ASX ANNOUNCEMENT **4 September 2023**

EBR Reports Positive Results from the SOLVE-CRT Randomised Sub-Study

Sunnyvale, California; 4 September 2023: EBR Systems, Inc. (ASX: **"EBR"**, **"EBR Systems"**, or the **"Company"**), developer of the world's only wireless cardiac pacing device for heart failure, is pleased to announce further positive results from SOLVE-CRT, following analysis of the randomised sub-study. Data from the randomised phase of the study was released on the 2nd September at the 2023 Asia-Pacific Heart Rhythm Society ("APHRS") Conference during the late-breaking clinical trials session in Hong Kong. The trial showed clinically and statistically significant improvement for those in the Treatment Group against patients in the Control Group. These strong results support the conclusion of the SOLVE-CRT trial primary outcomes reported in May 2023 and provide further evidence of the clinical benefit of WiSE® in reversing heart failure symptoms in this patient population. The Company remains on track to submit the final module of its pre-market ("PMA") application to the FDA, with approval expected during H2 2024.

Key Highlights:

- EBR's randomised phase of its pivotal SOLVE-CRT ("SOLVE") trial showed statistically significant efficacy outcomes in its Treatment Group (WiSE® system ON) against the Control Group (WiSE system OFF) for two populations
  - Entire Randomised Population
    - Treatment Group efficacy: 14.6%, Control Group efficacy: 5.2% (p = 0.005)
  - Primary Indications Population
    - Treatment Group efficacy: 18.2%, Control Group efficacy: 3.1%, (p = 0.002)
- The Entire Randomised Population contained patients who were categorised as previously untreatable ("PU"), high risk upgrades ("HRU") and non-responders ("NR")
  - The Primary Indications Population contained patients who were categorised as PU and HRU
- Results of the randomised sub-study support the conclusions of the primary study that the WiSE-CRT system is efficacious in treating heart failure patients with few other options
- The Company continues to execute on its commercialisation strategy, with PMA submission to the FDA remaining on track and approval expected during H2 2024

SOLVE-CRT Randomised sub-study results

Results from the Randomised Population demonstrated that patients in the Treatment Group experienced a 14.6% improvement in heart function (measured by reduction in left ventricular end systolic volume) compared to the Control Group, which experienced a 5.2% improvement in heart function. In the Primary Indications Population, patients in the Treatment Group experienced a 18.2% improvement in heart function compared to a 3.1% improvement in heart function for the Control Group. All outcomes analysed to date have been consistent with the Company's previous studies, showing significant improvement in reversing heart failure symptoms and physiology.

Table 1 – Efficacy Outcomes (*Improvement in heart function measured by reduction in left ventricular end systolic volume***)**

	Treatment Group *WiSE system ON*	**Control Group** *WiSE system OFF*	**p-value**
Entire Randomised Population (patient groups: PU, HRU, NR)	**14.6%**	**5.2%**	**p = 0.005**
Primary Indications Population (patient groups: PU, HRU)	**18.2%**	**3.1%**	**p = 0.002**

John McCutcheon, President and CEO of EBR Systems commented:

"We are immensely proud of these positive results from our randomised sub-study, which show our system generating a statistically significant benefit to patients who used our technology. The strong result supports our findings from the SOLVE-CRT trial and demonstrates the efficacy and safety of our WiSE CRT system. We will continue to advance PMA submission as we look forward to gaining FDA approval. We remain focused on progressing and executing our commercialisation strategy as we look to significantly improve the lives of many patients suffering from cardiac arrhythmia and heart failure."

The SOLVE-CRT study comprised of a Roll-In Study followed by a Pivotal Study. Due to the impact of the COVID-19 pandemic, the Pivotal Study, which was initially a randomised trial was concluded and redesigned to be completed as a single-arm, treatment only clinical trial. A total of 108 participants were enrolled in the randomised phase of SOLVE, where all participants received the WiSE implant and were randomised in a 1:1 ratio to either the Treatment Group (System ON) or Control Group (System OFF). Patient groups in the randomised sub-study included patients who were previously untreatable, were considered high risk upgrades, and non-responders. The outcome of the randomised sub-study reinforces the positive results previously reported for SOLVE which exceeded both efficacy and safety thresholds.

Data from the randomised sub-study was presented by Dr Prashanthan Sanders from The Royal Adelaide Hospital on 2nd September 2023 during the late-breaking clinical trial session of the Asia Pacific Heart Rhythm Society meeting in Hong Kong.

Next steps

EBR remains focused on supporting the expansion of clinical applications for WiSE through studies in Totally Leadless CRT and Leadless LBBAP/Conduction System Pacing. As the use of leadless pacing systems continues to expand, the need for a totally leadless CRT system increases, with WiSE potentially providing the means to upgrade leadless pacemakers to CRT.

The Company is well funded to support its commercialisation objectives and remains on track to submit the final module of its pre-market ("PMA") application to the FDA, with approval expected during H2 2024.

ENDS

This announcement has been authorised for release by the EBR Systems General Disclosure Committee, a committee of the Board of Directors.

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About EBR Systems (ASX: EBR)

Silicon Valley-based EBR Systems (ASX: EBR) is dedicated to superior treatment of cardiac rhythm disease by providing more physiologically effective stimulation through wireless cardiac pacing. The patented proprietary Wireless Stimulation Endocardially (WiSE) technology was developed to eliminate the need for cardiac pacing leads, historically the major source of complications and reliability issues in cardiac rhythm disease management. The initial product is designed to eliminate the need for coronary sinus leads to stimulate the left ventricle in heart failure patients requiring Cardiac Resynchronisation Therapy (CRT). Future products potentially address wireless endocardial stimulation for bradycardia and other non-cardiac indications.

EBR Systems' WiSE® Technology

EBR Systems' WiSE technology is the world's only wireless, endocardial (inside the heart) pacing system in clinical use for stimulating the heart's left ventricle. This has long been a goal of cardiac pacing companies since internal stimulation of the left ventricle is thought to be a potentially superior, more anatomically correct pacing location. WiSE technology enables cardiac pacing of the left ventricle with a novel cardiac implant that is roughly the size of a large grain of rice. The need for a pacing wire on the outside of the heart's left ventricle – and the attendant problems – are potentially eliminated. WiSE is an investigational device and is not currently available for sale in the US.

Forward-Looking Statements

This announcement contains or may contain forward-looking statements that are based on management's beliefs, assumptions, and expectations and on information currently available to management. Forward-looking statements involve known and unknown risks, uncertainties, contingencies and other factors, many of which are beyond the Company's control, subject to change without notice and may involve significant elements of subjective judgment and assumptions as to future events which may or may not be correct.

All statements that address operating performance, events or developments that we expect or anticipate will occur in the future are forward-looking statements, including without limitation our expectations with respect to our ability to commercialize our products including our estimates of potential revenues, costs, profitability and financial performance; our ability to develop and commercialize new products including our ability to obtain reimbursement for our products; our expectations with respect to our clinical trials, including enrolment in or completion of our clinical trials and our associated regulatory submissions and approvals; our expectations with respect to the integrity or capabilities of our intellectual property position.

Management believes that these forward-looking statements are reasonable as and when made. You should not place undue reliance on forward-looking statements because they speak only as of the date when made. EBR does not assume any obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise. EBR may not actually achieve the plans, projections or expectations disclosed in forward-looking statements, and actual results, developments or events could differ materially from those disclosed in the forward-looking statements.

