MSP feature.

Primary Effectiveness Endpoint

- Percent of MSP pts with an Improved CCS at 12 months, compared to pre-determined performance rate of 5%
- limited to pts w/ MSP ON, ≥ 93% pacing

SMART MSP: *Design & Disposition*



Patient Demographics

Demographics were similar between all patients and MSP treatment arm

Demographics	All	MSP
N	528	78
Age (years)	66.8±10.8	66.7±11.0
Sex (women)	182 (34.5%)	27 (34.6%)
NYHA (I / II)	6 (1.1%) / 211 (40.0%)	2 (2.6%) / 34 (43.6%)
NYHA (III / IV)	306 (58.0%) / 5 (0.9%)	42 (53.8%) / -
Ischemic Cardiomyopathy	216 (40.9%)	30 (38.5%)
Atrial Fibrillation	120 (22.7%)	19 (24.4%)
Left bundle branch block	430 (81.4%)	62 (79.5%)
Right bundle branch block	59 (11.2%)	12 (15.4%)
IV conduction delay	27 (5.1%)	3 (3.8%)
QRS duration (ms)	158.1±20.6	155.1±17.7
ACEi/ARB/ARNI	406 (76.9%)	60 (76.9%)
Aldosterone antagonists	191 (36.2%)	24 (30.8%)
Beta blockers	486 (92.0%)	73 (93.6%)

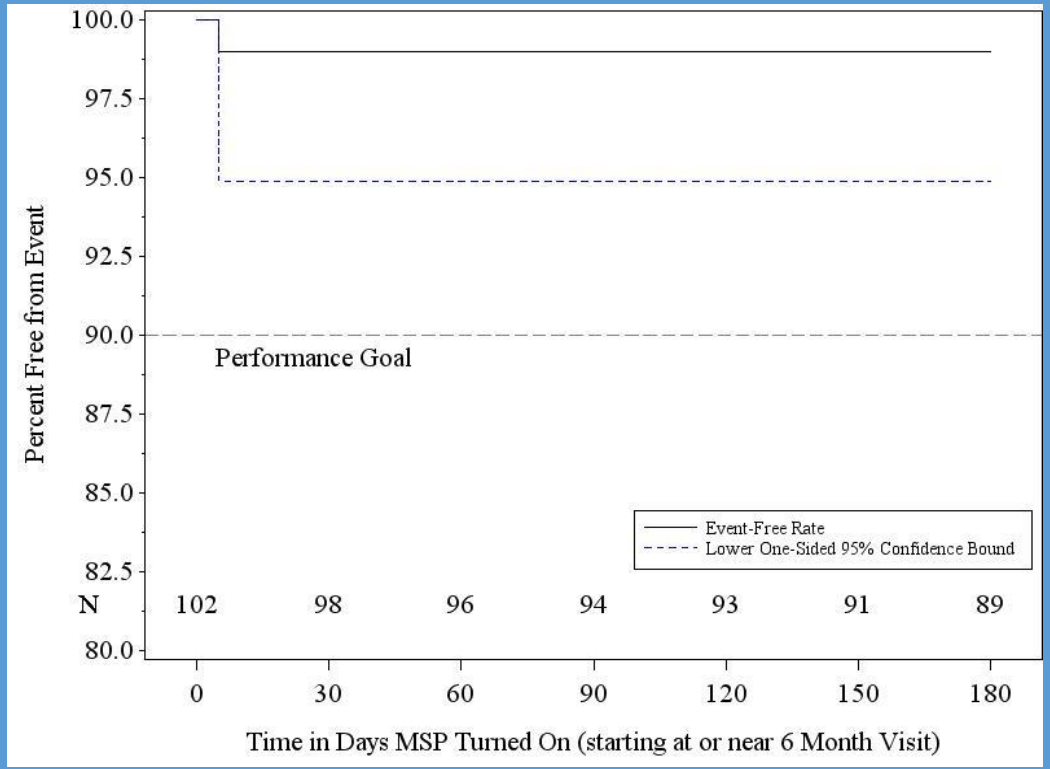
MSP-Related Complications

Complications determined as ‘related / possibly related’ to the LV MSP feature counted against the endpoint

1 LV MSP feature related complication was reported of 102 Non-Responders

99% LV MSP Complication - Free Rate

Time to Complication



MSP Effectiveness

Primary Effectiveness Criteria:
Percent of MSP pts with an Improved CCS at 12 Months, compared to 5% goal.

