November 11, 2026

Urgent: Important Safety Information
Medical Device Correction for the WiSE CRT System

Dear Healthcare Provider,

EBR Systems, Inc. (EBR) is providing this important safety communication related to the **use of diagnostic ultrasound imaging, including transthoracic echocardiography (TTE), in patients implanted with the WiSE CRT System (WiSE System)**. This communication provides updated information about the risk of inappropriate pacing, the factors identified as increasing that risk, and the precautions that healthcare professionals should follow when TTE is clinically indicated. **EBR IS NOT REQUESTING ANY RETURN OF PRODUCT FROM YOUR FACILITY.**

Please share this communication with all personnel who order, schedule, perform, supervise, or provide clinical support for echocardiography or other diagnostic ultrasound procedures involving patients with a WiSE System.

WARNING: Transthoracic echocardiography (TTE) or other low frequency ultrasound can cause the implanted electrode to deliver inappropriate pacing, which may lead to ventricular fibrillation and/or death. Before performing TTE on a patient with a WiSE CRT System, follow the Precautions outlined below.

WiSE Operating Principle & Unique Risk

The WiSE System provides leadless left ventricular endocardial pacing. Unlike conventional cardiac resynchronization therapy systems, which deliver left ventricular pacing through a coronary sinus lead, the WiSE System uses ultrasound-mediated energy transfer. A subcutaneously implanted Transmitter generates ultrasound pulses, and a small Electrode implanted in the left ventricle converts that ultrasound energy into electrical energy that paces the heart.

This ultrasound-based design enables the Electrode to be leadless and ultra-compact and allows it to be implanted directly on the left ventricular endocardium. These intentional design characteristics also mean that the Electrode can be sensitive to ultrasound originating from an external source. Under certain circumstances, ultrasound energy generated during TTE may be received by the Electrode and converted into inappropriate pacing.

This interaction is not ordinarily associated with other CRT systems because they do not use ultrasound energy for CRT pacing. Because the WiSE System uses ultrasound energy to enable leadless left ventricular pacing, externally applied diagnostic ultrasound may, under certain circumstances, result in inappropriate pacing during TTE. If the inappropriate pacing occurs at a vulnerable time in the cardiac cycle, it can produce a serious or life-threatening ventricular arrhythmia.

Reported Events

Across global clinical, post-market, compassionate-use, and commercial experience through October 26, 2026, EBR identified 17 reported events of ultrasound-induced inappropriate pacing among 586 implanted patients (2.9%). One event resulted in death. The overall occurrence rate observed during commercial experience (1.2%) has not exceeded that observed during the clinical and other global experience (3.6%).

Table 1. Reported Ultrasound-Induced Inappropriate Pacing Events

Experience	Patients Implanted	Reported Events	Deaths
Clinical and Other Global[1]	420	15 (3.6%)	0
U.S. Commercial[2]	166	2 (1.2%)	1 (0.6%)
Total	586	17 (2.9%)	1 (0.2%)

[1] Clinical and Other Global Experience includes patients implanted through clinical studies, prior European commercial and post-market experience, compassionate use or derogation pathways, and other non-U.S. access pathways. It includes the WiSE-CRT Study, SELECT-LV, SOLVE-CRT, the EU Post-Market Surveillance Registry, and compassionate use/derogation cases.
[2] U.S. Commercial Experience includes patients implanted in the United States after FDA PMA approval in April 2025.

Reported occurrence rates should be interpreted cautiously[*]. They are based on complaints reported to EBR and may be affected by differences in recognition, documentation, reporting, ultrasound technique, and the number of TTE procedures performed per patient. The rate does not represent the probability of an event during an individual TTE examination.

Factors Associated with Increased Risk

Factors that may increase the risk of inappropriate pacing have been associated with:

- First 30 days after Electrode implantation
- Apical or near-apical Electrode implant location
- High Mechanical Index settings
- Low frequency ultrasound
- Echo imaging from apical views

[*] FDA notes that Medical Device Report (MDR) data are not intended to be used to evaluate adverse event rates and that the incidence or prevalence of an event cannot be determined from this passive reporting system alone. See FDA, *About Manufacturer and User Facility Device Experience (MAUDE) Database, "Limitations of Medical Device Reports (MDRs)"*.

These factors may increase the energy received by the Electrode, but their absence does not eliminate the risk. Accordingly, the precautions below should be followed for every TTE examination involving a patient with an implanted WiSE System.

Precautions When Performing TTE on a Patient with an Implanted WiSE System

Below are important precautions to take prior to/during diagnostic imaging:

- Monitor patients by ECG at all times during any diagnostic echocardiography with an implanted WiSE Electrode so that inappropriate rhythms can be more readily detected and addressed. Inappropriate stimulation may present as Premature Ventricular Contractions (PVCs) or non-sustained Ventricular Tachycardia (VT) and should be suspected as device interaction.
- Keep external defibrillation equipment in the room for immediate use in case of emergency when performing ultrasound imaging on patients with a WiSE System Electrode. A physician or appropriately trained medical staff should be immediately available to manage any observed induced arrhythmias.
- Use the lowest power setting that provides a clinically adequate image.
- Avoid prolonged imaging of the implanted Electrode.
- When performing continuous wave Doppler imaging, avoid allowing the implanted Electrode to be intersected by Doppler interrogation line.
- In the event of inappropriate pacing, immediately remove the probe from the patient and discontinue imaging, and respond to any induced arrhythmias.

Future Labeling

EBR is updating the Instructions for Use and Echo Protocol and will provide them on the EBR Systems' eIFU website.

Additional Actions for Implanting Centers and Ordering Clinicians

- Place this communication and the WiSE Echo Protocol where echocardiography personnel can access them at the point of care.
- Ensure that patients receive the WiSE System Implant Card and Patient Information Booklet and are reminded to present their implant cards before medical tests or procedures.
- Remind your patients that a medical alert bracelet or pendant is available to supplement the WiSE System Implant Card and Information Booklet which directs healthcare providers to a website (echo-tips.com) with these precautions.
- Review local scheduling and handoff processes so that other members of the patient's healthcare team (e.g., echocardiography laboratory, referring physician) are informed when a patient has a WiSE System.

Product Use and Availability

This communication does not require device return, explant, or reprogramming, and the labeling update does not change the intended performance of the device. This communication reinforces the known ultrasound interaction and ensures that established imaging precautions are applied consistently. Healthcare professionals should determine whether diagnostic imaging is clinically indicated and communicate to other members of the patient's healthcare team the precautions. Perform in accordance with the WiSE CRT System labeling and the WiSE Echo Protocol. Continue routine patient follow-up and device management according to the applicable Instructions for Use.

Reporting and Questions

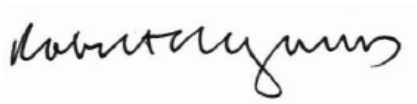
Report suspected adverse events and product complaints through your institution's established process and to EBR. Adverse events may also be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax.

If you have any questions regarding the content of this notification, please contact your EBR representative or EBR Customer Service.

Telephone	+1 (408) 720-1906
Email	compliance@ebrwise.com
Instructions for Use & Patient Information Booklet	ebrsystemsinc.com/resources#eIFU
Echo Protocol	echo-tips.com

EBR is committed to putting patients first in all we do. As always, EBR will continue to provide clinical support for your WiSE System procedures. We will also continue to monitor the clinical experience with the WiSE System, listen to physician feedback, and update you on any important information we learn through our post-market surveillance programs. We are grateful to our physician partners with whom we have collaborated in the preparation of this update.

Sincerely,



Robert Canby, M.D.
Chief Medical Officer

WiSE® Cardiac Resynchronization Therapy (CRT) System

INSTRUCTIONS FOR USE

Common Section

For use with:

- **WiSE CRT Electrode Catheter (M1000)**
- **WiSE CRT Delivery Sheath (M2000)**
- **WiSE CRT Battery (M3100)**
- **WiSE CRT Transmitter (M4100)**
- **WiSE CRT Programmer (M5100)**

CAUTION: Limited to investigational use outside of the United States.

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LBL-05300 Rev. B

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1 SYSTEM DESCRIPTION

The WiSE CRT System is an implantable, cardiac device capable of pacing the heart without a lead (**Figure 1**). A subcutaneously implanted Transmitter generates ultrasonic pulses that travel to a receiver implanted in the heart. This receiver, also known as the Receiver Electrode or Electrode, converts ultrasonic waves into electrical energy to stimulate cardiac tissue. The WiSE CRT System is not intended to be a life-sustaining device.

The WiSE CRT System applies this leadless technology to stimulate the endocardial surface of the left ventricle (LV). Working in conjunction with a standard commercially available pacemaker (with or without leads) or defibrillator already implanted in the patient, the WiSE System replaces the pacing function of a coronary sinus (CS) lead to achieve cardiac resynchronization therapy (CRT). The WiSE CRT System synchronizes with the co-implant using sensing electrodes in the Transmitter and Battery. As the co-implant paces the right ventricle (RV), the Transmitter generates ultrasound pulses that are received by the Electrode and converted to electrical energy to pace the LV. The sequence of sensing, transmitting, receiving, and stimulating the LV is essentially simultaneous with the co-implanted device's RV pacing output and provides biventricular (BiV) pacing, an operation analogous to standard CRT pacing devices.

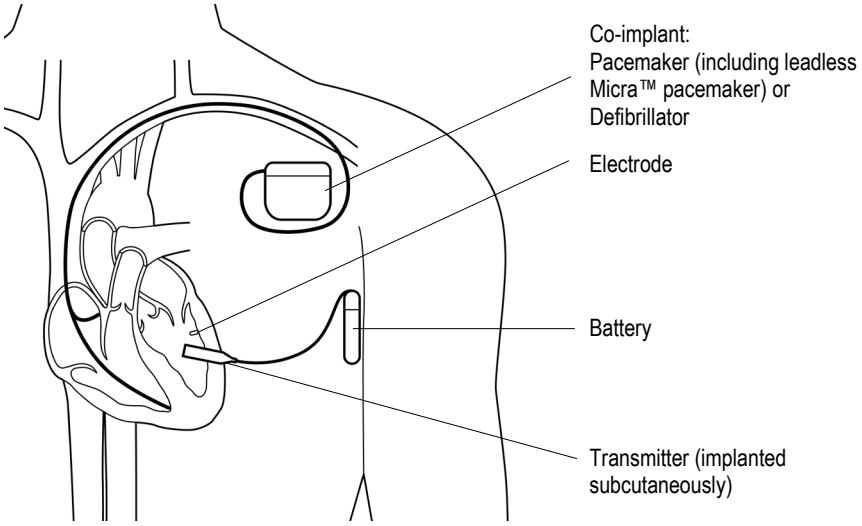


Figure 1**. Implanted WiSE CRT System Components with Co-Implant Device**

The WiSE CRT System has five main components (**Figure 1**):

1. **M1000 (Model 1000) - Electrode Catheter:** A single use catheter used to implant the Electrode, comprising the Electrode and Delivery Catheter (or Electrode Catheter or Catheter). The Electrode is implanted in the LV; it receives ultrasound energy and converts it into electrical energy for endocardial pacing.
2. **M2000 (Model 2000) - Delivery Sheath:** A single use deflectable guide Sheath used in combination with the M1000 Electrode Catheter.
3. **M3100 (Model 3100) - Battery:** A power source implanted subcutaneously in the mid-axial area of the left thorax, connected to the Transmitter by a cable.