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HEART HEALTH
Centre for Heart
Rhythm Disorders

THE UNIVERSITY of ADELAIDE

Results of a Leadless Ultrasound-Based Cardiac Resynchronization System in Heart Failure

The SOLVE-CRT Randomised Sub-study Results

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on behalf of the SOLVE-CRT Investigators

Disclosure

Advisory Board: Medtronic, Abbott Medical, Boston-Scientific, CathRx, Pacemate

Research Funding: Medtronic, Abbott Medical, Boston-Scientific, Microport, Becton Dickenson

Background

Despite the well-established role of CRT in heart failure, major limitations of CRT include:

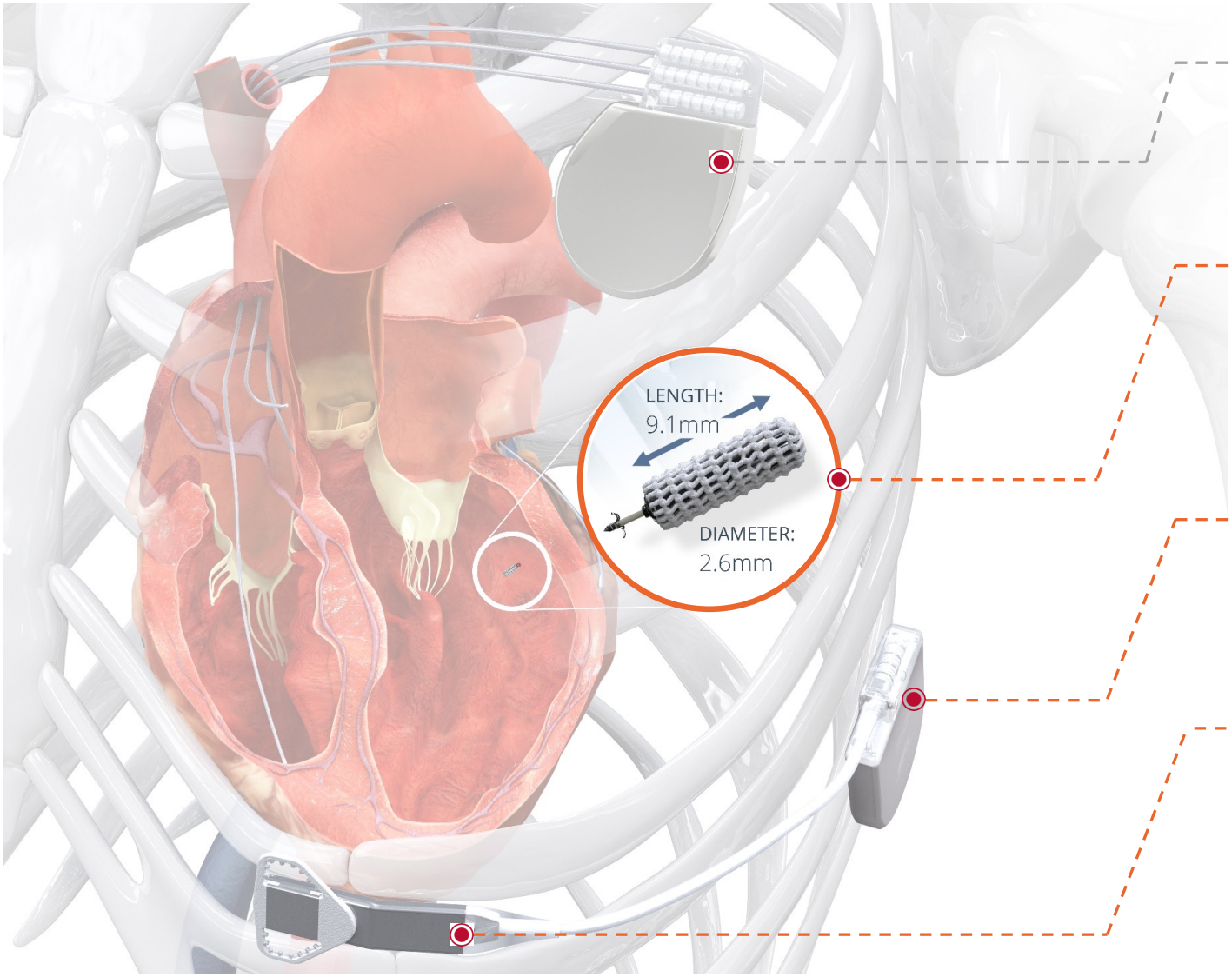
- High incidence of unsuccessful coronary sinus (CS) lead placement
- Upgrading ICDs in high-risk patients
- High rates of CRT non-responders (30-50%)

The WiSE CRT System is designed to overcome the limitations of traditional CRT pacing by providing wireless, left ventricular (LV) endocardial pacing as an alternative to the epicardial CS lead

Prior non-randomised studies with the WiSE CRT System have shown high implant success rates and improvement in LV remodeling and heart failure symptoms[1,2,3,4]

[1]Delnoy, et al. (2014) – Europace, [2]Reddy, et al. (2017) – JACC , [3]Okabe T, et al. (2021), Heart Rhythm, [4]Singh et al. 2023 HRS LBCT

SOLVE-CRT Device



CO-IMPLANT DEVICE

Existing pacemaker, ICD or CRT provides RV pacing

RECEIVER ELECTRODE

Implanted endocardially, this Electrode converts ultrasound into electrical energy to pace the LV

BATTERY

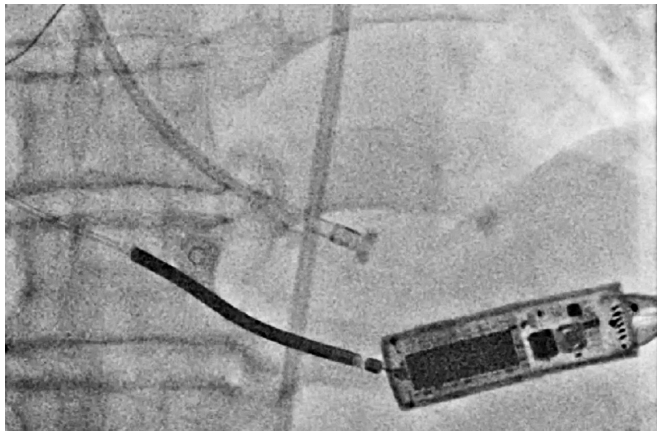
Implanted subcutaneously at the left mid-axillary line, powers the Transmitter

TRANSMITTER

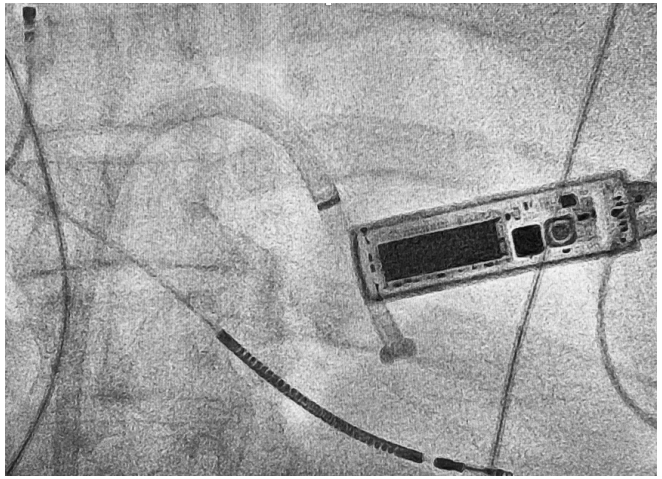
Phased array ultrasound Transmitter synchronizes with RV pacing pulse to transmit ultrasound energy to the Receiver Electrode