Sensitivity analysis:
Examination of Conversion rate with different criteria revealed the same ~50% in MSP patients:

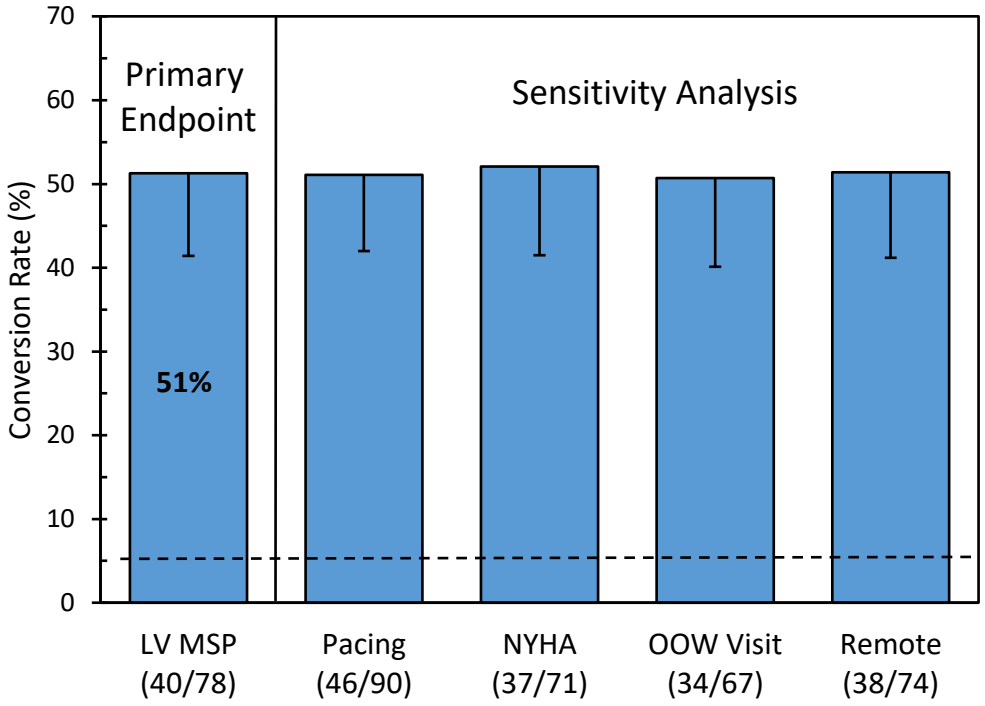
Pacing (including pts that did not have 93% pacing)

NYHA (excluding pts from 2 sites that used 'unqualified' NYHA assessors)

OOW (excluding pts with 12-month follow-up outside window)

Remote (excluding pts with virtual follow-ups)

