Lead Evaluation for Defibrillation and Reliability in Left Bundle Branch Area Pacing (LEADR LBBAP)

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The purpose of this study is to confirm the safety and defibrillation efficacy of the Next Generation ICD Lead when placed in the Left Bundle Branch Area Pacing (LBBAP) location in an Implantable Cardioverter Defibrillator (ICD) or Left Bundle...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON57056

Source
ToetsingOnline

Brief title
LEADR LBBAP

Condition

- Cardiac arrhythmias

Synonym
ventricular tachyarrhythmias

Research involving
Human

Sponsors and support

Primary sponsor: Medtronic B.V.
Source(s) of monetary or material Support: Medtronic.Inc.

Intervention

Keyword: Cardiac Resynchronization Therapy, ICD Lead, Left Bundle Branch Pacing

Outcome measures

Primary outcome

Primary Efficacy Objective:

Demonstrate the percentage of patients successfully defibrillated at implant with the Next Generation ICD Lead when placed in LBBAP location exceeds a pre-specified threshold of 88%. Successful implant defibrillation is defined as:

• First induced SSVA episode successfully terminated with an 18J or maximum output minus 10 Joule (M-10J) shock, or

• First therapy of the second induced SSVA episode successfully terminated with a M-10J shock, or

• First therapy after a system reposition of an induced SSVA episode successfully terminated with a M-10J shock, or

• Two consecutively induced SSVA episodes successfully terminated with a M-10J shock.

Primary Safety Objective:

Estimate the Next Generation ICD Lead-related major complication rate at 3-months post implant when the Next Generation ICD Lead implant is attempted in the LBBAP location.

Secondary outcome

Ancillary Objectives

• Estimate the success rate of LBBAP Next Generation ICD Lead placement at implant.

• Characterize pacing capture thresholds at a 0.4 ms pulse duration at implant and 3-months when the Next Generation ICD Lead is placed in the LBBAP location

• Characterize R-wave sensing amplitude at implant and 3-months when the Next Generation ICD Lead is placed in the LBBAP location

• Characterize pacing impedance at implant and 3-months when the Next Generation ICD Lead is placed in the LBBAP location

• Characterize intrinsic (at implant) and paced (at implant and 6 months) ECG measurements

• Characterize the change in Kansas City Cardiomyopathy Questionnaire (KCCQ) score from baseline to 6 months

For LOT-CRT implanted subjects only:

• Characterize the change in Left Ventricular End-Systolic Volume Index (LVESVi) from baseline to 6 months

• Characterize the change in Left Ventricular Ejection Fraction (LVEF) from baseline to 6 months

• Characterize the Clinical Composite Score (CCS) when assessed at 6 months

Study description

Background summary

I refer to section 3.1 of the Clinical Investigational plan version 2.0.

Study objective

The purpose of this study is to confirm the safety and defibrillation efficacy of the Next Generation ICD Lead when placed in the Left Bundle Branch Area Pacing (LBBAP) location in an Implantable Cardioverter Defibrillator (ICD) or Left Bundle Branch-Optimized Cardiac Resynchronization Therapy (LOT-CRT) patient population.