Receiver Electrode Implant Procedure

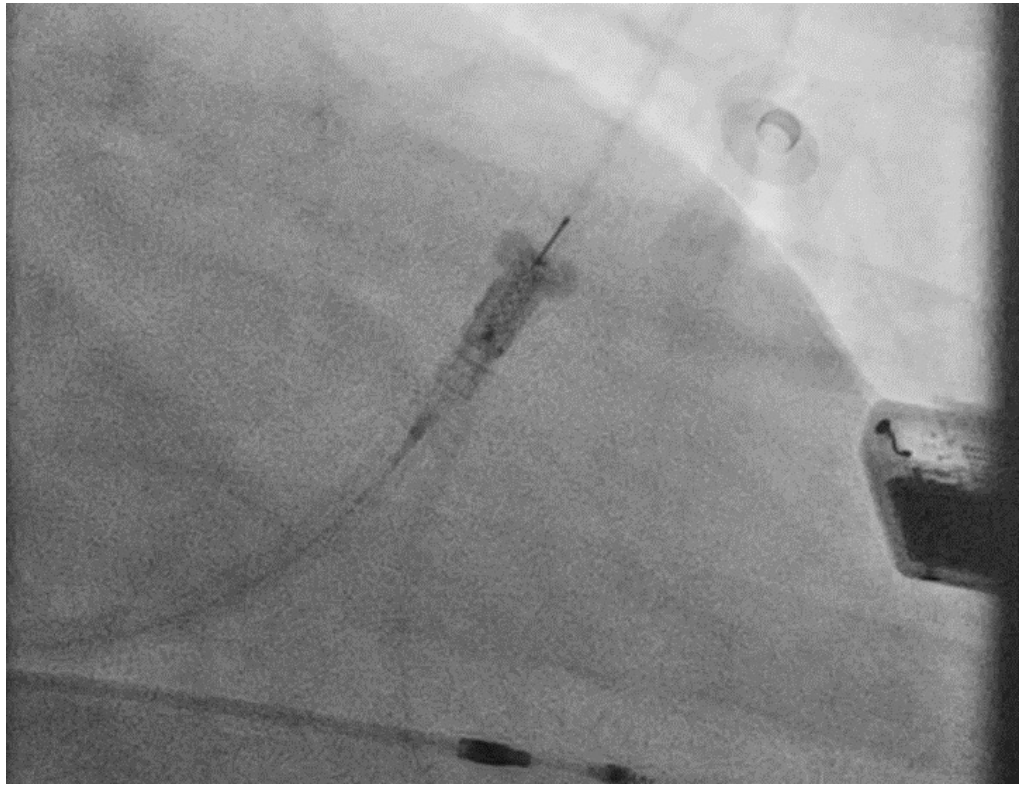
Retrograde Aortic Approach



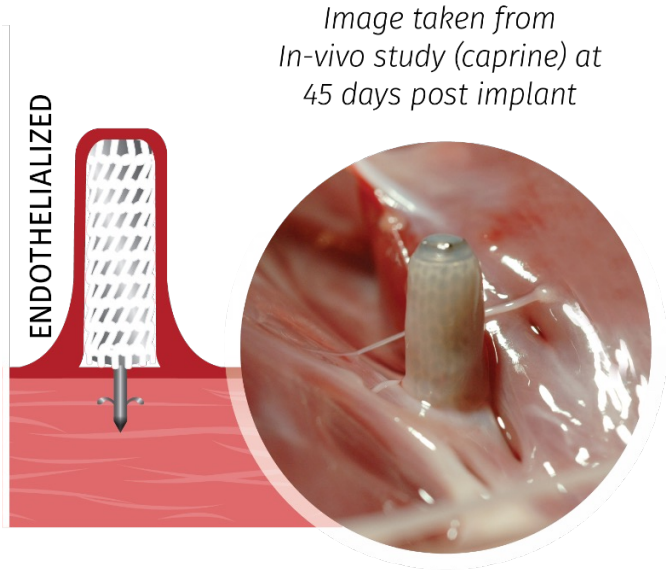
Transseptal Approach



Anchoring Sequence



Secure Attachment



Endothelializes for a low risk of thromboembolic events

SOLVE-CRT Protocol Overview

Aim: Pivotal study to assess the safety and effectiveness of the WiSE® CRT System

Design: International, multi-center, 3-part study: (i) Roll-in, (ii) Randomised, and (iii) Single-arm

Study Population

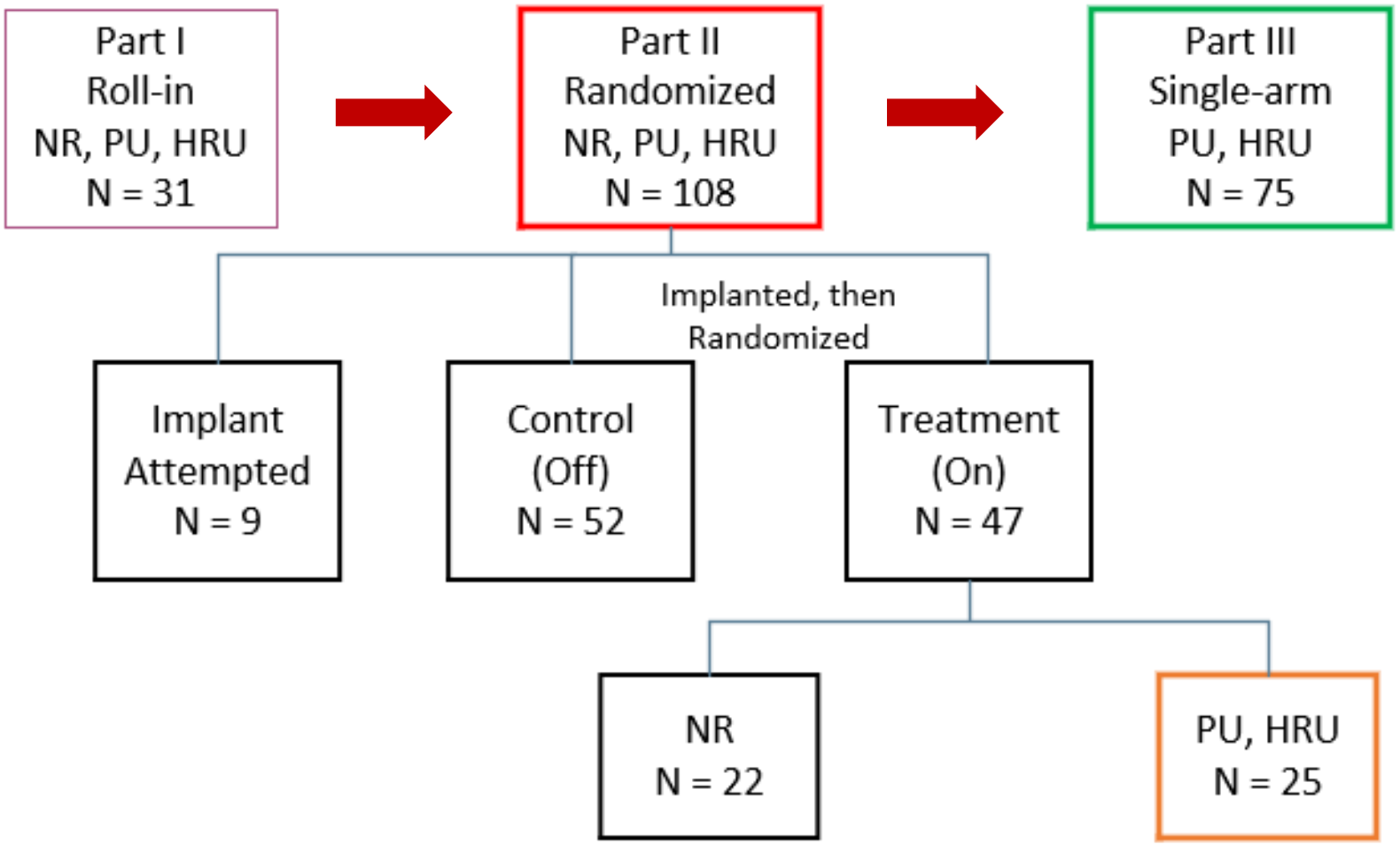
Patients indicated for CRT and

- Previously untreatable (PU), or
- Considered a high-risk upgrade (HRU) to conventional CRT, or
- Non-responders (NR) to CRT – Randomised part only

Primary Population: Patients indicated for CRT and

- Previously untreatable (PU), or
- Considered a high-risk upgrade (HRU) to conventional CRT