CCS Responders at 12 months



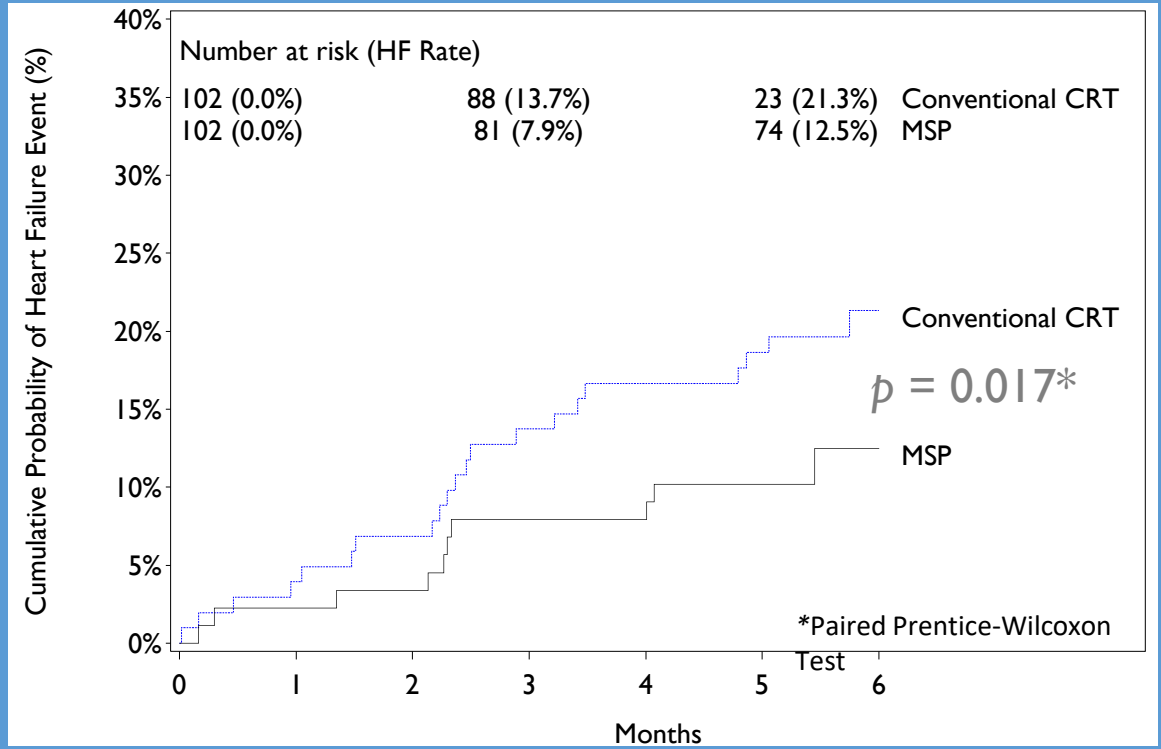
*limited to pts w/ MSP ON, ≥ 93% pacing, and complete CCS data

Heart Failure Events

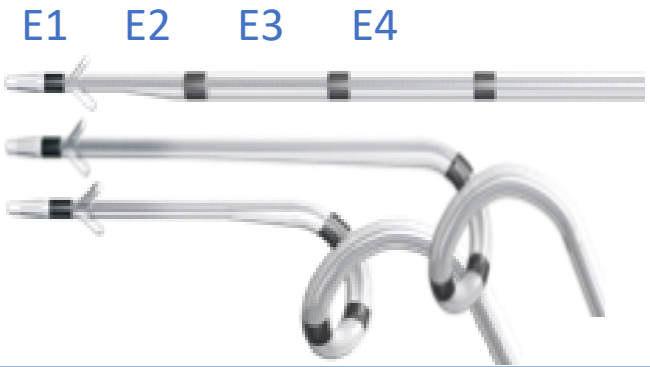
Analysis of time to first HF event in MSP treated pts shows a lower rate of HF on MSP compared to CRT only treatment

	CRT	MSP
HF Event	21 (20.6%)	11 (10.8%)