Study design

The LEADR LBBAP study is a prospective, pre-market, pivotal, non-randomized, multi-site, interventional, global study designed to allow controlled access of the Next Generation ICD Lead for placement in a LBBAP application. The study is expected to be conducted at up to 40 study sites. Participating geographies may include but are not limited to: Australia, Mainland China, Japan, Hong Kong, Malaysia, Europe, Middle East, and Africa (EMEA), Canada, and the United States. Approximately 300 subjects, including a minimum of 150 LOT-CRT implant attempts (no minimum requirement for ICD implant attempts), will be enrolled. Assuming one lead is used per subject, as well as a 6% increase to account for system revisions, sterility compromised products, etc., it is expected that approximately 320 Next Generation ICD Leads will be used in the study. Medtronic may decide to stop or pause ICD or LOT-CRT enrollments (in all or in specific regions), for example to manage total (or per cohort) sample size. In addition, Medtronic may decide to keep enrollments open in specific regions/sites beyond 300 enrollments to address local needs. The final study sample size will depend on enrollment rate and/or timing of official enrollment closure (see section 15.10.1). A sample size of at least 160 subjects completing the defibrillation protocol at implant with the Next Generation ICD Lead placed in the LBBAP location will provide at minimum 90.4% power to test the study*s primary efficacy objective provided the true defibrillation success rate is at least 95.5%.
Subjects will be considered enrolled into the study upon signing the Informed Consent Form (ICF) and will be followed prospectively from consent to implant, 3-months post-implant, 6-months post-implant, and at subsequent 6-month intervals until study closure. Enrolled subjects from all geographies will be followed until at least 3-months post-implant (ICD-indicated subjects) or 6-months post-implant (CRT-indicated subjects).
There is no minimum number of subjects to be enrolled per study site. Enrollment parameters are included in the study to avoid introduction of bias to the study results due to disproportionate enrollment. Enrollment should not exceed 10% (i.e., 30 subjects if 300 subjects are enrolled) of the final sample size at any individual site. Enrollment will be competitive across study sites. The per-study site enrollment cap may be increased upon Sponsor approval.

The first enrollment is projected to occur in 2024. Successfully implanted study subjects will be followed until study closure, with an Exit electronic

Case Report Form (eCRF) entered for each subject. Official study closure is defined as when all enrolled subjects have been followed until at least 3 months (ICD-indicated subjects) or 6 months post-implant (CRT-indicated subjects) or have been exited, and applicable regulatory authority agency or governing body requirements have been satisfied per the Clinical Investigation Plan (CIP) and/or by a decision by Medtronic or regulatory authority to stop or close the study. The duration of individual subject participation will vary based on timing of study site activation and their enrollment. The approximate duration for each subject participant will be 1.5 to 3 years. The expected study duration is approximately 3 years from first site activation until the study closure criteria are met. Official study closure is anticipated in 2027.

Intervention

Please see visit schedule overview in CIP section 9.2, table 7

Enrollment/Baseline visit - Visit 1
- Physical Exam - a general exam that will include height and weight
- Demographics: including age, gender, race, and ethnicity (if allowed per local regulations)
- New York Heart Association (NYHA classification (assessment of heart failure) and general cardiovascular and surgical medical history will be reviewed
- Assessment for an ICD or CRT-D implant, in the case of CRT-D, an echocardiogram will be needed within 60 days of the baseline visit
- Quality of Life Survey

Implant visit - Visit 2
- Within about 30 days of the enrollment visit, the implant will be scheduled.
- Pregnancy test
- The Medtronic CRT-D or ICD device will be implanted
- In case the Next Generation ICD Lead is not attempted to be implanted or is not implanted at completion during the Implant visit, the patient will be exited from the study
- If a Next Generation ICD Lead implant is attempted, but not successfully placed in the LBBAP location or the right ventricle (RV) location, the patient will be exited from the study after monitoring for at minimum 30 days to ensure there are no problems..

Following the successful implant, the following tests will be done:
- 12-Lead Electrocardiogram (ECG)
- Defibrillation testing may take place
- Moving X-ray

Defibrillation Testing During the Implant
-In case the device needs to be repositioned during defibrillation testing, the patient may have additional fluoroscopy to get extra pictures of your lead and device before repositioning the lead.
-In case the device does not successfully provide appropriate therapy (shock),

the device may be removed and replaced with another device from your body and could be replaced with another lead

Pre-discharged checks from the hospital, the following procedures will be done:
-Electrical testing
-Chest x-rays

3 and 6-month follow-up visits - Visits 3 and 4
- Electrical testing of the device implanted
-Chest x-rays (at either the 3 or the 6-month visit, but not both)
-12-Lead ECG (6-month visit only)
- Quality of Life survey (6-month visit only)
In case the CRT-D device is done during the implant, the following procedures are completed at the 6-month follow-up visit : Transthoracic echocardiogram (TTE) (a test that uses sound waves to create pictures of your heart)

Long-term follow-up visits - Visit 5 and any additional visits beyond 5

Depending on when you were enrolled in this study you may have these visits at 12 months after the implant and every 6 months thereafter. These visits may be in the office or as phone call visits.