Primary Analysis



Safety Population
n = 183

Part II: Randomization
n = 108

+

Part III: Single Arm
n = 75

Efficacy Population
n = 100

PU or HRU
n = 25

+

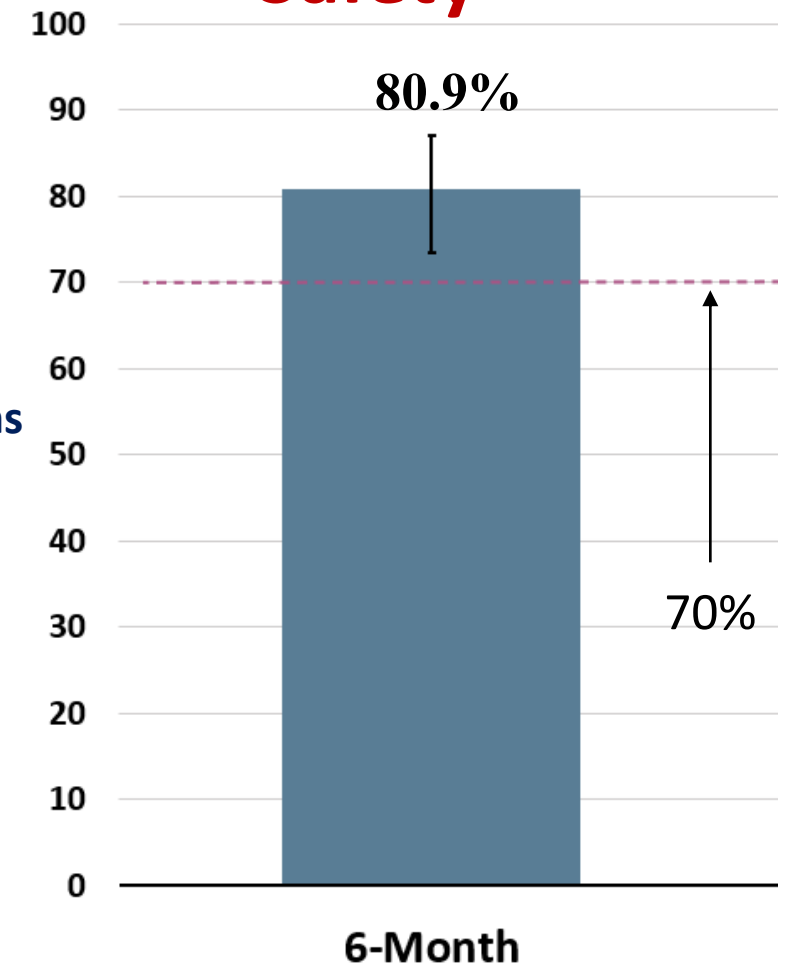
Part III: Single Arm
n = 75

Primary Endpoints*

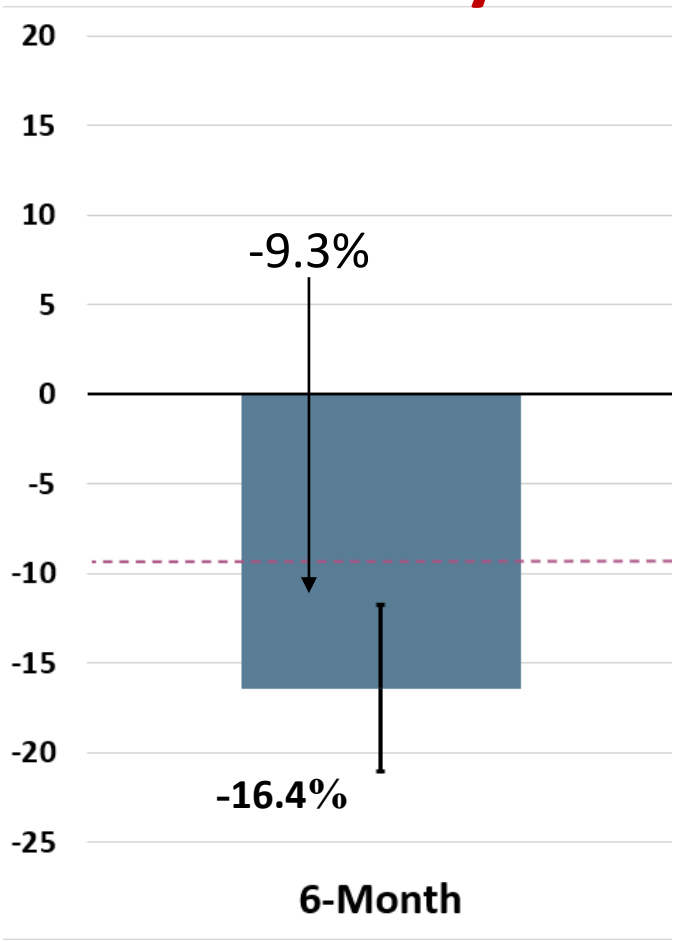
Safety

Freedom from Type I Complications (%)