Time to First Heart Failure Event

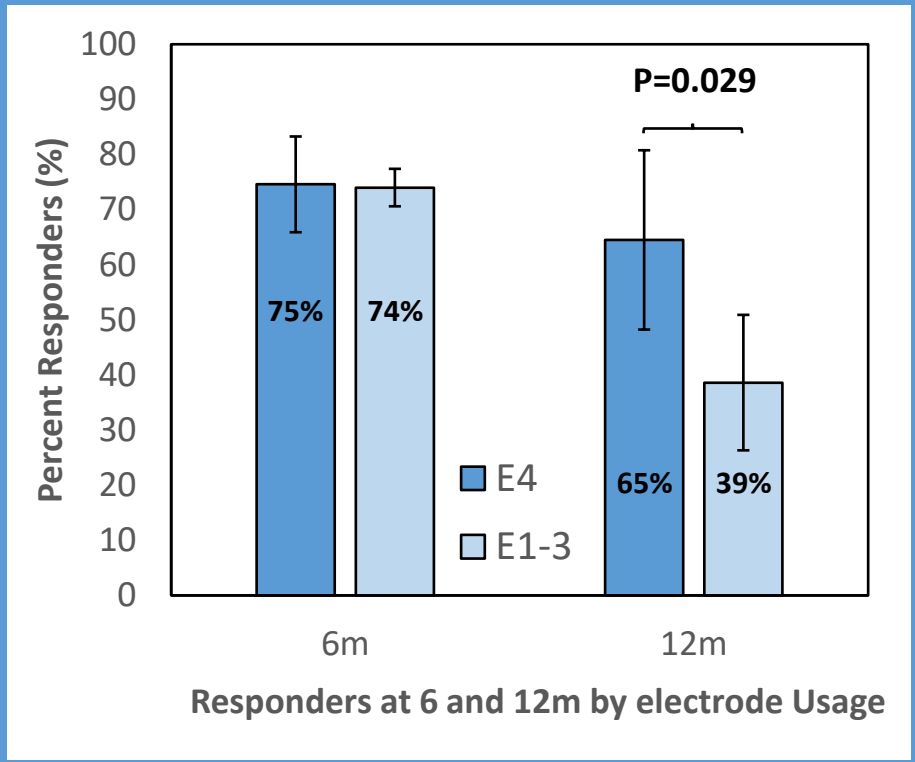


LV Electrode and CCS



Significantly more MSP pts paced from the E4 LV electrode converted to responders

LV Electrode & CCS Response



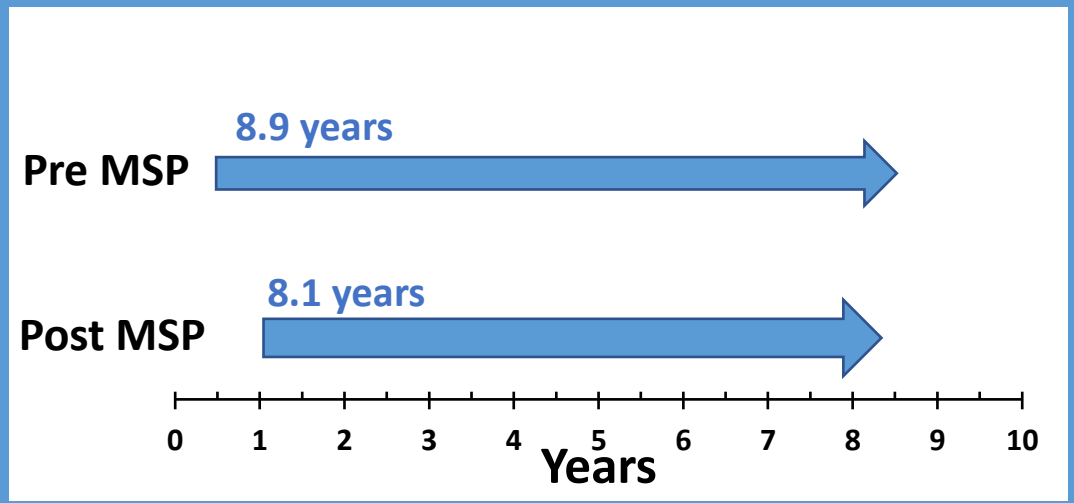
Responders at 6 and 12m by electrode Usage

Battery Life

Programmer estimate of remaining battery life in years*:

- Pre-MSP @ 6 m 8.9±2.1 yrs
- Post-MSP @ 12 m 8.1±2.2 yrs

Estimate of remaining battery



* Data are Mean ± SD

Conclusions

Multisite LV pacing is a safe and effective tool that can convert CRT Non-Responders to Responders, with minimal impact on device battery life

Future effort should focus on identifying:

- Sub-populations that may further benefit from MSP
- Optimal programming and vector selection for MSP
- Impact of early MSP activation in CRT recipients

On behalf of the SMART-MSP Investigators

Thank You

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RESONATE™HF, RESONATE™, RESONATE™X4, VIGILANT™, VIGILANT™X4, MOMENTUM™, MOMENTUM™ X4 CRT-D

– MANUAL 360198-002

INDICATIONS AND USAGE

- These Boston Scientific Cardiac Resynchronization Therapy Defibrillators (CRT-Ds) are indicated for patients with heart failure who receive stable optimal pharmacologic therapy (OPT) for heart failure and who meet any one of the following classifications: Moderate to severe heart failure (NYHA Class III-IV) with EF ≤ 35% and QRS duration ≥ 120 ms; or left bundle branch block (LBBB) with QRS duration ≥ 130 ms, EF ≤ 30%, and mild (NYHA Class II) ischemic or nonischemic heart failure or asymptomatic (NYHA Class I) ischemic heart failure.

CONTRAINDICATIONS

- There are no contraindications for this device.