4. **M4100 (Model 4100) - Transmitter:** An ultrasound energy device implanted subcutaneously in the thorax.

The Battery and the Transmitter together may be referred to as Pulse Generator.

5. **M5100 (Model 5100) - Programmer:** An external portable touch screen tablet with a communication module used to adjust parameters on the Pulse Generator and to assist with implant and follow-up of the System.

Note: Read the entire Instructions for Use (IFU) for all components of the WiSE CRT System to understand a complete description of its use.

2 INDICATIONS

- The WiSE CRT System is indicated for the following adult patients who are at least 22 years of age, are indicated for cardiac resynchronization therapy (CRT), have an existing or are eligible for an implanted right ventricular pacing system, and are in one of the following two categories: Patients in whom previous coronary sinus (CS) lead implantation was unsuccessful, or where an implanted lead has been turned off, referred to as "**previously untreatable**";
- Patients with previously implanted pacemakers or Implantable Cardioverter-Defibrillators (ICDs) in whom standard CRT upgrade is not advisable due to known relative contraindications for CS lead or CRT device implantation, referred to as "**high-risk upgrades**".

These categories are defined as follows:

Previously Untreatable:

Patients who have a full or partial CRT system and are deemed as 'previously untreatable' for one of the following reasons:

- CS lead implant was attempted but abandoned due to any of the following: difficult CS access or anatomy, inadequate lead location, inadequate pacing thresholds, phrenic nerve stimulation (PNS), or other procedural challenges;
- Left ventricular (LV) lead that was implanted but not operational includes patients in whom the LV lead is inoperative or programmed off due to improper function such as high threshold, non-capture, PNS, lead failure, lead dislodgement, or suboptimal LV lead location.

High Risk Upgrades:

Patients in whom standard CRT upgrade is not advisable due to known relative contraindication to CS lead implant, for example:

- Risk of venous occlusion or lesion precluding implant (e.g., multiple existing leads in situ);
- Risk of pocket infection at co-implanted device site (e.g., co-implant initial placement or Battery change within last 12 months);

- Considered high risk for CS implant due to co-morbidities (e.g., history of ischemic cardiomyopathy (ICM) or ventricular tachycardia (VT) with risk of epicardial pacing induced VT)

There is insufficient evidence to support the use of the WiSE CRT System in prior CRT non-responders.

The safety and effectiveness of the WiSE CRT System has not been established with leadless pacemaker co-implants that utilize conductive communication (e.g., Abbott Aveir).

3 CONTRAINDICATIONS

The WiSE CRT System is contraindicated for the following:

- Patients on triple anticoagulant who cannot tolerate periprocedural stopping of anticoagulation therapy.
- Patients who cannot tolerate, or are allergic or hypersensitive to, procedural anticoagulation or contrast agents, or to the post-procedural antiplatelet regimen.

4 WARNINGS

- Do not apply therapeutic ultrasound to the WiSE CRT Electrode, Transmitter, or Battery; this can cause untimed electrical stimulation and excessive heating of tissue around and/or damage to implanted components.
- Do not apply diathermy directly over the implanted WiSE CRT System components.
- Do not apply radiofrequency ablation (RFA) close enough to the Electrode to damage the tissue that it is stimulating.
- Do not apply therapeutic radiation over the implanted WiSE CRT System components. Damage to the electronic components of the WiSE CRT System might not be immediately detectable.
- Do not use transcutaneous nerve stimulation (TENS) in close proximity to the WiSE CRT System.

5 PRECAUTIONS

5.1 GENERAL PRECAUTIONS

Do not directly place defibrillation pads over implanted Transmitter or Battery to prevent damage.

5.2 PATIENT PROCEDURE

Based on location and type of a left atrial (LA) or LV thrombus, the physician should determine the patient's suitability for the procedure.

5.3 ELECTRODE IMPLANT LOCATION

Apical LV stimulation in CRT has been shown to be arrhythmogenic. The myocardium is commonly the thinnest at the apex and might be more susceptible to perforation, and apical placement results in shorter distances between the Electrode and apical transthoracic echocardiographic (TTE) views. Hence, apical implant locations are not recommended.

5.4 ULTRASOUND

Be cautious when exposing the patient to sources of ultrasound. This includes the use of imaging devices such as those used in echocardiography. There is a slight potential that the Electrode implanted in the LV of the heart could receive ultrasound pulses and convert them to untimed electrical pacing stimulation. Below are considerations to take prior/ during ultrasound imaging:

- The potential for untimed electrical pacing stimulation is highest in the first 30 days after implant.
- ECG monitoring is recommended during any diagnostic echocardiography in patients with an implanted WiSE CRT System so that inappropriate rhythms can be more readily detected and addressed.
- When performing ultrasound imaging on patients with a WiSE CRT System, a defibrillator should be available in case of emergency.
- In the event of extra pacing stimulation, discontinue imaging and remove probe from patient. If more imaging is necessary consider alternative options such as reducing the power output, a different imaging mode, or adjusting the imaging position.

5.5 PATIENT ENVIRONMENTS

Patients will be provided with a WiSE CRT System Implant Card and Information Booklet that carry similar information. Please remind your patient to:

- Carry the Implant Card at all times, especially during travel and when visiting any medical facility or personnel.
- Review the Information Booklet for important information.
- Avoid or seek medical guidance before entering areas that have signs or are otherwise documented as restricted for persons with implanted pacemakers.

Avoid close proximity and extended exposure to sources of electromagnetic interference. Electromagnetic interference may cause implanted medical devices to inappropriately sense, inhibit therapy, or operate incorrectly. The following are specific sources to be avoided:

- AC and DC motors/ power sources including automobile alternators
- Arc welding equipment
- Large radiofrequency (RF) transmit sources such as radar
- Hand-held radio transmitters (e.g., remote-control devices)
- Electronic article surveillance (anti-theft) devices
- Cell phones and personal music players

  Portable and mobile RF communications equipment can affect medical electrical equipment. Instruct patients to keep cell phones at least 15 cm (6 inches) away from implanted devices by

using the ear opposite the implant side of the body when in conversation. Instruct patients to avoid carrying cell phones or personal music players (e.g., iPod, mp3) in shirt pockets.

5.6 OTHER MEDICAL ENVIRONMENTS

Some devices used in medical environments may damage implanted devices or cause implanted medical devices to inappropriately sense, inhibit therapy, or operate incorrectly; these effects may not be immediately detectable.

General practice during any procedure that has the potential for operational interference is to temporarily turn the WiSE CRT System 'OFF' during the procedure by consulting the WiSE CRT System implanter's office. This will eliminate the possibility of inappropriate sensing and mistimed pacing. Once the procedure is completed, the System will need to be turned back 'ON' and proper device function verified. Instruct medical personnel on this potential for interference. Example of devices and procedures that may interfere with function of the WiSE CRT System include:

- Radiofrequency-based devices used for programming and communicating with other implantable devices such as pacemakers and defibrillators.
- Radiofrequency-based devices used for tissue ablation and/or cauterization.
- Lithotripsy therapy which delivers high intensity ultrasound to dissolve calcific deposits.
- Diathermy, which heats tissue by delivery of high frequency electromagnetic radiation, electric current, or ultrasonic waves.
- Therapeutic ionizing radiation
- Mechanical ventilators.
- Use caution with neurologic stimulation devices that cannot be turned off as they may interfere with the WiSE CRT System. Check with manufacturers for compatibility.

6 POST PROCEDURE CONSIDERATION

Based on physician assessment of individual patient characteristics, including bleeding risk, thromboembolic risk, and patient preference, post-implant antiplatelet therapy may be initiated. For patients prescribed Dual Antiplatelet Therapy (DAPT) alone, a minimum duration of three months is recommended, in accordance with current clinical guidelines and institutional protocols.

7 POTENTIAL ADVERSE EVENTS OR COMPLICATIONS

Potential adverse events relating to interventional procedures or this System may include but not be limited to:

- Access site and pocket complications (e.g., pain, bleeding, infection)
- Air embolism
- Allergic reactions to materials used in the devices, sedatives, other materials and drugs used in the course of implant procedures

- Aortic/ Mitral valve damage
- Arrhythmias
- Breach of Battery or Battery connections
- Cardiac tamponade/ pericardial effusion
- Chronic nerve damage
- Dissection of aorta or branch vessels including femoral artery (includes arterial perforation)
- Early Battery depletion/ malfunction
- Endocarditis
- Electronic or mechanical component failure
- Electrochemical burns
- Embolization of the non-anchored Electrode or other delivery system material
- Excessive bleeding
- Excessive fibrotic growth
- Fluid accumulation in implant pockets
- Foreign body reaction
- General surgery and anesthesia-related risks and complications such as hypotension, hypertension, respiratory failure, syncope, cardiac failure, renal failure, anemia, and death.
- Hypersensitivity to the device materials
- Inappropriate synchronization/ pacing (over-sensing, under-sensing)
- Hematoma at surgical incision, device pocket, or arterial insertion sites
- High rate or competitive ventricular pacing
- Infection and/or sepsis
- Interference from other ultrasound sources that affect System performance or cause the Electrode to pace
- No pacing therapy or no pacing capture leading to worsening heart failure
- Mechanical injury causing tissue damage
- Migration of device that may or may not require surgical revision
- Myocardial infarction
- Myocardial tissue injury or perforation
- Overexposure to X-ray fluoroscopic radiation - Radiation skin burns
- Phrenic nerve stimulation leading to diaphragmatic pacing
- Pneumothorax

- Psychological disturbances (dependency, depression, fear of Battery depletion, fear of malfunction)
- Reset of programmed device parameters
- Skin erosion overlying implanted device
- Septal defect
- Stroke or transient cerebrovascular episodes
- Thermal tissue injury from Transmitter elements
- Thrombus formation and thromboembolism

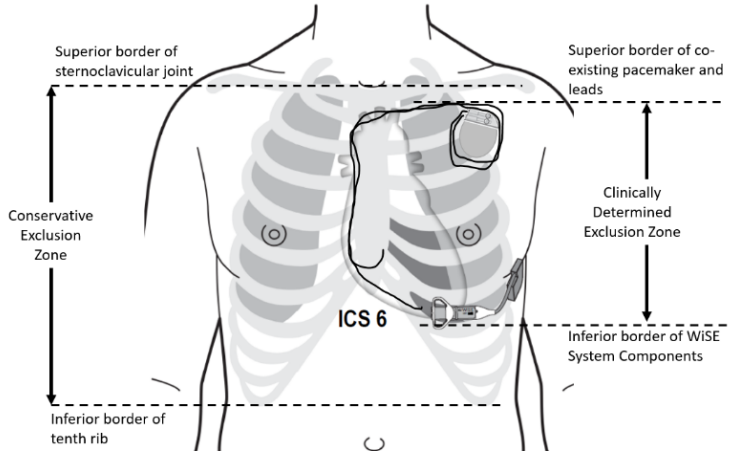
8 MRI SAFETY INFORMATION

8.1 MR CONDITIONAL

<table>
<tr><td colspan="2">

MR Conditional</td></tr>
<tr><td colspan="2">Non-clinical testing has demonstrated the implanted devices (Electrode, Battery, and Transmitter) of the “WiSE Cardiac Resynchronization Therapy (CRT) System” are MR Conditional. A patient with these implanted devices can be safely scanned in an MR system meeting the following conditions. Failure to follow these conditions may result in injury.</td></tr>
<tr><td>Additional Resources for magnetic resonance imaging (MRI) Safety Information</td><td>www.WiSEIFU.com
Phone: +1 (408) 720-1906
Email: techsupport@ebrsystemsinc.com</td></tr>
<tr><td>Parameter</td><td>Conditions of Use</td></tr>
<tr><td>Device Name</td><td>Implanted devices of WiSE CRT System for MR Conditional consisting of:
▪ Electrode M1000
▪ Battery M3100
▪ Transmitter M4100</td></tr>
<tr><td>Static Magnetic Field Strength (B_0)</td><td>1.5 Tesla (T), 3 T</td></tr>
<tr><td>Type of Nuclei</td><td>Hydrogen</td></tr>
<tr><td>Static Magnetic Field (B_0) Orientation</td><td>Horizontal, cylindrical bore</td></tr>
</table>