p <0.001



Efficacy

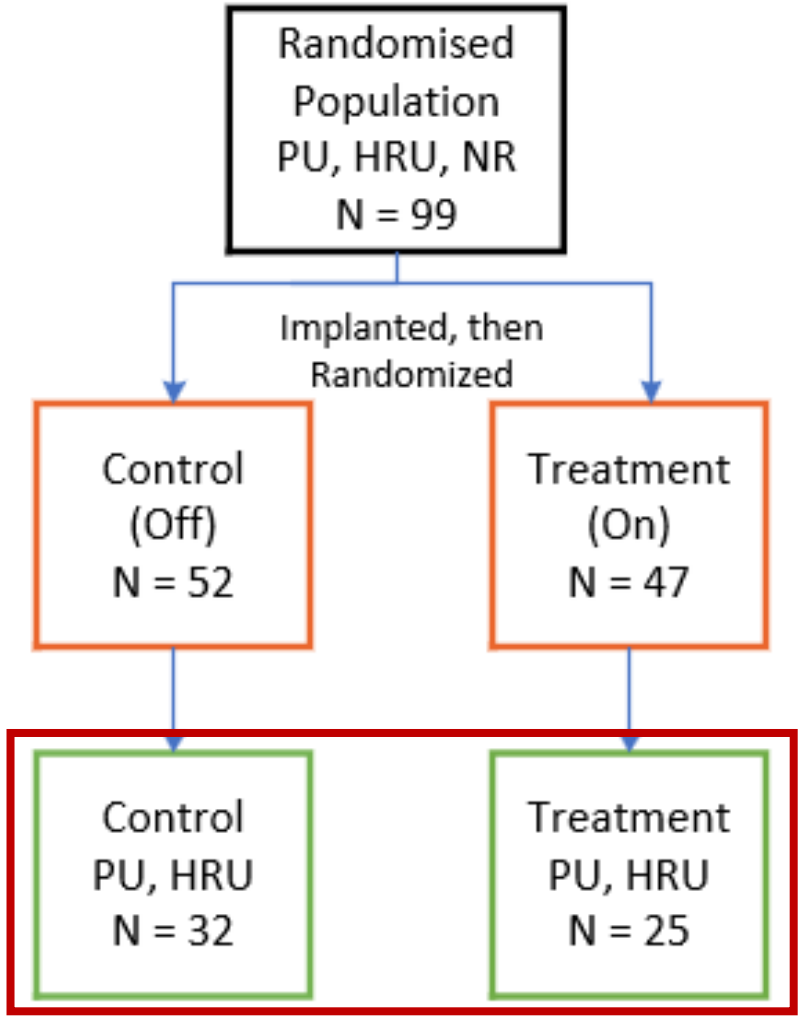


% ΔLVESV

p = 0.003

**Primary results presented at 2023 HRS, New Orleans*

Randomised Efficacy



Primary Efficacy Population

PU = Previously untreatable
HRU = High risk upgrade
NR = Non responder

Baseline Characteristics

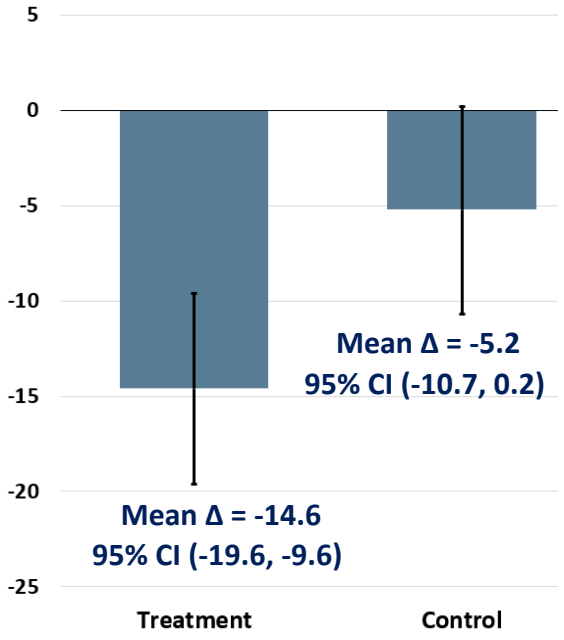
	Treatment	Control	p-value
Female, N (%)	13/47 (27.7)	9/52 (17.3)	0.216‡
Age at enrollment (Years)	68.1±8.3	67.4±11.3	0.735†
Previously Untreatable, N (%)	20/47 (42.6)	28/52 (53.9)	
High Risk Upgrade, N (%)	5/47 (10.6)	4/52 (7.7)	0.525‡
Non-responder, N (%)	22/47 (46.8)	20/52 (38.5)	
Left ventricular ejection fraction (%),	29.5±7.8	28.3±8.3	0.484†
Left ventricular end systolic volume (ml)	149.7±61.2	157.5±63.0	0.536†
Left ventricular end diastolic volume (ml)	207.8±72.7	215.0±68.6	0.615†
Ischemic, N (%)	24/47 (51.1)	25/52 (48.1)	0.767‡
Atrial fibrillation, N (%)	9/47 (19.2)	8/52 (15.4)	0.620‡
Renal dysfunction, N (%)	13/47 (27.7)	11/52 (21.2)	0.451‡
COPD, N (%)	5/47 (10.6)	10/52 (19.2)	0.234‡
Diabetes, N (%)	17/47 (36.2)	19/52 (36.5)	0.970‡
NYHA Class II, N (%)	13/47 (27.7)	18/52 (34.6)	0.456‡
NYHA Class III, N (%)	34/47 (72.3)	34/52 (65.4)	
ACEI, ARB, or ARNI use, N (%)	43/47 (91.5)	47/52 (90.4)	0.849‡
SGLT2 inhibitor, N (%)	0/47 (0.0)	0/52 (0.0)	--
Beta-blocker use, N (%)	47/47 (100)	50/52 (96.2)	0.174‡
Aldosterone Antagonist, N (%)	33/47 (70.2)	31/52 (59.6)	0.271‡

†T-test
‡Pearson chi-square test

Efficacy – Randomised Population

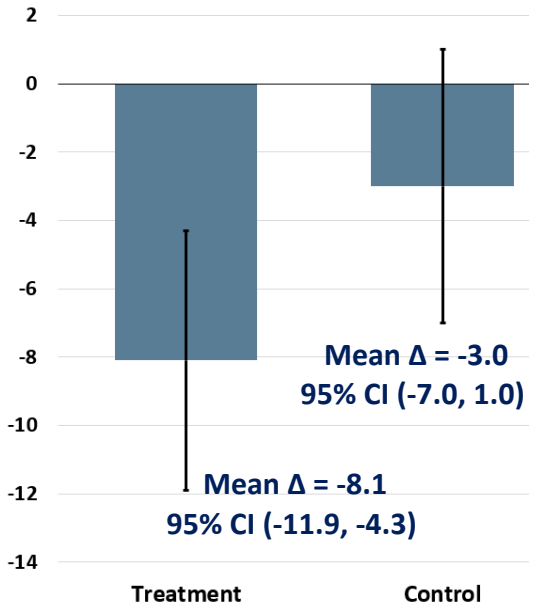
LVESV (%)

p=0.005‡



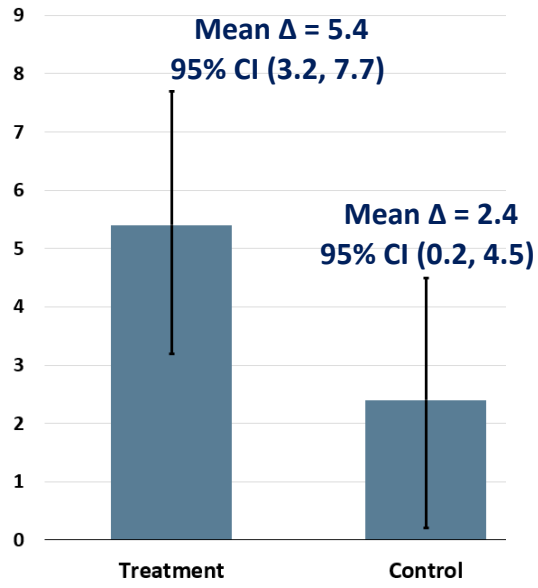
LVEDV (%)

p=0.027‡



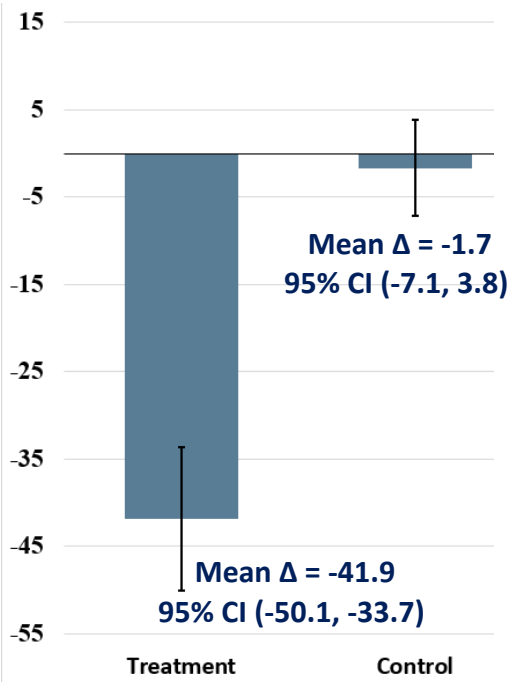
LVEF (%)

p=0.048‡



QRS (ms)