WARNINGS

- Read this manual thoroughly before implantation to avoid damage to the pulse generator and/or lead. For single patient use only. Do not reuse, reprocess, or resterilize. Always have external defibrillation equipment available during implant and electrophysiologic testing. Ensure that an external defibrillator and medical personnel skilled in CPR are present during post-implant device testing should the patient require external rescue. Do not use defibrillation patch leads with the pulse generator system. Do not use this pulse generator with another pulse generator. Program the pulse generator Tachy Mode(s) to Off during implant, explant, or postmortem procedures. Do not kink, twist, or braid the lead with other leads. For leads that require the use of a Connector Tool, use caution handling the lead terminal when the Connector Tool is not present on the lead. Do not directly contact the lead terminal with any surgical instruments or electrical connections such as PSA (alligator) clips, ECG connections, forceps, hemostats, and clamps. Do not contact any other portion of the DF4–LLHH or DF4–LLHO lead terminal, other than the terminal pin, even when the lead cap is in place. Do not contact any other portion of the IS4–LLLL lead terminal, other than the terminal pin, even when the lead cap is in place. When implant a system that uses both a DF4–LLHH or DF4–LLHO and IS4–LLLL lead, ensure that the leads are inserted and secured in the appropriate ports. Do not use atrial tracking modes in patients with chronic refractory atrial tachyarrhythmias. Do not use atrial-only modes in patients with heart failure. Left ventricular lead dislodgement to a position near the atria can result in atrial oversensing and left ventricular pacing inhibition. Physicians should use medical discretion when implanting this device in patients who present with slow VT. Advise patients to seek medical guidance before entering environments that could adversely affect the operation of the active implantable medical device, including areas protected by a warning notice that prevents entry by patients who have a pulse generator. RESONATE HF, RESONATE, and MOMENTUM devices except for those with an RA: IS-1; RV: IS-1/DF-1; LV: LV-1 lead connection are considered MR Conditional. VIGILANT devices are considered MR Conditional. For these devices, unless all of the MRI Conditions of Use are met, MRI scanning of the patient does not meet MR Conditional requirements for the implanted system, and significant harm to or death of the patient and/or damage to the implanted system may result. For potential adverse events applicable when the Conditions of Use are met or not met, refer to the MRI Technical Guide. Do not subject a patient with an implanted pulse generator and/or lead to diathermy. If desired, ensure that Patient Triggered Monitor (PTM) is enabled prior to sending the patient home by confirming the magnet response is programmed to Store EGM. Once the PTM feature has been triggered and the magnet response set to Inhibit therapy the patient should not reapply the magnet.

PRECAUTIONS

- For specific information on precautions, refer to the following sections of the product labeling: clinical considerations, sterilization and storage, implantation, device programming, environmental and medical therapy hazards, hospital and medical environments, follow up testing, explant and disposal, supplemental precautionary information. Advise patients to avoid sources of EMI because EMI may cause the pulse generator to deliver inappropriate therapy or inhibit appropriate therapy.

POTENTIAL ADVERSE EVENTS

- Based on the literature and on pulse generator and/or lead implant experience, the following alphabetical list includes the possible adverse evets associated with the included devices: Air embolism; Allergic reaction; Bleeding; Bradycardia; Cardiac tamponade; Chronic nerve damage; Component failure; Conductor coil fracture; Death; Electrolyte imbalance/dehydration; Elevated thresholds; Erosion; Excessive fibrotic tissue growth; Extracardiac stimulation (muscle/nerve stimulation); Failure to convert an induced arrhythmia; Fluid accumulation; Foreign body rejection phenomena; Formation of hematomas or seromas; Heart block; Inability to defibrillate or pace; Inappropriate therapy (e.g., shocks and antitachycardia pacing (ATP) where applicable, pacing); Incisional pain; Incomplete lead connection with pulse generator; Infection including endocarditis; Insulating myocardium during defibrillation with internal or external paddles; Lead dislodgement; Lead fracture; Lead insulation breakage or abrasion; Lead perforation; Lead tip deformation and/or breakage; Local tissue reaction; Loss of capture; Myocardial infarction (MI); Myocardial necrosis; Myocardial trauma (e.g., tissue damage, valve damage); Myopotential sensing; Oversensing/undersensing; Pacemaker-mediated tachycardia (PMT); Pericardial rub, effusion; Pneumothorax; Pulse generator migration; Shunting current during defibrillation with internal or external paddles; Syncope; Tachyarrhythmias, which include acceleration of arrhythmias and early, recurrent atrial fibrillation; Thrombosis/thromboemboli; Valve damage; Vasovagal response; Venous occlusion; Venous trauma (e.g., perforation, dissection, erosion); Worsening heart failure.

