Safety and Performance of Electrodes implanted in the LV

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5.1 Primary study objectives:5.1.1 SafetySafety of the device has been defined as 1. Device-related complications (24 hour perioperative and one month) 2. Procedure-related complications (24 hour perioperative and one month) 5.1.2…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON40357

Source
ToetsingOnline

Brief title
SELECT-LV

Condition

- Heart failures

Synonym
Wireless Stimulation Endocardially for Cardiac Resynchronization Therapy

Research involving
Human

Sponsors and support

Primary sponsor: EBR Systems Inc.
Source(s) of monetary or material Support: EBR Systems;Inc.

Intervention

Keyword: Cardiac Resynchronization Therapy, Endocardial Stimulation, Wireless

Outcome measures

Primary outcome

20.4 Primary endpoint(s) analysis

20.4.1 Safety

Primary endpoint - Device-related complications (24 hours perioperative and one month):

A primary endpoint for evidence of safety will be the number of patients with major device-related complications. This endpoint will be assessed at two time points, the perioperative device-related complications (from implant to 24 hours post implant) and the one month (30 day) device-related complications (from 24 hours post implant to 30 days post implant). The definition of a major device-related complication is a complication in which the WiCS-LV system is directly or indirectly responsible for a serious adverse event. All serious adverse events will be reviewed and adjudicated by an independent Clinical Events Committee.

Primary endpoint - Procedure-related complications (24 hours perioperative and one month):

A primary endpoint for evidence of safety will be the number of patients with major procedure-related complications. This endpoint will be assessed at two time points, the perioperative procedure-related complications (from implant to

24 hours post implant) and the one month (30 day) procedure-related complications (from24 hours post implant to 30 days post implant). The definition of a major procedure-related complication is a serious adverse event occurring as a direct result of the implant procedure. All serious adverse events will be reviewed and adjudicated by an independent Clinical Events Committee.

20.4.2 Performance

Primary endpoint - bi-ventricular pacing at one month:

The primary endpoint for evidence of clinical performance will be chronic bi-ventricular pacing. This will be demonstrated by obtaining 12 lead EKG*s at the 1 month (30 day) follow-up assessment. Twelve lead EKG*s will be obtained without pacing (if the patient is not pacemaker-dependent, during RV pacing (by temporarily programming off the WiCS-LV system), and during bi-ventricular pacing. Bi-ventricular capture will be demonstrated by comparing the paced QRS morphology during bi-ventricular pacing to that during RV-only pacing. Note that in order to meet this endpoint, two performance criteria are met, both the appropriate recognition of the co-implant RV pacing output (successful detection) and LV pacing (successful capture).

Secondary outcome

20.5 Secondary endpoint(s) analysis

20.5.1 Safety

Secondary endpoint - Device-related complications up to 6 months:

Device-related complications will be tabulated in the same manner as the

primary endpoint, but extended to 6 months post implant. All serious adverse events will be reviewed and adjudicated by an independent Clinical Events Committee.

Secondary endpoint - Major complications up to 6 months:
All serious adverse events regardless of cause will be tabulated. All serious adverse events will be reviewed and adjudicated by an independent Clinical Events Committee.

Surveillance evaluation annually for 5 years:
All serious adverse events will be tabulated. Data regarding battery depletion and device replacement will be collected.

20.5.2 Performance

Secondary endpoint - left ventricular pacing at one, 2 and 6 months:
The secondary endpoint for evidence of clinical performance will be chronic left ventricular pacing. This will be demonstrated by obtaining 12 lead EKG*s at the one, 2 and 6 month follow-up assessments. Normally, the 12 lead EKG will be obtained after temporarily reducing the co-implanted pacemaker rate and operating the WiCS-LV system in temporary VOO mode at a higher rate to capture the left ventricle alone. However, there may be instances where it is clinically preferable to demonstrate left ventricular capture by comparing the paced QRS morphology during bi-ventricular pacing to that during right ventricular pacing alone (by temporarily programming off the WiCS-LV system).

Secondary endpoint - bi-ventricular pacing at 2 and 6 months:

Bi-ventricular pacing as a secondary endpoint will be demonstrated by obtaining 12 lead EKG*s at the 2 and 6 month follow-up assessments. Twelve lead EKG*s will be obtained without pacing (if the patient is not pacemaker-dependent, during RV pacing (by temporarily programming off the WiCS-LV system), and during bi-ventricular pacing. Bi-ventricular capture will be demonstrated by comparing the paced QRS morphology during bi-ventricular pacing to that during RV-only pacing. Note that in order to meet this endpoint, two performance criteria are met, both the appropriate recognition of the co-implant RV pacing output (successful detection) and LV pacing (successful capture).