Maximum Spatial Field Gradient	20 T/m (2000 gauss/cm)
Maximum Switched Gradient Slew Rate per Axis	200 mT/m/ms
Maximum Switched Gradient Amplitude per Axis	45 mT/m
RF Polarization (RF Excitation)	Multichannel-2 (MC-2) or circular polarization (CP)
RF Transmit Coil Type	• No local RF transmit coils inside the exclusion zone. • No restrictions on RF transmit coil type when placed outside of the exclusion zone.
RF Receive Coil	Any receive RF coil may be used.
MR System (RF) Operating Mode or Constraints	• 1.5 T: Normal operating mode • 3 T: Normal operating mode
Maximum Whole-Body Specific Absorption Rate (SAR)	2 W/kg (normal operating mode)
Maximum Head SAR	3.2 W/kg (normal operating mode)

Anatomy Scan Region Restrictions	Any scan landmark is acceptable with the exclusion zone placed outside the MR bore.  The exclusion zones are defined as follows: • Conservative Exclusion Zone: It extends from the superior border of the sternoventricular joint to the inferior border of the 10th rib. OR • Clinically Determined Exclusion Zone: It is based on the actual location of the implanted components and determined by palpation of the implanted WiSE CRT

	System and the co-implanted pacemaker system or by X-ray imaging. The conservative exclusion zone must be used if the implanted components cannot be unambiguously identified.
Patient Characteristics	• Scanning patients who have multiple MR Conditional items present is acceptable as long as the MR labeling conditions for all items can be satisfied. • The patient has no broken leads from the co-implanted pacemaker or leads with intermittent electrical contact, as confirmed by lead impedance history.
Patient Position in Scanner	It is mandatory that the MR exclusion zone defined above is observed.
Item Configuration	The following configurations are allowed to enter the MR environment: • A WiSE CRT System with all components implanted • A WiSE CRT System with a subset of components implanted • The implanted WiSE CRT System is implanted with a co-implanted pacemaker system. MR scans are only allowed if the co-implanted pacemaker is also MR Conditional. In addition to the conditions listed above for the implanted WiSE CRT System, all MR scan conditions for the co-implanted MR Conditional pacemaker must be met as well.
Scan Duration	2 W/kg whole-body average SAR for 60 minutes of continuous RF (a sequence or back-to-back series/scan without breaks) in compliance with the exclusion zone
Required Programming Setting	The following programming has to be completed before the patient enters the MR environment: • Implanted WiSE CRT System to OFF-mode **and** • Co-implanted pacemaker MRI Conditional implant mode enabled
Instructions to be Followed Before, During, or After the MRI Exam	The following has to be completed after the patient leaves the MR environment: • The WiSE CRT System and the co-implanted pacemaker programmed to their pre-scan settings. • A system check of the WiSE CRT System and the co-implanted pacemaker to ensure the safe operation.

8.2 EXCLUSION ZONE

Safe scanning of patients with the implanted devices of the WiSE CRT System and the co-implanted pacemaker system requires that both implanted systems are placed outside the MR bore. This is achieved by defining two types of exclusion zones:

- Conservative Exclusion Zone and
- Clinically Determined Exclusion Zone.

The **conservative exclusion zone** covers all possible implant locations of the implanted WiSE CRT System and the co-implanted pacemaker system. It is wider and therefore conservative and can be defined by a physician using easily identifiable anatomical landmarks. The **clinically determined exclusion zone** is narrower, allowing scanning closer to the actual implant locations and thereby expanding the accessible MR scan landmarks for the patient's benefit.

For all scans, the chosen MR exclusion zone (i.e., conservative or clinically determined) for the implanted devices of the WiSE CRT System **must be placed entirely outside** the MR bore.

8.3 WARNINGS FOR MRI SAFETY

Scans must be conducted with the chosen exclusion zone placed entirely outside the MR bore. Placing the exclusion zone inside the MR bore can result in serious and permanent injury including coma, paralysis, or death.

In addition to the scan conditions for the implanted devices of the WiSE CRT System, all scan conditions for the co-implanted MR Conditional pacemaker system must be met.

No local RF transmit coil must be placed over the exclusion zone. The implanted devices of the WiSE CRT System must not be exposed to any RF or gradient fields. Placing a local RF transmit coil over the exclusion zone can result in serious and permanent injury including coma, paralysis, or death.

Discontinue the MRI immediately if the patient becomes unresponsive to questions or experiences any heating, pain, shocking sensations, uncomfortable stimulation, or unusual sensations.

MR scans must be conducted using the stated MRI equipment and scan conditions. Failure to follow all warnings and guidelines related to MRI can result in serious and permanent injury including coma, paralysis, or death.

To ensure the safe operation of the MR Conditional co-implanted pacemaker and the implanted WiSE CRT System perform system check of the implanted devices of the WiSE CRT System and the co-implanted pacemaker after the MR scan.

The Programmer (M5100) has not been evaluated for safety in the MR environment. It has not been tested for heating or unwanted movement in the MR environment. The safety of the Programmer (M5100) in the MR environment is unknown and should not be used in the MR environment. The presence of the Programmer in a MR environment may result in injury or device malfunction.

9 REQUIRED WISE CRT SYSTEM COMPONENTS

Refer to the individual Instructions for Use provided with each WiSE CRT System component for information on their implantation and use (**Table 1**).

Table 1. WiSE CRT System Components Instructions for Use

WiSE CRT System Component	Model Number	Instruction for Use
Electrode Catheter & Delivery Sheath	M1000 M2000	LBL-05301
Battery and Transmitter	M3100 M4100	LBL-05302
Programmer	M5100	LBL-05303

10 MEDICAL ALERT BRACELET/ PENDANT

A medical alert bracelet or pendant is an option that is available for patients implanted with the WiSE CRT System to supplement the WiSE CRT System Implant Card and Information Booklet provided to patients. The bracelet/ pendant has an engraved statement that directs the healthcare providers to a website (echo-tips.com) This website provides precautions for potential medical interactions and information to consider when using ultrasound imaging on patients with an implanted WiSE CRT System.

To request the optional medical alert bracelet or pendant, contact EBR at techsupport@ebrsystemsinc.com or +1 (408) 720-1906.

11 SUMMARY OF CLINICAL STUDY

EBR performed a prospective, multi-center, multi-national, pivotal clinical study to establish a reasonable assurance of safety and effectiveness of the WiSE CRT System for the delivery of BiV pacing for CRT in patients with advanced HF. The SOLVE-CRT clinical study was conducted under an Investigational Device Exemption (IDE). The treated population included patients who had previously failed conventional CRT, who had not responded to conventional CRT, or who were high risk upgrades (HRU) for conventional CRT. The study was a global trial including investigational sites from the United States (US), European Union (EU), United Kingdom (UK), and Australia (AU).

11.1 STUDY PURPOSE

The purpose of the SOLVE-CRT clinical study was to demonstrate the safety and effectiveness of the WiSE CRT System.

11.2 STUDY DESIGN

The SOLVE-CRT study was a prospective pivotal clinical trial comprised of three separate, multi-center, multi-country parts:

- Part I Roll-In (n=31), single-arm, open label
- Part II Randomized (n=108), two-arm, randomized 1:1, double-blind
- Part III Single-Arm (n=75), single arm, open label

Part I Roll-In of the study was introduced to provide physicians with implant experiences prior to enrolling patients in the randomized arm of the trial. After enrolling 31 participants, the Roll-In Part was concluded as the results demonstrated low complication rates. Enrollment into Part II Randomized was ongoing was affected by the COVID-19 pandemic and was paused in March 2020 after 108 patients were enrolled at 36 centers. As a result of COVID-19, the trial was modified to include Part III Single-Arm, non-randomized part, to complete the study.

All Part II Randomized participants underwent implantation of the WiSE CRT System which was initially programmed to 'Off. The participants in Part II Randomized were then assigned employing a 1:1 randomization to either the Treatment-Arm ('WiSE On') or Control-Arm ('WiSE Off'). After 6 months of follow up, the Control-Arm patients could cross over to the Treatment-Arm. Part I Roll-In participants and Part III Single-Arm participants were programmed to 'WiSE On' following the procedure. All patients in Parts I, II, and III adhered to the same 6 month follow up schedule.

Participants were followed up for six months after implantation of the WiSE CRT System for primary endpoint analyses. Primary endpoint analyses were from the pivotal parts of the study—Part II (Randomized) and Part III (Single-Arm).

11.3 INCLUSION AND EXCLUSION CRITERIA

11.3.1 Inclusion Criteria

Enrollment in the SOLVE-CRT Clinical study was limited to patients who met the following inclusion criteria:

	Inclusion Criteria
1	Patient with a class I or IIa (1) or (2) indication for implantation of a CRT device according to current available guidelines (with additional QRS criteria on Class IIa (1)):
	a. Class I: New York Heart Association (NYHA) II, III, IV, ejection fraction (EF) ≤ 35%[1], left bundle branch block (LBBB), QRS ≥ 150 ms[2]
	b. Class IIa (1): NYHA II, III, IV, EF ≤ 35%, LBBB, QRS ≥ 130 to < 150 ms
	c. Class IIa (2): NYHA II, III, IV, EF ≤ 35%, non-LBBB, QRS ≥ 150 ms
2	Patient is a:
	a. 'Non-responder' (NR) (Part I and Part II - Roll-In and Randomized Only): [This criterion is not applicable to Part III Single-Arm]: Patients who have a CRT system that is functional and despite an adequate trial of Guideline Directed Medical Therapy (GDMT)[1] and attempts at optimal device programming[2] the patient has not responded to therapy for a minimum of 6 months. Non-response is defined as:

[1] Source documentation should be provided to support non-response despite trial of GDMT which should include an angiotensin converting enzyme inhibitor (ACEI), or angiotensin receptor blocker (ARB), or angiotensin receptor–neprilysin inhibitor (ARNI) in conjunction with evidence-based beta-blocker therapy and aldosterone antagonists, or other cardiac medications (e.g., diuretics, nitrates, digitalis, etc.) that were attempted (Yancy 2013; Yancy 2017). ACEI, ARB or ARNI and beta blocker, aldosterone blockade should be at a stable dose for 30 days. During the 30-day period immediately preceding enrollment, daily dose may increase by no more than 100% from the dose at the beginning of the 30-day stability period and may decrease by no more than 50% from the dose at the beginning of the 30-day stability period.