- For a list of potential adverse events associated with MRI scanning, refer to the MRI Technical Guide

- Patients may develop psychological intolerance to a pulse generator system and may experience the following: Dependency; Depression; Fear of premature battery depletion; Fear of a device malfunction. Additionally, potential adverse events associated with the implantation of a coronary venous lead system include: Allergic reaction to contrast media; Breakage/failure of implant instruments; Prolonged exposure to fluoroscopic radiation; Renal failure from contrast media used to visualize coronary veins. Rx only. 92436222 (Rev. A)

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Directions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions.

CAUTION: The law restricts these devices to sell by or on the order of a physician. Indications, contraindications, warnings and instructions for use can be found in the product labelling supplied with each device. Products shown for INFORMATION purposes only and may not be approved or for sale in certain countries. This material not intended for use in France

Left Ventricular Pace/Sense Leads– ACUITY X4™

– Manual 359160-004

Indications

- This Boston Scientific lead is indicated for use as follows: Intended for chronic, left-ventricular pacing and sensing via the coronary venous system when used in conjunction with a compatible pulse generator. The Boston Scientific ACUITY X4 lead is a steroid-eluting (dexamethasone acetate) IS4 quadripolar lead.

Contraindications

- Use of this Boston Scientific lead is contraindicated for the following patients: Patients with a hypersensitivity to a maximum single dose of 0.54 mg dexamethasone acetate.

Warnings

- Read the manual thoroughly before implantation to avoid damage to the pulse generator and/or lead. Such damage can result in patient injury or death. For single patient use only. Do not reuse, reprocess, or resterilize. Always have external defibrillation equipment available during implant and electrophysiologic testing. Ensure that an external defibrillator and medical personnel skilled in CPR are present during post-implant device testing should the patient require external rescue. When using a right ventricular (RV) pace/sense lead in conjunction with this left coronary venous pace/sense lead, it is recommended that a polyurethane- insulated lead be used. Lead fracture, dislodgment, abrasion, or an incomplete connection can cause a periodic or continual loss of pacing or sensing or both. Although pliable, the lead is not designed to tolerate excessive flexing, bending or tension. Do not kink, twist, or braid the lead with other leads as doing so could cause lead insulation abrasion damage or conductor damage. Use caution handling the lead terminal when the Connector tool is not present on the lead. Do not directly contact the lead terminal with any surgical instruments or electrical connections such as PSA (alligator) clips, ECG connections, forceps, hemostats and clamps. Do not contact any other portion of the lead terminal, other than the terminal pin, even when the lead cap is in place. When implanting a system which uses both a DF4-LLHH/LLHO and IS4-LLLL lead, ensure that the leads are inserted and secured in the appropriate ports. Implant of the system cannot be performed in an MRI site zone III (and higher). Only use the Connector Tool for electrical connections to pacing system analyzers or similar monitors. Take care to obtain appropriate electrode position.. When connecting the lead to the pulse generator, it is very important that proper connetions are made. Unless all of the MRI Conditions of Use are met, MRI scanning of the patient does not meet MR Conditional requirements for the implanted system, and significant harm to or death of the patient and/or damage to the implanted system may result. For potential adverse events applicable when the Conditions of Use are met or not met, refer to the MRI Technical Guide. Do not subject a patient with an implanted pulse generator and/or lead to diathermy since diathermy may cause fibrillation, burning of the myocardium, and irreversible damage to the pulse generator because of induced currents.

Precautions

- Refer to the lead product labeling for cautions specific to clinical considerations, sterilization and storage, handling, implantation, hospital and medical environments, and follow-up testing. Failure to observe these cautions could result in incorrect lead implantation, lead damage and/or harm to the patient.

Potential Adverse Events

- Potential adverse events include, but are not limited to the following: allergic/physical/physiologic reaction, death, erosion/migration, fibrillation or other arrhythmias, lead or accessory breakage (fracture/insulation /lead tip), hematoma/seroma, inappropriate or inability to provide therapy (pacing/sensing), infection, procedure-related, and component failure. In rare cases severe complications or device failures can occur.
- *Refer to the product labeling for specific indications, contraindications, warnings/precautions and adverse events. Rx only. 92436276 (Rev. A)*

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Directions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions

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