20.5.3 Preliminary Evidence of Efficacy

Secondary endpoint - Clinical composite score at 6 months:

The clinical composite score is a measure incorporating the parameters of all cause mortality, hospitalizations for heart failure, NYHA functional classification, and patient global assessment (29). The clinical composite score has been utilized as an endpoint in a number of clinical studies of CRT device systems (4,5,30). The NYHA functional classification assigns patients to one of four classes (I, II, III, or IV) depending on the degree of symptoms needed to elicit symptoms (28). The patient global assessment is a measure of the whether the patient*s overall status has changed since the start of the study, and if so, in which direction and to what magnitude. The NYHA classification and patient global assessment will be made by the Investigator. The clinical composite score classifies the patient as improved, unchanged, or

worsened depending on the clinical response during and the clinical status at 6 months. Patients are considered improved if at 6 months the NYHA class is decreased by at least one class or the patient global assessment is better (or both) and they did not experience mortality or hospitalization for heart failure.

Secondary endpoint - Change in echocardiographic left ventricular end-systolic volume, left ventricular end-diastolic volume, and ejection fraction at 6 months:
The values of the above parameters obtained from the pre-implant study will be compared to the values obtained after 6 months as a measure of cardiac reverse remodeling. A reduction in LV end-systolic volume and/or end-diastolic volume of >= 10% will be considered a positive echocardiographic response (31). An absolute increase in EF by >= 5% will also be considered a positive echocardiographic response.

Study description

Background summary

Bi-ventricular pacing is the pacing modality used to accomplish Cardiac Resynchronization Therapy (CRT). CRT is recommended for use by both European Society of Cardiology/European Heart Rhythm Association (ESC/EHRA) Guidelines and ACC/AHA/HRS Guidelines for a number of subsets of heart failure patients based on evidence from large scale randomized trials demonstrating benefits in symptoms, function, and survival.

Study objective

5.1 Primary study objectives:

5.1.1 Safety
Safety of the device has been defined as
1. Device-related complications (24 hour perioperative and one month)
2. Procedure-related complications (24 hour perioperative and one month)
5.1.2 Performance
Performance of the device has been defined as:
1. Bi-ventricular pacing capture (documented on 12 lead EKG at one month)
5.2 Secondary study objectives:
5.2.1 Safety
1. Device-related complications up to 6 months
2. Major complications up to 6 months
3. Surveillance by annual registry survey
5.2.2 Performance
1. Left ventricular pacing capture (documented on 12 lead EKG at one, 2 and 6 months)
2. Bi-ventricular pacing capture (documented on 12 lead EKG at 6 months)
5.2.3 Preliminary evidence of efficacy
1. Clinical composite score (all-cause mortality, HF hospitalization, NYHA class, and patient global assessment (16)) at 6 months
2. Change in echocardiographic left ventricular end-systolic volume, left ventricular end-diastolic volume, and ejection fraction at 6 months

Study design

This study is a multicenter, prospective, open-label, and non-comparative clinical investigation. The study will be conducted in up to 7 clinical centers in EU member states.

The purpose of this Clinical Investigation Plan is to collect data on the safety and performance of the WiCS-LV system. It is designed to satisfy requirements for clinical data and post market clinical follow-up for the Active Implantable Medical Devices Directive (AIMDD 90/385/EEC), Annex 7, as amended in December 2008. A complete risk assessment was performed to determine the design of the Clinical Investigation Plan.

Intervention

Summary of implant steps:
1. Prepare femoral artery access with introducer and arterial closure device.
2. Administer intravenous heparin to attain an ACT level in the range of 200-250 sec.
3. Introduce Delivery System*s Sheath and Dilator into femoral artery introducer and advance into the artery.
4. Inflate Sheath*s distal tip balloon and then advance Sheath and Dilator into the LV.

5. Exchange Dilator for the Catheter mounted with the Electrode and position the Sheath at target LV implant site.
6. Evaluate intracardiac electrogram with the Electrode.
7. Perform transthoracic echocardiography imaging of the Electrode in the Sheath with a commercial instrument to confirm a Transmitter acoustic window location on the chest wall.
8. Anchor the Electrode into the LV tissue, confirm tissue attachment using contrast dye, and confirm intracardiac electrogram and acceptable electrical pacing thresholds.
9. Disconnect the Electrode from the Catheter.
10. Release the Electrode from the Sheath.
11. Retract the Sheath and Catheter in to the femoral artery and deflate the Sheath*s distal tip balloon.
12. Remove the Delivery Catheter System via the femoral introducer.
13. Perform transthoracic echocardiography imaging of the Electrode implanted in the LV with a commercial instrument to determine the Transmitter acoustic window location on the chest wall and mark the chest location.
14. After ACT level is lowered to an acceptable level (approximately 180 sec), make skin incisions and subcutaneous pockets for the Transmitter and Battery modules.
15. Tunnel the cable to the lateral Battery pocket using standard techniques with a trocar or other suitable blunt instrument.
16. Insert Battery into the lateral Battery pocket, connect to Transmitter cable, and secure cable in place.
17. Insert the Transmitter stability accessory into the intercostal space and secure to the intercostal muscle.
18. Insert and secure Transmitter into the accessory. Fill area with saline or sterile conductive gel.Using the Programmer, evaluate RV pacing detection and LV pacing capture.
19. Demonstrate bi-ventricular pacing capture as recorded on EKG.
20. Secure Battery in place and close skin incisions. Optionally, a drain and/or negative pressure bandage may be applied to eliminate air around the implanted Transmitter.
21. Document final program settings for WiCS-LV and co-implant.