[2] Attempts at programming for high percentage of BiV pacing and optimization of timing intervals should have been attempted and must be documented.

	Inclusion Criteria
	i. Ejection fraction has remained unchanged or worsened (defined as < 5% increase since implant), **and**
	ii. The patient's clinical status based on the totality of available clinical evidence (such as NYHA class, exercise tolerance, quality of life (QOL), or global assessment) has remained unchanged or worsened, as determined by the local Site Enrollment Committee.
	b. 'Previously Untreatable' (PU) (Part I, Part II, and Part III- Roll-In, Randomized, and Single-Arm): Patients who have a full or partial CRT system, who meet general inclusion criteria, and are deemed as 'previously untreatable' for one of the following reasons:
	i. Patients in whom CS lead implantation for CRT has failed.
	Coronary sinus lead implant was attempted but abandoned due any of the following: difficult CS access or anatomy, inadequate lead location, inadequate pacing thresholds, persistent phrenic nerve pacing, or other procedural challenges.
	ii. CS lead implanted but has been programmed OFF[1].
	Left ventricular lead that was implanted but not operational includes patients in whom the LV lead is inoperative or programmed 'Off' due to improper function such as high threshold, non-capture, phrenic nerve pacing, lead failure, lead dislodgement, or suboptimal LV lead location
	c. 'High Risk Upgrade' (HRU) (Part I, Part II, and Part III): Patients in whom standard CRT upgrade is not advisable due to known relative contraindication to CS lead implant, for example:
	i. Risk of venous occlusion or lesion precluding implant (e.g., multiple existing leads in situ)
	ii. Risk of pocket infection at co-implanted device site (e.g., co-implant placement or battery change within last 12 months)
	iii. Considered high risk for CS implant due to co-morbidities (e.g., history of ICM or VT with risk of epicardial pacing induced VT)
3	Patients on a stable GDMT.
4	Patient must be 18 years old or over.
5	Patient has signed and dated informed consent.
6	Patient has suitable anatomy for implant of the WiSE CRT System (e.g., adequate acoustic window, LV wall thickness in target implant area ≥ 5 mm, absence of LV wall structural abnormalities which may preclude implant).

11.3.2 Exclusion Criteria

Patients were excluded from the SOLVE-CRT study if they met any of the exclusion criteria in the table below.

	Exclusion Criteria
1	Pure RBBB
2	LVEDD ≥ 8cm
3	Non-ambulatory or unstable NYHA class IV
4	Contraindication to heparin, chronic anticoagulants, or antiplatelet agents
5	Triple anticoagulant patients who cannot tolerate periprocedural stopping of anticoagulation therapy
6	Attempted device implant (pacemaker, implantable cardioverter defibrillator (ICD), CRT, LV lead) or successful co-implant within prior 30 days.
7	Patients with planned or expected lithotripsy treatment post implant
8	Life expectancy of < 12 months
9	Chronic hemodialysis
10	Stage 4 or 5 renal dysfunction defined as eGFR < 30
11	Grade 4 mitral valve regurgitation
12	Noncardiac implanted electrical stimulation therapy devices
13	Patients with a prosthetic aortic valve and a non-viable transseptal approach for the electrode implant
14	Patients with a prosthetic mitral valve and a non-viable retrograde aortic approach for the electrode implant
15	Unstable angina, acute myocardial infarction (MI), coronary artery bypass surgery (CABG), or percutaneous transluminal coronary angioplasty (PTCA) within the past 1 month
16	Correctable valvular disease that is the primary cause of HF
17	Recent cerebrovascular accident (CVA) or transient ischemic attack (TIA) (within the previous 3 months)
18	Patients with a history of paroxysmal or persistent atrial fibrillation (AF)/ flutter are excluded if they have had a documented AF episode > 30 min or a cardioversion in the past 30 days from screening.
19	Patients with permanent AF are excluded if they have intact atrioventricular (AV) node conduction (RV pacing < 95%)
20	Already included in another clinical study that could confound the results of this study
21	Pregnancy
22	Known drug or alcohol addiction or abuse
23	Moderate or severe aortic stenosis

	Exclusion Criteria
24	Participant unable to attend follow-up at the investigative center or unable, for physical or mental reasons, or to comply with the trial's procedures
25	For Part II Randomized patients, those who will not tolerate being randomized to the Control Group for 6 months

11.4 STUDY ENDPOINTS

Per the Clinical Investigation Plan, the study was considered a success when both the primary safety endpoint and the primary effectiveness endpoint were achieved.

11.4.1 Primary Safety Endpoint (Part II and Part III)

The primary safety endpoint for the SOLVE-CRT study was freedom from Type I complications at 6 months post implant compared to a performance goal of 70% for all participants in Part II and Part III of the study (n=183). Type I complications included AEs caused by any component of the investigational system or specific procedure-related events.

11.4.2 Primary Effectiveness Endpoint (PU-HRU of Part II and Part III):

The primary effectiveness endpoint for the SOLVE-CRT study was the mean relative (%) change in left ventricular end systolic volume (LVESV) as assessed by echocardiography at 6 months post implant compared to a performance goal of -9.3%. All echocardiograms were evaluated by a blinded echocardiographic core lab.

11.5 SUBJECT ACCOUNTABILITY AND DEMOGRAPHICS

11.5.1 Subject Accountability

The first subject was enrolled and the first implant with the WiSE CRT System occurred on January 17, 2018. The last subject completed the 6-month follow-up visit on February 9, 2023. The study database was frozen for analysis on February 15, 2023, and included 214 subjects enrolled. There were 68 investigational sites. **Figure 2** displays the disposition of all 214 enrolled subjects.

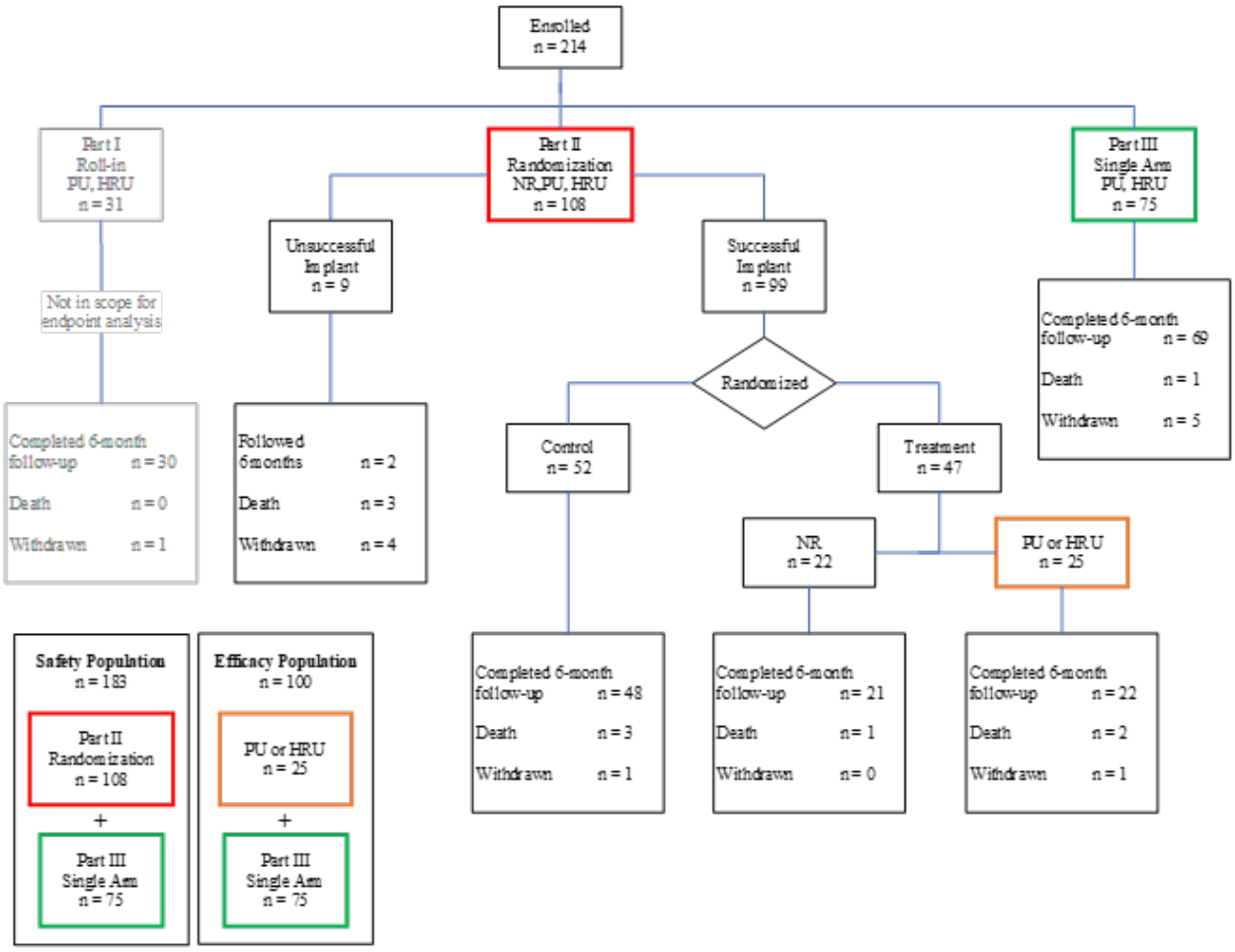


Figure 2. Patient Disposition and Analysis Groups

11.5.2 Subject Demographics and Baseline Parameters

Baseline CRT Indication

All participants in the SOLVE-CRT study met standard indications for CRT therapy. Indication classes were defined as:

- Class I: NYHA II, III, IV, EF ≤ 35%, LBBB, QRS ≥ 150 ms
- Class IIa(1): NYHA II, III, IV, EF ≤ 35%, LBBB, QRS ≥ 130 to < 150 ms
- Class IIa(2): NYHA II, III, IV, EF ≤ 35%, non-LBBB, QRS ≥ 150 ms

As shown in **Table 2** indications for CRT in the safety population were Class I (68.9%), Class IIa(1) (13.7%), and Class IIa(2) (17.5%). Twenty-four percent (24%) of participants in the safety population were Non-Responders (NR)s, 60.1% were PUs, and 15.8% were HRUs.

For the effectiveness population, indications for CRT were Class I (64.0%), Class IIa(1) (14.0%), and Class IIa(2) (22.0%). Seventy-five percent (75.0%) of participants in the effectiveness population were PUs and 25.0% were HRUs.

The NYHA assessment in the SOLVE-CRT trial was performed by a heart specialist who was either the Principal Investigator or the Sub-Investigator of the Study.