p<0.001†



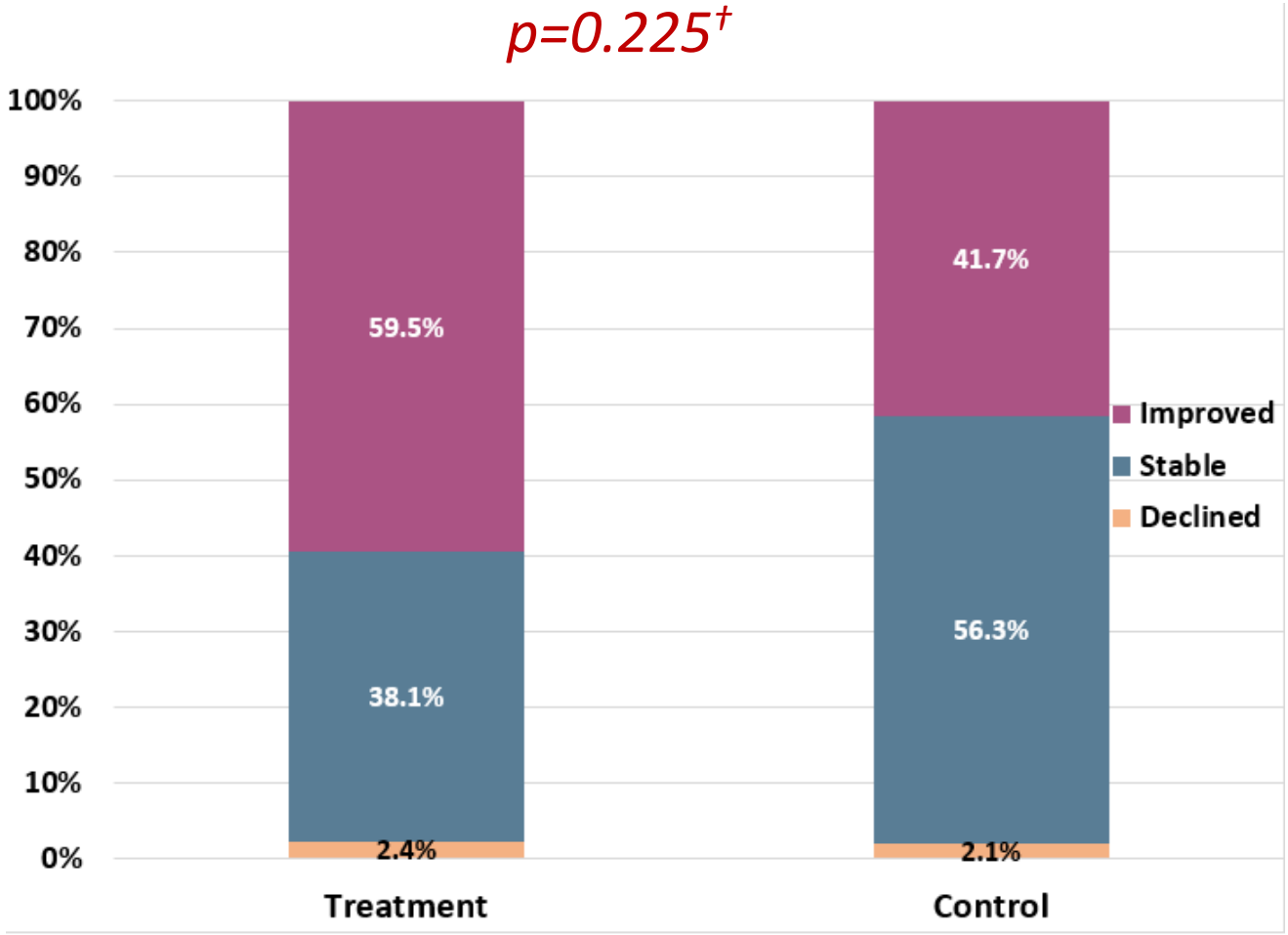
- Clinically and statistically significant evidence of reverse remodelling and electrical response

†T-test
‡Wilcoxon rank-sum test

Heart Failure Symptoms

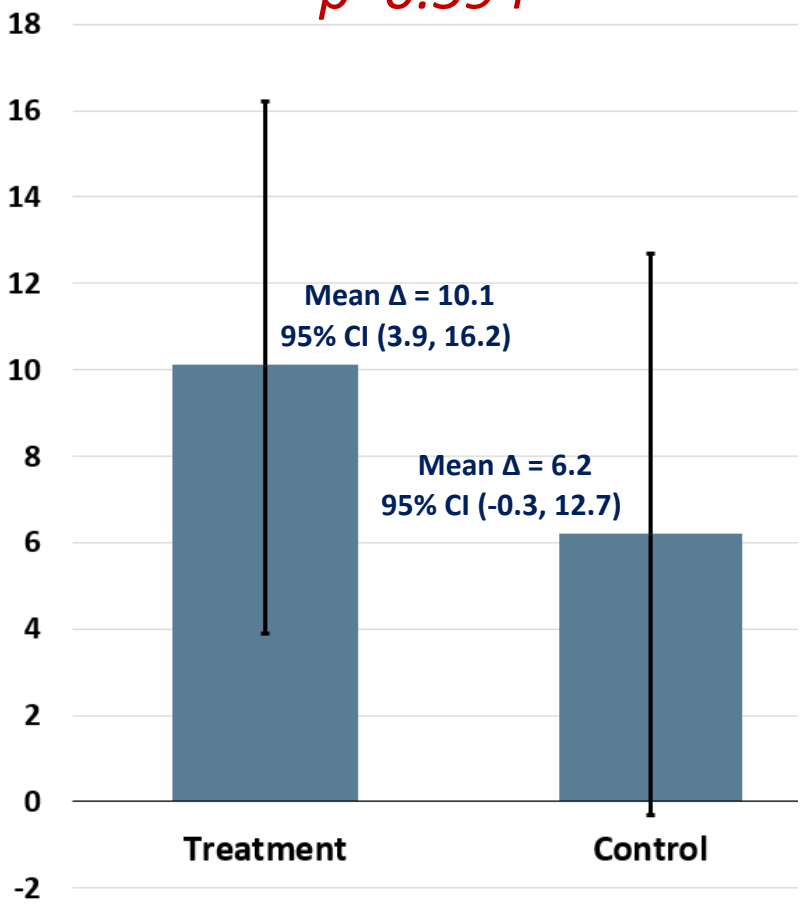
NYHA

p=0.225†



KCCQ

p=0.594‡

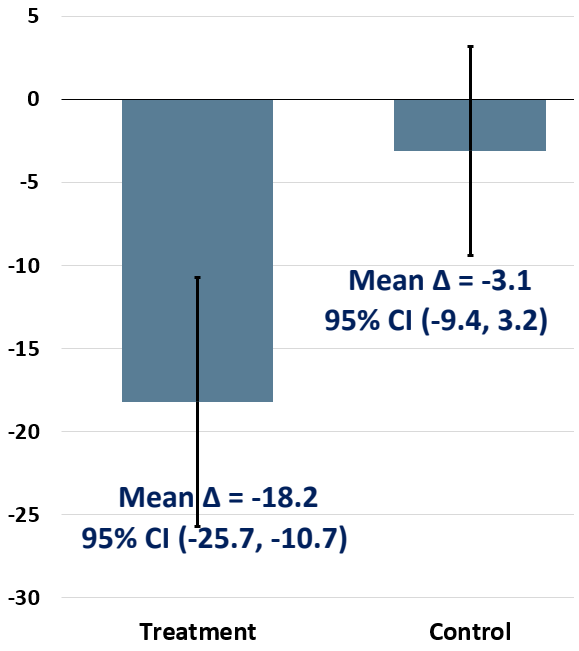


†Pearson chi-square test
‡Wilcoxon rank-sum test

Efficacy – Primary Population

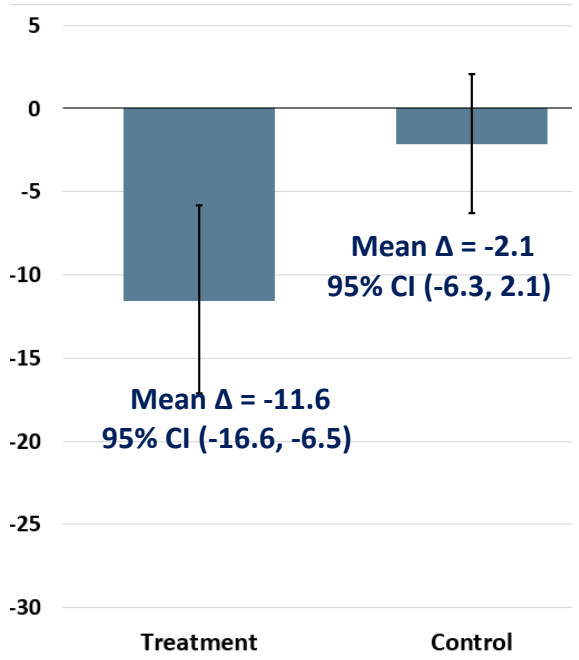
LVESV (%)