At the discretion of the operator, the implant procedure may be assisted by transesophageal echocardiography or intracardiac ultrasound.

Study burden and risks

The WiCS-LV system is associated with some potential discomforts and risks common to all implantable pacing systems, as well as certain unique potential discomforts and risks.

Potential discomforts and risks common to all implantable pacing systems include the following:
• Air embolism

• Allergic reactions to medications used including renal failure from contrast media
• Arrhythmias
• Cardiac tamponade
• Chronic nerve damage
• Death
• Electrochemical burns
• Excessive bleeding
• Excessive fibrotic growth
• Foreign body reaction
• Hematoma
• Embolization of device or materials
• Infection
• Migration of device
• Myocardial tissue injury or perforation
• Myocardial infarction
• Pain
• Pneumothorax
• Radiation skin burns
• Stroke or transient cerebrovascular episodes
• Thromboembolism
• Vascular damage

Potential discomforts and risks of the WiCS-LV system not associated with implantable pacing systems but having similarities to left heart catheterization or the implantation of other devices within the left heart (such as stents, clips, septal closure devices, and appendage occlusion devices) include the following:
• Aortic or mitral valve damage
• Dissection of aorta or branch vessels
• Femoral artery pseudoaneurysm
• Embolization of device or material, thrombi, or air to systemic circulation increasing stroke and peripheral vascular occlusion risk

Potential discomforts and risks of the WiCS-LV system not associated with implantable pacing systems but having similarities to other diagnostic and therapeutic devices utilizing ultrasound energy (such as ultrasound imaging instruments, physical therapy) related to ultrasound bioeffects include the following:
• Thermal injury from ultrasonic transducer elements overheating
• Mechanical injury causing tissue damage

These risks are minimized by operating at substantially lower levels (duty cycle and amplitudes) than those used in commercially available echocardiographic imaging instruments. The system has safeguard circuitry to prevent energy levels from exceeding programmed limits.

There is one potential risk of the WiCS-LV system not associated with other devices:
• Implanted Electrode may receive ultrasound pulses from other ultrasound devices (such as echocardiographic imaging instruments) and convert those pulses to stimulation pulses.

This risk is minimized by the very short, narrow pulse durations used in echocardiographic imaging devices and by limiting the electrical output of the Electrode to amplitudes lower than the expected stimulation thresholds at these pulse durations. Additionally, warnings are placed in the Technical Manual and Investigators are trained for this specific risk.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients with standard indications for CRT based upon the most recent ESC/EHRA guidelines AND meeting criteria for one of these two categories:
1. Patients with previously implanted pacemakers or ICD*s and meeting standard indications for CRT but in whom standard CRT is not advisable due to known high risk - referred to as *upgrades*. Justifications for not using standard CRT must be documented in a CRF.
2. Patients in whom coronary sinus lead implantation or attempted implantation for CRT has failed to provide demonstrable therapy benefit - referred to as *untreated*
Investigator

Exclusion criteria

Study patients responding to the following criteria are excluded from enrollment:
1. Inability to comply with the study follow-up or other study requirements
2. History of chronic alcohol/drug abuse and currently using alcohol/drugs
3. Non-ambulatory (or unstable) NYHA class 4
4. Contraindication to heparin
5. Contraindication to both chronic anticoagulants and antiplatelet agents
6. Triple anticoagulation therapy (warfarin, clopidogrel, ASA, and other agents)
7. Thrombocytopenia (platelet count <150,000)
8. Contraindication to iodinated contrast agents
9. Intracardiac thrombus by transesophageal echocardiography
10. Age less than 18 years or greater than 75
11. Attempted IPG implant within 3 days
12. Life expectancy of less than 12 months
13. Chronic hemodialysis
14. Stage 4 or 5 renal dysfunction defined as GFR <30
15. Grade 4 mitral valve regurgitation
16. Myocardial infarction within one month
17. Major cardiac surgery within one month
18. History of a pericardial effusion in prior procedures
19. Female of childbearing potential, pregnant, or breastfeeding (a pregnancy test will be obtained where applicable)
20. Non-cardiac implanted electrical stimulation therapy devices

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-03-2014
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	WiCS-LV System
Registration:	No

Ethics review

Approved WMO Date:	16-09-2013
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	10-10-2013
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	04-11-2013
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	02-06-2014
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	26-08-2014

Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL44156.075.13