Table 2. Indications for CRT

Indication	Safety Population (N=183) n/N (%)	Effectiveness Population (N=100) n/N (%)
Class I	126/183 (68.9%)	64/100 (64.0%)
Class IIa(1)	25/183 (13.7%)	14/100 (14.0%)
Class IIa(2)	32/183 (17.5%)	22/100 (22.0%)
Non-Responder	44/183 (24.0%)	0/100 (0.0%)
Previously Untreatable	110/183 (60.1%)	75/100 (75.0%)
Failed CS lead implant	68/183 (37.2%)	48/100 (48.0%)
CS lead turned off	42/183 (23.0%)	27/100 (27.0%)
High Risk Upgrade	29/183 (15.8%)	25/100 (25.0%)

Baseline Demographics & Medical History

Table 3 summarizes the baseline demographics and medical history of participants in the SOLVE-CRT study. Overall, there were no significant differences in demographics or medical history between the safety and effectiveness populations.

The mean age in the safety population was 68.1 ± 10.28 years and 68.2 ± 10.47 years in the effectiveness population, with 66.7% and 67.0% over 65 years of age, respectively. Most patients were male (77.0% in the safety population and 76.0% in the effectiveness population) and white (85.8% in the safety population and 82.0% in the effectiveness population).

Most had NYHA class III symptoms (65.4% safety, 65.0% effectiveness). In addition, about half of the participants in each population had a history of atrial tachyarrhythmia and non-ischemic cardiomyopathy, and about one-third in each population had a history of VT. Study participants in both populations had histories of coronary artery disease, cerebrovascular disease, renal dysfunction, pulmonary disorder, or other medical conditions. These characteristics of the study population are consistent with advanced HF with multiple comorbidities and a poor prognosis.

Table 3. Baseline Demographics and Medical History

Variable	Safety Population (N=183)	Effectiveness Population (N=100)
	Mean ± SD (N) (Min-Max) or n/N (%)	Mean ± SD (N) (Min-Max) or n/N (%)
Age (Years)	68.1 ± 10.28 (183) (32 – 88)	68.2 ± 10.47 (100) (36 – 88)
Age ≥65 Years	122/183 (66.7%)	67/100 (67.0%)
Male	141/183 (77.0%)	76/100 (76.0%)
Body Mass Index (BMI) (kg/m^2)	30.8 ± 5.75 (183) (19 – 51)	30.6 ± 5.45 (100) (19 – 50)
Systolic Blood Pressure (SBP) (mmHg)	119.2 ± 18.69 (183) (79 – 200)	117.5 ± 17.68 (100) (79 – 180)
Diastolic Blood Pressure (DBP) (mmHg)	70.3 ± 10.58 (183) (44 – 100)	69.5 ± 10.45 (100) (44 – 94)
Heart Rate (HR) (bpm)	70.0 ± 10.59 (183) (50 – 100)	70.4 ± 10.25 (100) (50 – 100)
Ethnicity		
Hispanic	7/183 (3.8%)	6/100 (6.0%)
Not Hispanic	170/183 (92.9%)	94/100 (94.0%)
Choose not to answer	6/183 (3.3%)	0/100 (0.0%)
Race		
American Indian or Alaska Native	1/183 (0.5%)	1/100 (1.0%)
Asian	2/183 (1.1%)	2/100 (2.0%)
Black	12/183 (6.6%)	10/100 (10.0%)
Native Hawaiian or Other Pacific Islander	1/183 (0.5%)	1/100 (1.0%)
White	157/183 (85.8%)	82/100 (82.0%)
Chose not to answer	10/183 (5.5%)	4/100 (4.0%)
NYHA		
Class I	0/182 (0.0%)	0/100 (0.0%)
Class II	63/182 (34.6%)	35/100 (35.0%)
Class III	119/182 (65.4%)	65/100 (65.0%)
Class IV	0/182 (0.0%)	0/100 (0.0%)
Rhythm Disorders		

Variable	Safety Population (N=183)	Effectiveness Population (N=100)
	Mean ± SD (N) (Min-Max) or n/N (%)	**Mean ± SD (N) (Min-Max) or n/N (%)**
History of atrial tachyarrhythmia	*92/183 (50.3%)*	*52/100 (52.0%)*
Supraventricular tachycardia	74/183 (40.4%)	46/100 (46.0%)
Atrial fibrillation	19/183 (10.4%)	5/100 (5.0%)
Persistent	3/183 (1.6%)	1/100 (1.0%)
Permanent	0/183 (0.0%)	0/100 (0.0%)
Paroxysmal	16/183 (8.7%)	4/100 (4.0%)
Prior cardioversion	6/183 (3.3%)	1/100 (1.0%)
Atrial flutter	8/183 (4.4%)	2/100 (2.0%)
History of ventricular tachyarrhythmia	*67/183 (36.6%)*	*34/100 (34.0%)*
Ventricular tachycardia	61/183 (33.3%)	31/100 (31.0%)
Ventricular fibrillation	18/183 (9.8%)	7/100 (7.0%)
Type of Cardiomyopathy		
Non-ischemic cardiomyopathy	94/183 (51.4%)	50/100 (50.0%)
Ischemic cardiomyopathy	87/183 (47.5%)	50/100 (50.0%)
Non-ischemic + ischemic cardiomyopathy	2/183 (1.1%)	0/100 (0.0%)
Associated Conditions/ Prior Surgeries		
Prior cardiac device implant	*183/183 (100.0%)*	*100/100 (100.0%)*
Pacemaker	28/183 (15.3%)	21/100 (21.0%)
ICD	69/183 (37.7%)	48/100 (48.0%)
CRT-P	11/183 (6.0%)	4/100 (4.0%)
CRT-D	124/183 (67.8%)	59/100 (59.0%)
LV lead	109/183 (59.6%)	51/100 (51.0%)
Other	18/183 (9.8%)	16/100 (16.0%)
Coronary artery disease history	*104/183 (56.8%)*	*60/100 (60.0%)*
Prior MI	74/183 (40.4%)	41/100 (41.0%)
Prior PTCA	55/183 (30.1%)	30/100 (30.0%)
Prior CABG	53/183 (29.0%)	30/100 (30.0%)
Unstable angina	6/183 (3.3%)	2/100 (2.0%)

Variable	Safety Population (N=183)	Effectiveness Population (N=100)
	Mean ± SD (N) (Min-Max) or n/N (%)	**Mean ± SD (N) (Min-Max) or n/N (%)**
Cardiac valve surgical history	*19/183 (10.4%)*	*14/100 (14.0%)*
Aortic valve replacement	8/183 (4.4%)	6/100 (6.0%)
Mitral valve repair or replacement	10/183 (5.5%)	7/100 (7.0%)
Other valve replacement	5/183 (2.7%)	5/100 (5.0%)
Cerebrovascular disease history	*28/183 (15.3%)*	*16/100 (16.0%)*
Prior stroke/ CVA	19/183 (10.4%)	11/100 (11.0%)
Prior TIA	10/183 (5.5%)	6/100 (6.0%)
Renal dysfunction history	*51/183 (27.9%)*	*31/100 (31.0%)*
eGFR	64.3 ± 22.20 (174) (25 – 146)	64.3 ± 21.95 (94) (29 – 146)
Pulmonary disorder history	*65/183 (35.5%)*	*38/100 (38.0%)*
Chronic obstructive pulmonary disease	25/183 (13.7%)	11/100 (11.0%)
Current smoker	6/183 (3.3%)	4/100 (4.0%)
Former smoker	56/183 (30.6%)	33/100 (33.0%)
Other conditions	*138/183 (75.4%)*	*74/100 (74.0%)*
Systemic hypertension	99/183 (54.1%)	63/100 (63.0%)
Diabetes	64/183 (35.0%)	31/100 (31.0%)
Insulin dependent	21/183 (11.5%)	8/100 (8.0%)
Non-insulin dependent	43/183 (23.5%)	23/100 (23.0%)
Dyslipidemia	94/183 (51.4%)	50/100 (50.0%)
Hyperthyroidism	5/183 (2.7%)	5/100 (5.0%)
Sleep apnea	43/183 (23.5%)	24/100 (24.0%)
Pulmonary artery hypertension	11/183 (6.0%)	3/100 (3.0%)
Peripheral vascular disease	16/183 (8.7%)	8/100 (8.0%)
Cancer	27/183 (14.8%)	15/100 (15.0%)

Baseline Endpoint Measurements

Baseline measurements for clinical variables used for primary safety and effectiveness endpoints are presented in

Table 4.

In the safety population, mean LVESV was 151.1 ± 67.21 ml, mean left ventricular end diastolic volume (LVEDV) was 210.4 ± 77.8 ml, and mean left ventricular ejection fraction (LVEF) was 29.8 ± 7.9%.

In the effectiveness population, mean LVESV was 146.3 ± 71.5 ml, mean LVEDV was 206.8 ± 83.6 ml, and mean LVEF was 31.1 ± 7.9%. Mean intrinsic QRS, paced QRS, Kansas City Cardiomyopathy Questionnaire (KCCQ) score, NT-proBNP level, and Acoustic Pacing Capture Threshold (APCT) are also presented in

Table 4**.**

The baseline endpoint measures were similar between the two study populations and describe a population of patients with advanced HF.

Table 4. Baseline Endpoint Measurements

Variable	Safety Population (N=183)	Effectiveness Population (N=100)
	Mean ± SD (N) Median (Min-Max) or n/N (%)	Mean ± SD (N) Median (Min-Max) or n/N (%)
Echocardiographic Parameters		
LVESV (ml)	151.1 ± 67.21 (181) 138.0 (31 – 409)	146.3 ± 71.51 (100) 125.5 (31 – 409)
LVEDV (ml)	210.4 ± 77.76 (181) 195.0 (49 – 476)	206.8 ± 83.58 (100) 185.5 (49 – 476)
LVEF (%)	29.8 ± 7.90 (181) 30.1 (9 – 56)	31.1 ± 7.89 (100) 31.0 (14 – 56)
Other		
Intrinsic QRS (ms)	165.7 ± 21.69 (92) 162.0 (122 – 231)	166.1 ± 21.10 (49) 162.0 (134 – 231)
Paced QRS (ms)	182.8 ± 26.59 (138) 179.3 (108 – 257)	184.9 ± 24.72 (82) 182.0 (131 – 246)
KCCQ overall summary score	54.7 ± 22.90 (182) 56.0 (3 – 100)	57.2 ± 21.38 (100) 59.8 (13 – 94)
NT-proBNP (pg/ml)	1626.2 ± 2172.41 (153) 882.0 (49 – 14974)	1761.6 ± 2463.09 (86) 1039.5 (49 – 14974)
Acoustic pacing capture threshold (APCT) (mJ)	0.5 ± 0.86 (110) 0.2 (0 – 6)	0.5 ± 0.57 (87) 0.3 (0 – 3)

Baseline Heart Medications

Table 5 provides details of background medical therapy. Overall, these results reflect contemporary medication usage trends and show that the study population was medically optimized for HF treatment prior to entry into the trial.