p=0.002†



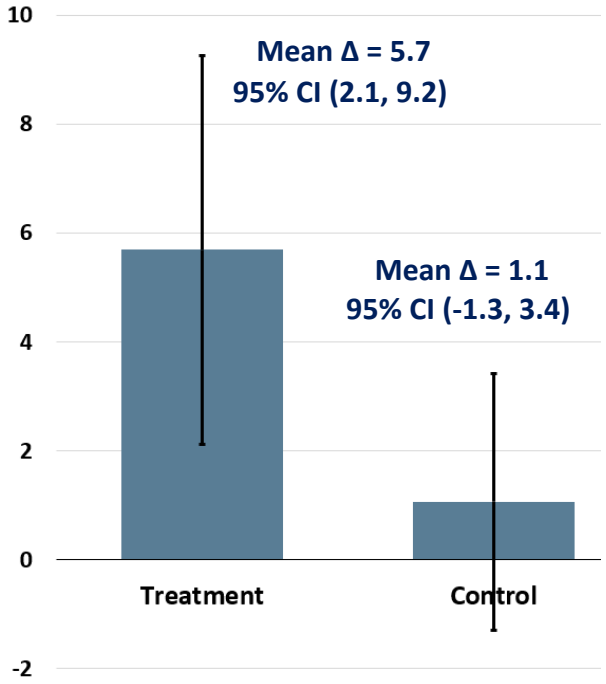
LVEDV (%)

p=0.004‡



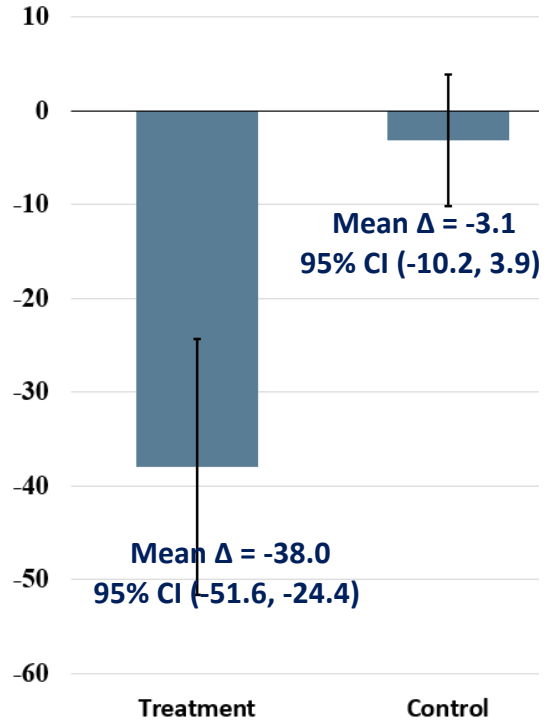
LVEF (%)

p=0.025†



QRS (ms)

p<0.001‡



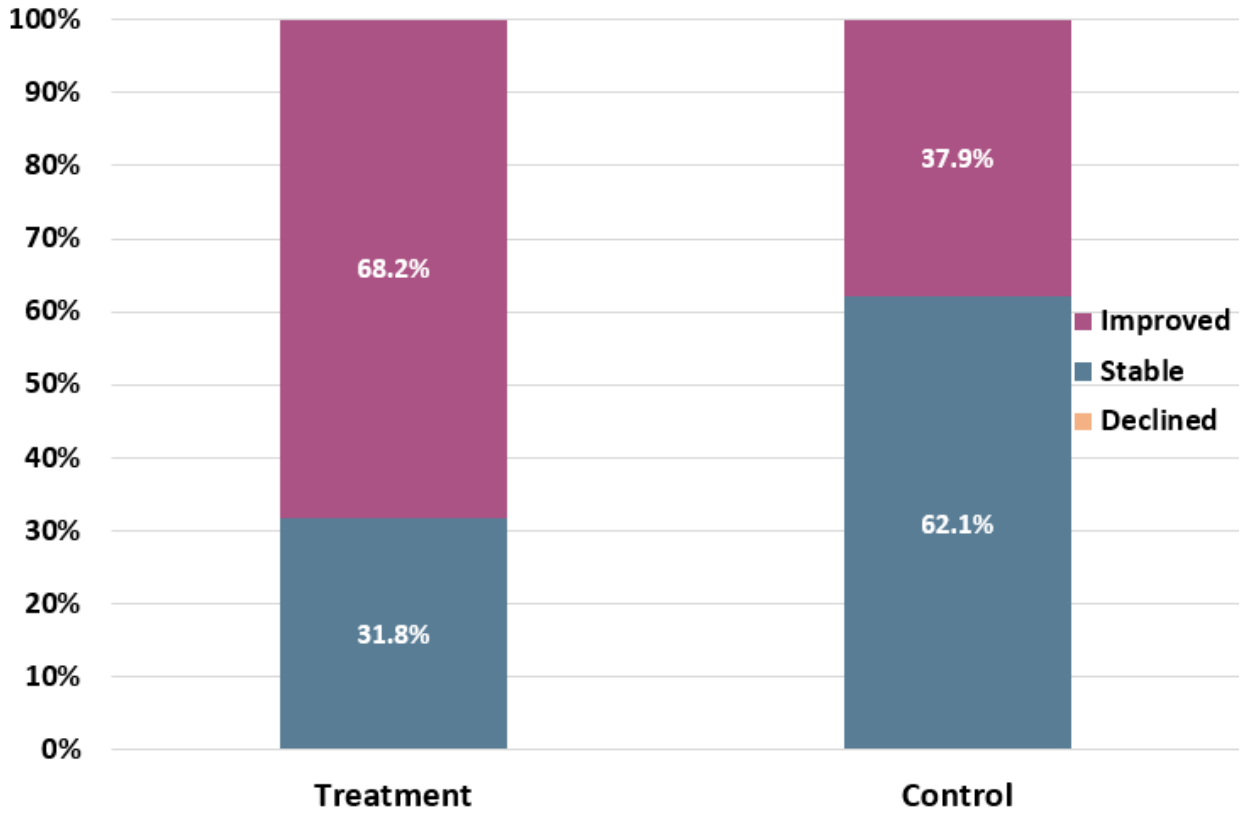
- Clinically and statistically significant evidence of reverse remodelling and electrical response