Table 5. Baseline Heart Medications for Participants

Medication Type	Safety Population (N=183) n/N (%)	Effectiveness Population (N=100) n/N (%)
ACE or ARB or ARNI	168/183 (91.8%)	93/100 (93.0%)
Angiotensin-Converting Enzyme (ACE) Inhibitor	59/183 (32.2%)	30/100 (30.0%)
Angiotensin Receptor Blocker (ARB)	74/183 (40.4%)	38/100 (38.0%)
Angiotensin Receptor-Neprilysin Inhibitor (ARNI)	68/183 (37.2%)	44/100 (44.0%)
Beta-Blocker	174/183 (95.1%)	94/100 (94.0%)
Aldosterone Antagonist	115/183 (62.8%)	58/100 (58.0%)
Sodium-Glucose Cotransporter-2 (SGLT2) Inhibitor	6/183 (3.3%)	6/100 (6.0%)
Diuretic	145/183 (79.2%)	81/100 (81.0%)
Digitalis	11/183 (6.0%)	6/100 (6.0%)
I_f Channel Inhibitor	4/183 (2.2%)	3/100 (3.0%)
Nitrate	37/183 (20.2%)	20/100 (20.0%)

11.6 RESULTS

The primary safety and effectiveness endpoints were met. Since both the primary effectiveness and safety endpoints met the pre-specified stopping rules for interim analysis, the trial was concluded.

11.6.1 Primary Safety Results

The primary safety analysis was based on all 108 participants from Part II Randomized and 75 participants from Part III Single-Arm of the study for a total of 183 patients in the safety population available for the 6-month evaluation. The key safety outcomes for this study are presented in **Table 6** and **Table 7.**

Adverse event details are reported in **Table 8** and **Table 9.**

In the safety population, there was an 80.9% rate (148/183 patients) of freedom from Type I complications with a lower bound of the one-sided 98.8% confidence interval of 73.4%, above the 70% performance goal ($p < 0.001$). Thus, the primary safety endpoint was achieved.

Further, a Kaplan-Meier sensitivity analysis was conducted, showing a freedom from Type I complications of 80.6%, with a lower confidence bound of 72.8%, above the performance goal of 70% which confirmed the success of the primary safety endpoint.

Table 6. Freedom from Type I Complication Rate through 6 Months (Safety Population)

Freedom from Type I Complication Rate (N=183)	Analysis Time Point	Lower Confidence Bound (LCB)	Performance Goal	Study Endpoint Conclusion
80.9%	Interim	73.4%	70%	**MET** ***p < 0.001***

Table 7. Kaplan-Meier Analysis for Freedom from Type I Complication Rate Estimate at 6 Months

Freedom from Type I Complications Kaplan-Meier Rate Estimate (N=183)	LCB	Performance Goal
80.6%	72.8%	70%

11.6.1.1 Adverse Events Summary

Adverse events reported from baseline to 6 months post implant were adjudicated by the Clinical Events Committee (CEC). The key safety outcomes for this study are presented in **Table 8** and **Table 9**. Both observations and complications were reported.

An observation was defined as an AE that does not result in invasive intervention or can be corrected by simple adjustments.

A complication was defined as an AE that results in injury, or significant or permanent disability and meets any one or more of the following:

1. An event that cannot be treated or resolved by simple adjustments/ treatments and requires invasive intervention, intravenous medication, blood product administration, hospitalization or re-hospitalization after discharge or prolonged hospitalization (> 48 hours) prior to discharge, or any combination thereof
2. A procedure- or device-related pericardial effusion or pseudoaneurysm resulting in a procedure
3. An event that results in significant or permanent loss of device function
4. An event that results in death

Complications were further defined by Type I, II, III, or IV.

- Type I complications were those that were caused by a component of the study device system (the WiSE CRT System Transmitter, Battery, Electrode, Catheter, Sheath, and/or Programmer), or specific procedure-related events including vascular events, stroke, pericardial effusion, and pocket events. Note that failure to implant or a failed implant attempt did not count as a Type I complication unless it was associated with an event that was classified as such.
- Type II complications were other procedure-related events not specifically caused by a component of the study device system, but that would not have occurred in the absence of the study implantation procedure.

- Type III complications were events that were caused by a change in the participant's condition unrelated to the implanted study device system or the implantation procedure.
- Type IV complications were pre-existing medical conditions or conditions that occurred while the participant was not enrolled in the Study.

Table 8 shows CEC-adjudicated AEs that occurred through 6 months post implant in the safety population of the SOLVE-CRT study. There were no unanticipated adverse device effects (UADEs).

Overall, 177 complications occurred in 86 of 183 participants in the safety population (47.0%). Of the 86 participants who experienced a complication, 19.1% (35/183) had a Type I, 7.7% (14/183) had a Type II, 12.6% (23/183) had a Type III, and 25.7% (47/183) had a Type IV complication.

Of the 35 participants who experienced a Type I complication, 6.6% had a study device system event, 2.7% had a vascular event, 1.6% had a stroke or other thromboembolic event, 3.8% had a cardiac perforation, and 6.6% had a pocket event. Four (4) cardiac perforations required surgical intervention and three (3) were treated with pericardiocentesis of which two (2) appeared to be related to the transseptal puncture. The cardiac perforations requiring surgical intervention occurred early in the study and prompted some additional safety measures for the implant, including the use of real time echocardiography during the Electrode implant. No LV perforations requiring surgical intervention were observed after the implementation of this mitigation.

In addition, the CEC adjudicated 169 observations in 82 of the 183 participants (44.8%) in the safety population.

Table 8. Adjudicated AEs with ≤ 6 Months Post Procedure

Adjudicated Adverse Events Categorization	Safety Population (N=183)
	N Patients (% Patients) [N Events]
No Complications of Any Type, N Patients (% Patients)	97 (53.0%)
Complications	***86 (47.0%) [177]***
Type I or II	43 (23.5%) [67]
Type I	***35 (19.1%) [43]***
Study device system event	12 (6.6%) [12]
Vascular event (not caused by closure device)	5 (2.7%) [5]
Stroke and other thromboembolic events (e.g., TIA)	3 (1.6%) [3]
Cardiac perforation	7 (3.8%) [7]
Surgically repaired	4 (2.2%) [4]
Pericardiocentesis	3 (1.6%) [3]
Pocket events	12 (6.6%) [15]
Other	1 (0.5%) [1]

Adjudicated Adverse Events Categorization	Safety Population (N=183)
	N Patients (% Patients) [N Events]
Type II	14 (7.7%) [24]
Type III	23 (12.6%) [32]
Type IV	47 (25.7%) [78]
Observations	82 (44.8%) [169]
UADEs	0 (0%) [0]

Type I Complications by Category

Table 9 shows the overall device and procedure-related (Type I) complication rate through 6 months was 19.1% (35 patients). Of the 183 participants in the safety population, 12 (6.6%; 3.4%, 11.2%) experienced a study device system event, including two (2) device migrations, two (2) failures to capture, one (1) device dislocation, one (1) ventricular tachyarrhythmias, one (1) medical device replacement, one (1) device component issue, two (2) device dislodgements, and two (2) device embolizations.

Five (5) participants (2.7%; 0.9%, 6.3%) had vascular events including one (1) retroperitoneal hematoma, one (1) leg ischemia, two (2) groin hematomas, and one (1) iliac artery perforation.

There were also three (3) participants (1.6%; 0.3%, 4.7%) who experienced a stroke or other thromboembolic event.

Further, 12 participants (6.6%; 3.4%, 11.2%) experienced a pocket event, including one (1) fatigue, four (4) hematomas, one (1) pneumothorax, one (1) wound dehiscence, one (1) wound infection, one (1) implant site erosion, one (1) implant site hematoma, one (1) incision site infection, one (1) acute anemia, one (1) device issue, and one (1) implant site pocket infection.

Finally, there were seven (7) participants (3.8%; 1.6%, 7.7%) with cardiac perforations, including three (3) with cardiac tamponade, two (2) with pericardial effusion, one (1) cardiac perforation, and one (1) pulseless electrical activity.

Table 9. Type I Complications through 6 Months by Category

Categorization	Safety Population (N=183)
	N Patients, (% Patients) [N Events], LCB, UCB
Study Device System Event	***12 (6.6%) [12], 3.4%, 11.2%***
Device migration	2 (1.1%) [2], 0.1%, 3.9%
Failure to capture	2 (1.1%) [2], 0.1%, 3.9%
Device dislocation	1 (0.5%) [1], 0.0%, 3.0%
Ventricular tachyarrhythmia	1 (0.5%) [1], 0.0%, 3.0%
Medical device replacement	1 (0.5%) [1], 0.0%, 3.0%

Categorization	Safety Population (N=183)
	N Patients, (% Patients) [N Events], LCB, UCB
Device component issue	1 (0.5%) [1], 0.0%, 3.0%
Device dislodgement	2 (1.1%) [2], 0.1%, 3.9%
Device embolization	2 (1.1%) [2], 0.1%, 3.9%
Vascular Event (not caused by closure device)	***5 (2.7%) [5], 0.9%, 6.3%***
Retroperitoneal hematoma	1 (0.5%) [1], 0.0%, 3.0%
Leg ischemia	1 (0.5%) [1], 0.0%, 3.0%
Groin hematoma	2 (1.1%) [2], 0.1%, 3.9%
Iliac artery perforation	1 (0.5%) [1], 0.0%, 3.0%
Stroke and Other Thromboembolic Events (e.g., TIA)	***3 (1.6%) [3], 0.3%, 4.7%***
Cerebrovascular accident	1 (0.5%) [1], 0.0%, 3.0%
Stroke	1 (0.5%) [1], 0.0%, 3.0%
Ischemic stroke	1 (0.5%) [1], 0.0%, 3.0%
Cardiac Perforation	***7 (3.8%) [7], 1.6%, 7.7%***
Cardiac tamponade	3 (1.6%) [3], 0.3%, 4.7%
Pericardial effusion	2 (1.1%) [2], 0.1%, 3.9%
Cardiac perforation	1 (0.5%) [1], 0.0%, 3.0%
Pulseless electrical activity	1 (0.5%) [1], 0.0%, 3.0%
Pocket Event	***12 (6.6%) [15], 3.4%, 11.2%***
Fatigue	1 (0.5%) [1], 0.0%, 3.0%
Hematoma	4 (2.2%) [4], 0.6%, 5.5%
Pneumothorax	1 (0.5%) [1], 0.0%, 3.0%
Wound dehiscence	2 (1.1%) [2], 0.1%, 3.9%
Wound infection	1 (0.5%) [1], 0.0%, 3.0%
Implant site erosion	1 (0.5%) [1], 0.0%, 3.0%
Implant site hematoma	1 (0.5%) [1], 0.0%, 3.0%
Incision site infection	1 (0.5%) [1], 0.0%, 3.0%
Acute anemia	1 (0.5%) [1], 0.0%, 3.0%
Device issue	1 (0.5%) [1], 0.0%, 3.0%
Implant site pocket infection	1 (0.5%) [1], 0.0%, 3.0%

Categorization	Safety Population (N=183)
	N Patients, (% Patients) [N Events], LCB, UCB
Other	***1 (0.5%) [1], 0.0%, 3.0%***
Anemia postoperative	1 (0.5%) [1], 0.0%, 3.0%
Total	**35 (19.1%) [43], 13.7%, 25.6%**

11.6.2 Primary Effectiveness Results

The effectiveness analysis was based on a total of 100 participants at 6 months post implant, 25 PU-HRU Part II participants randomized to the Treatment-Arm and 75 Part III Single-Arm participants at the 6-month time point. Key effectiveness outcomes are presented in **Table 10**.

Table 10 shows the absolute and relative changes in LVESV at 6 months post implant in comparison to baseline using imputed data. With imputation, measurements of LVESV were available at baseline and 6 months for 92 of 100 participants (92.0%) in the effectiveness population. The mean relative change in LVESV among those participants was -16.4 ± 22.50% (95% CI, -21.0% to -11.7%) with an upper confidence bound (UBC) below the -9.3% performance goal ($p = 0.003$), meeting the primary effectiveness endpoint. The absolute change in LVESV was -22.8 ± 36.22 ml (95% CI: -30.3, -15.3) which was also statistically significant ($p < 0.001$).

Table 10. Relative and Absolute Change in LVESV at 6 Months from Baseline (Imputed)

Characteristic	Effectiveness Population (N=100)	95% CI	Study Endpoint Conclusion
Baseline (ml)			
N	100	-----	-----
Mean	146.3	132.1, 160.5	-----
SD	71.51	-----	-----
Median (IQR)	125.5 (95.0, 170.5)	-----	-----
Min, Max	31.0, 409.0	-----	-----
Six Months (ml)			
N	92	-----	-----
Mean	125.4	109.3, 141.5	-----
SD	77.67	-----	-----
Median (IQR)	97.5 (75.0, 158.0)	-----	-----
Min, Max	30.0, 368.4	-----	-----
Absolute Change from Baseline at Six Months (ml)			

Characteristic	Effectiveness Population (N=100)	95% CI	Study Endpoint Conclusion
N	92	-----	-----
Mean	-22.8	-30.3, -15.3	-----
SD	36.22	-----	-----
Median (IQR)	-21.0 (-49.5, 0.0)	-----	-----
Min, Max	-123.0, 67.4	-----	-----
Relative Change from Baseline at Six Months (%)			
N	92	-----	-----
Mean	-16.4	-21.0, -11.7	MET (***p = 0.003***)
SD	22.50	-----	-----
Median (IQR)	-15.4 (-34.2, 0.0)	-----	-----
Min, Max	-64.1, 36.1	-----	-----

The primary effectiveness endpoint was also evaluated in the As Treated and Per Protocol analysis populations, and results were similar to the effectiveness population; namely, the primary effectiveness endpoint was met in both of these analysis populations.

Data Poolability

Data poolability was tested for the primary safety endpoint and the primary effectiveness endpoint by three poolability factors: 1) Study Part (Randomized vs Single-Arm), 2) Geography (US, EU, UK, AU), and 3) Study Site. Both primary endpoints passed ($p > 0.05$) poolability testing across all three factors.

11.6.2.1 Secondary Effectiveness Results

Secondary effectiveness endpoints were not formally tested. Proportion of participants or descriptive statistics are summarized.

Key secondary effectiveness outcomes are presented in **Table 11 to Table 15**. Secondary endpoints included KCCQ responders, percent BiV pacing, LVEF responders and APCT.

KCCQ Score

Among the 87 participants with KCCQ scores, 57 (65.5%) had an absolute increase of ≥ 5 points in their KCCQ score.

Table 11: KCCQ Responders from Pre-Implant to 6 months - by Analysis Population

	Proportion of subjects achieving an increase in KCCQ Overall Summary Score of 5 points or greater from pre-implant to 6 months
Analysis Population	**n/N (%)**
Efficacy Population	57/87 (65.5%)
Per Protocol	57/87 (65.5%)
As Treated	57/87 (65.5%)

Percent Biventricular Pacing

Among the 86 participants with BiV pacing data, the mean percent BiV pacing was 93.1 ± 13.0%. These results indicate the WiSE CRT System was able to deliver effective BiV pacing for CRT > 93% of the time in those participants.

Table 12: Mean % Bi-ventricular Pacing at 6 Months - by Analysis Population

	% Bi-ventricular Pacing at 6 Months
Analysis Population	**Mean ± SD (N)**
Efficacy Population	93.1 ± 12.96 (86)
Per Protocol	93.1 ± 12.96 (86)
As Treated	93.1 ± 12.96 (86)

LVEF Responders

Among the 89 participants with available data, 41 (46.1%) had an absolute increase in LVEF ≥ 5%.

Table 13: LVEF Responders from Pre-Implant to 6 months - by Analysis Population

	Proportion of subjects achieving an increase in LVEF of 5% or greater from pre-implant to 6 months
Analysis Population	**(N=100)**
	n/N (%)
Efficacy Population	41/89 (46.1%)
Per Protocol	41/89 (46.1%)
As Treated	41/89 (46.1%)

APCT

The APCT is a measure of the energy needed to deliver a pacing pulse at the capture threshold. Among the 83 participants with available data, 79 (95.2%) achieved an APCT of < 2.9 mJ indicating that in greater than 95% of participants, the WiSE CRT System could be programmed as intended to deliver BiV pacing for CRT.

Table 14: Proportion of Patients with APCT less than 2.9 mJ at 6 months

	Proportion of subjects with APCT less than 2.9 mJ
Analysis Population	**n/N (%)**
Efficacy Population	79/83 (95.2%)
Per Protocol	79/83 (95.2%)
As Treated	79/83 (95.2%)

APCT Stability

Among 75 participants with available data, 61 (81.3%) had a relative increase in APCT from pre-discharge to 6 months that was less than 3x, characterizing the stability of energy usage to maintain pacing through this period.

Table 15: Proportion of patients whose APCT relative increase from pre-discharge to 6 months is less than 3x by Analysis Population

	Proportion of patients whose APCT relative increase from pre-discharge to 6 months is less than 3x
Analysis Population	**n/N (%)**
Efficacy Population	61/75 (81.3%)
Per Protocol	61/75 (81.3%)
As Treated	61/75 (81.3%)

11.6.3 Subgroup Analyses for Primary Endpoints

Freedom from Type I Complications

A subgroup analysis for freedom from Type I complications through 6 months in the safety population was conducted (**Table 16**). Due to small sample size only descriptive statistics are provided.

Table 16. Subgroup Analysis of Freedom from Type I Complication Rate through 6 Months (Safety Population)

Variable	Subgroup	N	Freedom from Type I Complication Rate (%)
Overall	Safety Population	183	148/183 (80.9%)
Sex	Male	141	119/141 (84.4%)
	Female	42	29/42 (69.0%)
Race	White	157	125/157 (79.6%)
	Black	12	11/12 (91.7%)
	Other	4	4/4 (100.0%)
	Chose not to answer	10	8/10 (80.0%)
Age	≥ 65 years	122	98/122 (80.3%)
	< 65 years	61	50/61 (82.0%)
NYHA Class	Class II	63	51/63 (81.0%)
	Class III/IV	119	96/119 (80.7%)
LVESV at Baseline	≥ 150 mL	79	65/79 (82.3%)
	< 150 mL	102	81/102 (79.4%)

Variable	Subgroup	N	Freedom from Type I Complication Rate (%)
LVEDV at Baseline	≥ 200 mL	87	72/87 (82.8%)
	< 200 mL	94	74/94 (78.7%)
LVEF at Baseline	≥ 30%	97	76/97 (78.4%)
	< 30%	84	70/84 (83.3%)
Peripheral Artery Disease	Yes	16	12/16 (75.0%)
	No	167	136/167 (81.4%)
Chronic Obstructive Pulmonary Disorder	Yes	25	19/25 (76.0%)
	No	158	129/158 (81.6%)
Renal Dysfunction	Yes	51	37/51 (72.5%)
	No	132	111/132 (84.1%)
Atrial Fibrillation	Yes	19	12/19 (63.2%)
	No	164	136/164 (82.9%)
Diabetes	Yes	64	49/64 (76.6%)
	No	119	99/119 (83.2%)
Cancer	Yes	27	21/27 (77.8%)
	No	156	127/156 (81.4%)
Cardiac Valve Surgery	Yes	19	18/19 (94.7%)
	No	164	130/164 (79.3%)
Progression of HF	Device ≥ 3 years	102	85/102 (83.3%)
	Device < 3 years	81	63/81 (77.8%)
Co-Implant	CRT	122	98/122 (80.3%)
	ICD	42	34/42 (81.0%)
	IPG	15	12/15 (80.0%)
Eligibility for SOLVE-CRT	Previously untreatable	110	89/110 (80.9%)
	High risk upgrade	29	23/29 (79.3%)
	Non-responder	44	36/44 (81.8%)
Cardiomyopathy	Ischemic	87	72/87 (82.8%)
	Non-ischemic	94	74/94 (78.7%)

Variable	Subgroup	N	Freedom from Type I Complication Rate (%)
ACE	Yes	59	47/59 (79.7%)
	No	124	101/124 (81.5%)
ARB	Yes	74	63/74 (85.1%)
	No	109	85/109 (78.0%)
ARNI	Yes	68	57/68 (83.8%)
	No	115	91/115 (79.1%)
Beta-Blocker	Yes	174	141/174 (81.0%)
	No	9	7/9 (77.8%)
Mineralocorticoid Receptor Antagonist	Yes	115	97/115 (84.3%)
	No	68	51/68 (75.0%)
SGLT2 Inhibitor	Yes	6	5/6 (83.3%)
	No	177	143/177 (80.8%)
$CHADS_2$ Score	≥ 3	90	68/90 (75.6%)
	< 3	93	80/93 (86.0%)

Relative Change in LVESV

A subgroup analysis for relative change in LVESV was conducted (Table 14). Due to small sample size, only descriptive statistics are provided.

Table 17. Subgroup Analysis of Relative change in LVESV at 6 Months from Baseline

Variable	Subgroup	N	Mean relative change in LVESV at 6 Months from Baseline
Overall	Effectiveness Population	89	-17.7
Sex	Male	68	-17.0
	Female	21	-20.0

Variable	Subgroup	N	Mean relative change in LVESV at 6 Months from Baseline
Race	White	72	-21.0
	Black	9	-6.6
	Other	4	6.7
	Chose not to answer	4	-7.7
Age	≥ 65 years	56	-18.9
	< 65 years	33	-15.6
NYHA	Class II	33	-16.9
	Class III/IV	56	-18.1
LVESV at Baseline	≥ 150 ml	34	-15.3
	< 150 ml	55	-19.2
LVEDV at Baseline	≥ 200 ml	39	-18.9
	< 200 ml	50	-16.7
LVEF at Baseline	≥ 30%	49	-21.6
	< 30%	40	-12.9
Peripheral Artery Disease	Yes	7	-11.2
	No	82	-18.2
Chronic Obstructive Pulmonary Disorder	Yes	10	-2.6
	No	79	-19.6
Renal dysfunction	Yes	27	-14.8
	No	62	-18.9
Atrial fibrillation	Yes	5	-26.0
	No	84	-17.2
Diabetes	Yes	27	-9.6
	No	62	-21.2
Cancer	Yes	15	-26.4
	No	74	-15.9

Variable	Subgroup	N	Mean relative change in LVESV at 6 Months from Baseline
Cardiac Valve Surgery	Yes	13	-24.3
	No	76	-16.5
Progression of Heart Failure	Device ≥ 3 years	44	-13.6
	Device < 3 years	45	-21.7
Co-Implant	CRT	48	-17.0
	ICD	32	-18.7
	IPG	9	-17.6
Eligibility for SOLVE-CRT	Previously Untreatable	66	-16.6
	High Risk Upgrade	23	-20.9
Cardiomyopathy	Ischemic	45	-12.9
	Non-ischemic	44	-22.6
ACE	Yes	26	-10.2
	No	63	-20.8
ARB	Yes	34	-19.3
	No	55	-16.7
ARNI	Yes	40	-20.2
	No	49	-15.6
Beta-Blocker	Yes	84	-17.5
	No	5	-21.3
Mineralocorticoid Receptor Antagonist	Yes	51	-16.8
	No	38	-18.9
SGLT2 Inhibitor	Yes	5	1.1
	No	84	-18.8

11.7 DEATH EVENT SUMMARY

There have been 10 deaths that occurred prior to 6 months among the 183 enrolled subjects in the safety population. All deaths have been adjudicated by the Clinical Events Committee (CEC). The 10 deaths were from any cause (5.5%); four of those deaths were from a cardiac cause (2.2%).