†T-test
‡Wilcoxon rank-sum test

Heart Failure Symptoms

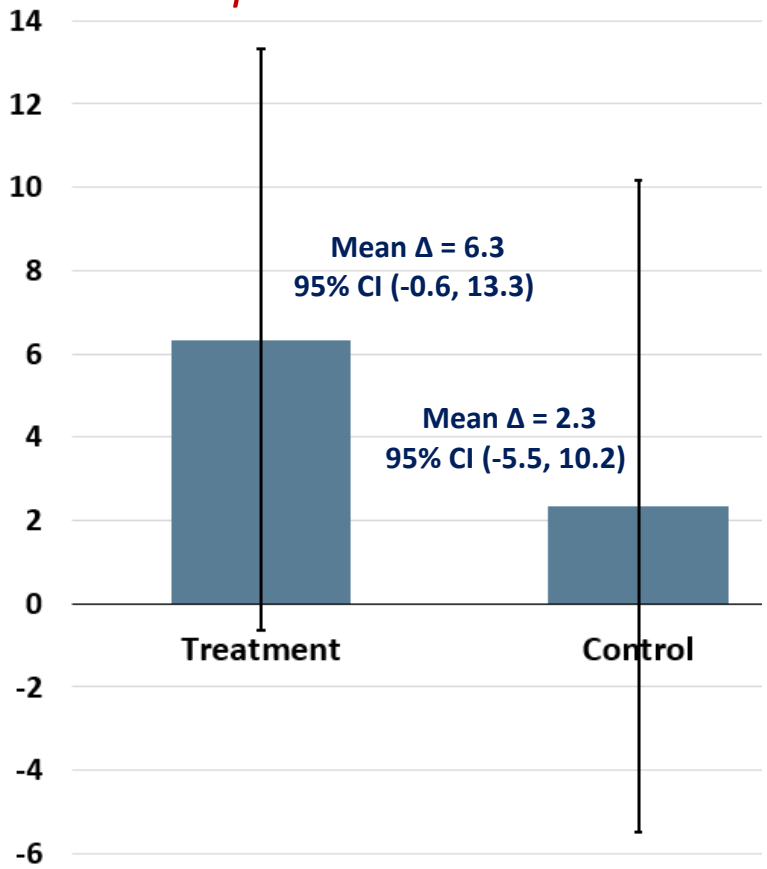
NYHA

p=0.032†



KCCQ

p=0.939‡



†Pearson chi-square test
‡Wilcoxon rank-sum test

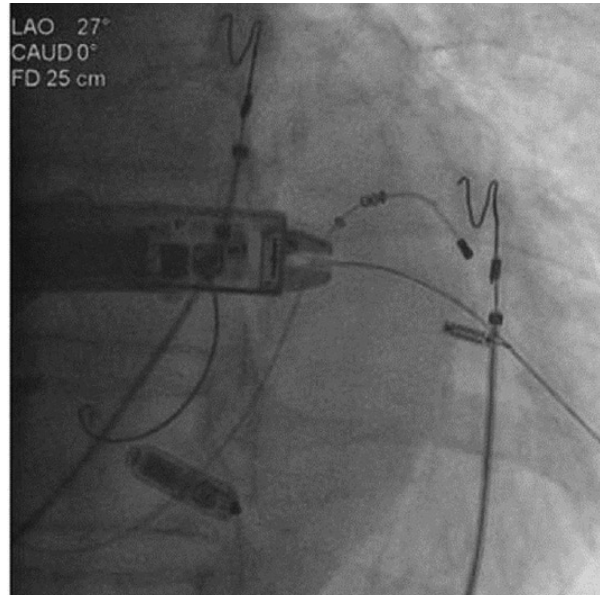
Limitations and Strengths

Limitations	Strengths
▪ COVID impact on protocol ▪ Short follow-up duration ▪ Under-powered, subset analysis	▪ Prospective, multi-center ▪ Randomised arm was blinded, sham-controlled ▪ Blinded Echo Core Lab

Future Considerations

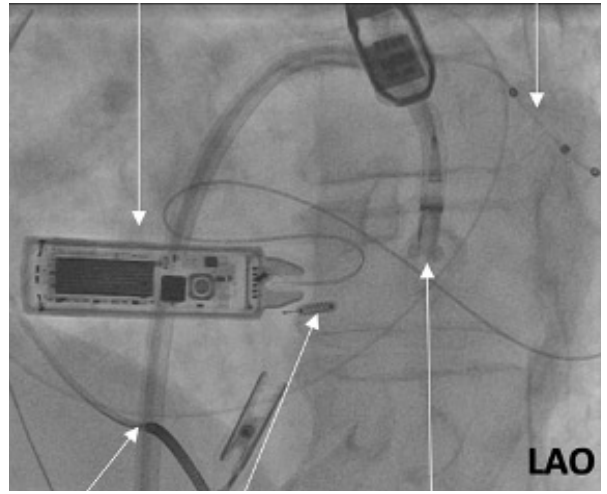
Pairing with a leadless pacemaker to achieve Totally Leadless CRT

- As the use of leadless pacing systems continues to expand, the need for a Totally Leadless CRT system increases
  - WiSE potentially provides the means to upgrade leadless pacemakers to CRT
  - 1 patient with Micra® in SOLVE-CRT
- Initial multi-center experience published 2020[4]
- Updated experience presented at APHRS2022
  - Included 3 *de novo* pts, 5 upgrades chronic devices, 6 replacements of infected / failed conventional CRT systems



Leadless LBBAP / Conduction System Pacing

- LBB is located sub-endocardially on the LV septum
  - Leadless LV endocardial approach might allow direct targeting of LBB – studies required
- Initial multi-center experience published 2022[5]
  - Included 2 animals, 8 humans



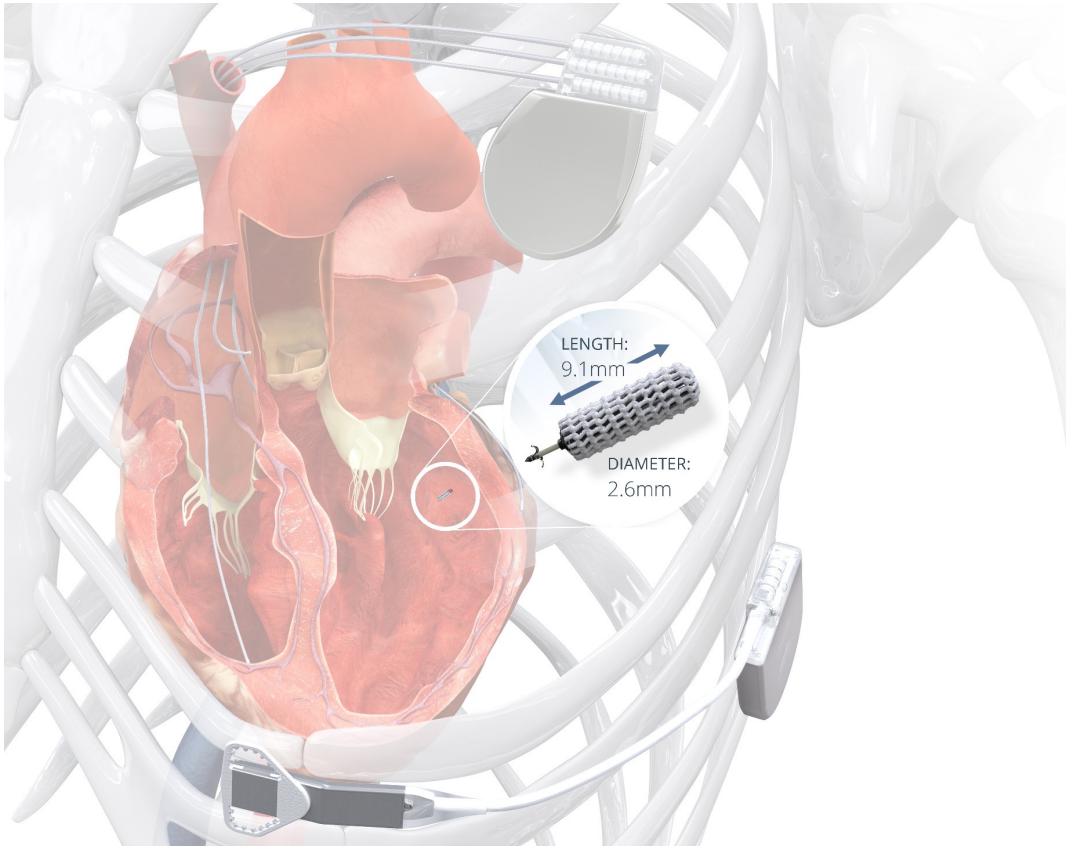
[4]Carabelli, et al. (2020) – Europace, [5]Elliott, et al. (2022) – Heart Rhythm

Conclusions

The pivotal SOLVE-CRT study has demonstrated that leadless, ultrasound-based endocardial pacing with the WiSE CRT System is:

- ✓ Feasible
- ✓ Safe
- ✓ Efficacious

Randomised analysis supports primary results



Acknowledgements

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- Eligibility Review Committee
- Coordination and Data Management Teams
- EBR Clinical & Study Monitoring Teams

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Ohio State Univ, US	The Heart Hosp Baylor Plano, US	Baptist Health Lexington, US	Sydney Adventist Hosp, AU	KUMC, US
Methodist Physicians Clin, US	Stern Cardiovascular Ctr, US	Prairie Heart, US	Texas Heart Institute, US	Northside Hosp, US
Univ of Michigan, US	St. Vincent's Jacksonville, US	University of Iowa, US	MUSC, US	Minneapolis Heart Institute Foundation, US
Royal Adelaide Hosp, AU	Cleveland Clinic, US	University of Virginia, US	Houston Methodist, US	CHU Rennes Hosp, EU
Rutgers-New Jersey Med School, US	Broward Health, US	Sentara, US	Michigan Heart, US	University Erlangen, EU
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Manchester Heart Center, UK	Ochsner, US	CHU Nord-Hospital Albert Michallan, EU	William Beaumont Hosp, US	Royal Melbourne Hosp, AU
Monash Heart, AU	Peace Health SHMC, US			

Thank you!

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