11.8 CLINICAL STUDY CONCLUSION

The clinical study results demonstrated the safety and effectiveness of the WiSE CRT System in a population indicated for a CRT.

The primary safety endpoint was met as the freedom from procedure-or device-related (Type I) complications at 6-month post implant were 80.9% (lower boundary of the one-sided 98.8% CI, 73.4%) exceeded the pre-specified performance goal of 70% ($p<0.001$). The primary effectiveness endpoint was met with a 16.4% (95% Confidence Interval [CI], 11.7% to 21.0%) reduction in mean LV end systolic volume (LVESV), which was statistically significant compared to the -9.3% performance goal ($p = 0.003$).

The SOLVE-CRT study prospectively evaluated the WiSE CRT System, a novel leadless endocardial CRT system, in patients with a failed standard CRT implant due to lead issues or who could not be upgraded to a standard CRT system due to known relative contraindications. This study showed that leadless ultrasound-based endocardial pacing is feasible, safe, and clinically efficacious with an implant success rate (95.5%), an 80.9% freedom from Type I complications, and a mean reduction of 16.4%..

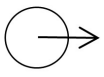
12 SYMBOL GLOSSARY

12.1 SYMBOLS FROM STANDARDS

SYMBOL	STANDARD REFERENCE	STANDARD TITLE	SYMBOL TITLE	EXPLANATORY TEXT
	ISO 15223-1: 2021, Clause 5.1.1	Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied.	Manufacturer	Indicates the medical device manufacture
	ISO 15223-1: 2021, Clause 5.1.3	Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied.	Date of manufacture	Indicates the date when the medical device was manufactured
	ISO 15223-1: 2021, Clause 5.1.4	Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied.	Use-by date	Indicates the date after which the medical device is not to be used

SYMBOL	STANDARD REFERENCE	STANDARD TITLE	SYMBOL TITLE	EXPLANATORY TEXT
	ISO 15223-1: 2021, Clause 5.1.6	Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied.	Catalogue number	Indicates the manufacturer's catalogue number so that the medical device can be identified
	ISO 15223-1: 2021, Clause 5.1.7	Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied.	Serial number	Indicates the manufacture's serial number so that a specific medical device can be identified
	ISO 15223-1: 2021Clause 5.2.11	Medical devices - Symbols to be used with information to be supplied by the manufacturer	Single Sterile Barrier Sterilized using ethylene oxide treatment	Indicates a medical device that has been sterilized using ethylene oxide and has a single sterile barrier
	ISO 15223-1: 2021, Clause 5.2.12	Medical devices - Symbols to be used with information to be supplied by the manufacturer	Double Sterile Barrier Sterilized using ethylene oxide treatment	Indicates a medical device that has been sterilized using ethylene oxide and has a double sterile barrier
	ISO 15223-1: 2021, Clause 5.4.2	Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied.	Do not reuse	Indicates a medical device that is intended for one use, or for use on a single patient during a single procedure
	ISO 15223-1: 2021, Clause 5.2.6	Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied.	Do not resterilize	Indicates a medical device that is not to be resterilized

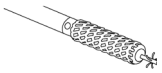
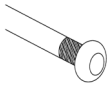
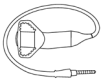
SYMBOL	STANDARD REFERENCE	STANDARD TITLE	SYMBOL TITLE	EXPLANATORY TEXT
	IEC 60601-1, Table D.2, Symbol 10	Medical electrical equipment — Part 1: General requirements for basic safety and essential performance.	Follow instructions for use	Refer to instruction manual/booklet.
	ISO 15223-1: 2021, Clause 4.3	Medical devices - Symbols to be used with information to be supplied by the manufacturer	Consult instructions for use or consult electronic instructions for use.	Refer to electronic format of instruction manual/booklet.
	21 CFR 801.109, Subpart D	Exemptions from Adequate Directions for Use Sec. 801.109 Prescription devices.	Prescription Use Only	Indicates that only professionals licensed by the law of the State in which the practitioner practices to use or order the use of the device can prescribe this device
	ISO 15223-1:2021, Clause 5.2.8	Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied.	Do not use if the package is damaged.	Indicates a medical device that should not be used if the package has been damaged or opened
	ISO 15223-1: 2021, Clause 5.4.4	Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied.	Caution	Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself
	ISO 15223-1: 2021, Clause 5.3.7	Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied.	Temperature limit	Indicates the temperature limits to which the medical device can be safely exposed

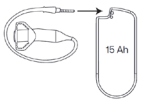
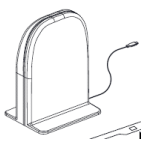
SYMBOL	STANDARD REFERENCE	STANDARD TITLE	SYMBOL TITLE	EXPLANATORY TEXT
1	ISO 80000-1: 2009 Section 3.1, note 3	Quantities and units — Part 1: General	Quantity	Quantity of package contents
	ISO 7000-3079	Graphic symbols for use on equipment	Open here	To identify the location where the package can be opened and to indicate the method of opening it
	IEC 60601-1-2:2020, Clause 5.1.1	Medical electrical equipment — Part 1-2: General requirements for basic safety and essential performance — Collateral standard: Electromagnetic compatibility — Requirements and tests	Non-ionizing electromagnetic radiation	To indicate generally elevated, potentially hazardous, levels of nonionizing radiation, or to indicate equipment or systems e.g., in the medical electrical area that include RF transmitters or that intentionally apply RF electromagnetic energy for diagnosis or treatment
	ISO 27185: 2012 Clause 6.8	Medical devices – Symbols to be used with cardiac rhythm management device labels and information to be supplied	Implantable Device	To indicate an implantable device
	IEC 60417-5035	Graphical symbols for use on equipment.	Output	To identify an output terminal when it is necessary to distinguish between inputs and outputs
	IEC 60417-5031	Graphical symbols for use on equipment.	Direct current	To indicate on the rating plate that the equipment is suitable for direct current only; to identify relevant terminals

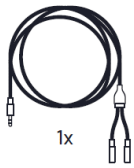
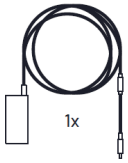
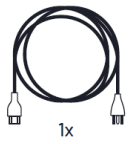
SYMBOL	STANDARD REFERENCE	STANDARD TITLE	SYMBOL TITLE	EXPLANATORY TEXT
	IATA Dangerous Goods Regulations, Section 7.3.18	IATA Dangerous Goods Regulations	Class 9 - Miscellaneous Dangerous Goods	Indicates that the package contains Lithium Metal Batteries Contained in Equipment, Hazard Class UN3091
 4GV/X11.1/S/** USA/+CG0117	IATA Dangerous Goods Regulations, Section 6.0.4.2	IATA Dangerous Goods Regulations	UN Specification Packaging	The packaging meets UN Packaging Code 4GV`, Performance Level X for Packaging Group I for Gross Mass weight of 11.1 kg, Solids. The year of manufacture and the manufacturer identification are as indicated on the package.
	IEC 60417 - 5009	Graphical symbols for use on equipment.	On/Off (push/push)	To identify power on/off button
	ISO 7000-3650	Graphical symbols for USB connection	USB port/plug	To identify USB port
	Dell	Graphical symbols for use on equipment.	Power Plug	To identify power plug connection
	47 CFR Part 15	Federal Communication Commission Number (FCC ID 2AMRX-5100) (FCC ID 2AMRX-4100)	FCC	Complies with United States Radio communication requirements

SYMBOL	STANDARD REFERENCE	STANDARD TITLE	SYMBOL TITLE	EXPLANATORY TEXT
	ASTM F2503: 2020	Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment	MR Conditional	To signify that the device is MR conditional and should be used under specific conditions

12.2 SYMBOLS NOT FROM STANDARDS

SYMBOL	REFERENCE	REFERENCE TITLE	SYMBOL TITLE	EXPLANATORY TEXT
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Electrode Catheter M1000	Left ventricular pacing system triggered by co-implant
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Sheath M2000	Left ventricular pacing system implantation sheath
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Battery M3100, 15 Ah	Energy source for the implanted components of the WiSE CRT System
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Transmitter M4100	Left ventricular pacing system triggered by co-implant
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Programmer M5100	External communication instrument used to adjust WiSE CRT System parameters and assist with system implant and follow-up
	EBR Systems, Inc.	Not Applicable	Ultrasound Cardiac Device	Ultrasound is transmitted from the device into the body. The ultrasound is converted by the system to an electrical output in the heart.

SYMBOL	REFERENCE	REFERENCE TITLE	SYMBOL TITLE	EXPLANATORY TEXT
	EBR Systems, Inc.	Not Applicable	Inappropriate Battery Connection	Do not connect battery to the heart.
	EBR Systems, Inc.	Not Applicable	Open here	Indicates the location to peel away the sterile barrier.
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Electrode Catheter M1000, Extension Cable	Cable connected between the Electrode Catheter and equipment for electrogram monitoring and pacing
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Electrode Catheter M1000, Reference Needle	Reference needle used as a far field reference and connected to equipment for electrogram monitoring and pacing
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Delivery Sheath M2000, Syringe	Used to inflate the Delivery Sheath's balloon
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Delivery Sheath M2000, Flush Extension Line	Extension with hub to connect to and to flush
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Delivery Sheath M2000, Pigtail Dilator with Insertion Tool	Used over a guidewire to support access to left ventricle
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Delivery Sheath M3100, Torque Wrench	Torque wrench used to secure connection between Transmitter and Battery
	EBR Systems, Inc.	Not Applicable	Connector Type	Connection between Transmitter and Battery
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Programmer M5100, Radio Input Module (RIO)	Support communication between the Programmer and WiSE CRT System

SYMBOL	REFERENCE	REFERENCE TITLE	SYMBOL TITLE	EXPLANATORY TEXT
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Programmer M5100, Recording System Connection Cable	Marker events cable for RIO
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Programmer M5100, AC Power Adapter	AC power adapter
	EBR Systems, Inc.	Not Applicable	WiSE CRT System Programmer M5100, AC Power Adapter United States Power Cord	Power cord for AC Power adapter
	Dell	IEC 60417 - 5009	Lock	Indicates to lock the M5100 tablet
	Dell	Not Applicable	Graphical symbol for Display Port USB-C port	Indicates a USB-C port can be used for video output
	Dell	Not Applicable	Graphical symbols for SuperSpeed (SS) USB port	Indicates a SS USB port is available. This port is used for the M5100 COM module



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