At each of the long-term follow-up visits, the following will occur:
-Electrical testing (only be done at in-office visits)
-Information regarding the device and other problems that the patient is having device-related or not will be collected

Unscheduled follow-up visits
- Electrical testing can be done
-Information regarding the device and other problems that the patient is having device-related can be reviewed

Study burden and risks

Risk/Benefit rational CIP section 10.4:
In addition to the extensive pre-clinical testing, bench testing, and computational modeling, a formal risk analysis and risk assessment for the Next Generation ICD Lead was performed according to EN ISO 14971:2019 and were used to ensure that the level of risk is acceptable prior to starting clinical investigations. The risk management activities reduced the risks to as low as possible and concluded that the residual risks associated with these hazards are acceptable when weighed against the benefits. The risk management file for the Next Generation ICD Lead will be updated periodically for impact to the product*s overall residual risk for issues that are identified during the clinical investigational study and following market release, in accordance with EN ISO 14971:2019.
A risk management plan/report establishes the strategy for performing

systematic and comprehensive evaluation of potential safety risks associated with the use or performance of the Next Generation ICD Lead for the investigational study, in accordance with EN ISO 14971:2019.
The risk management plan describes inputs to the hazard analysis as well as the structure of the hazard analysis activities performed for the Next Generation ICD Lead project. The chosen strategy was to perform hazard analysis for the therapy to capture potential risks associated with design inputs and then also perform hazard analyses for the new lead to capture potential risks associated with the design outputs (i.e., finished devices). The hazard analysis leverages the relevant risk analysis inputs such as failure analysis and use error analysis. Furthermore, the hazard analysis captures the pertinent risk controls that serve to minimize the residual risk to as low as possible. This plan may be updated in future phases of the device development lifecycle.
A systematic process is in place to continuously collect, analyze, and assess data relevant to the safety performance of the system during human use. Furthermore, the information gained during the investigational study will be leveraged during the planning and execution of the risk management activities throughout all phases for this project and for commercial release.
In summary, the anticipated risks of the Next Generation ICD Lead placed in the LBBAP location are consistent with the risks of similar market-approved transvenous ICD and catheter-delivered pacing leads. The potential benefits of having the Next Generation ICD Lead implanted in the LBBAP location are also consistent with the benefits of ICD therapy and similar market-approved transvenous ICD leads. Additionally, due to the smaller lead diameter of the Next Generation ICD Lead and the novel catheter delivery in tachycardia application, potential benefits may be seen in long term reliability, the ease of extraction and the potential to target specifically selected sites with the use of a catheter delivery system. The Next Generation ICD Lead may also be an alternative for subjects with small vasculature anatomies. Furthermore, the benefits for pediatric subjects, described in detail in section 10.3, outweigh the risks based on lower body mass. Therefore, it is concluded that the potential benefits related to the use of the Next Generation ICD Lead placed in the LBBAP location have been determined to outweigh any potential risks and justify the implementation of this investigation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1.Subject meets current local clinical practice guidelines for implantation of ICD (single or dual chamber) or CRT-D system* and will undergo one of the following:
a) De novo Medtronic ICD system implant (single or dual chamber) or
b) De novo Medtronic CRT-D system implant and is intended to also undergo LV lead implant (for patients indicated for CRT-D according to locally approved indications/indications*)
2. Subject is 12 years of age or older and also is greater than 30 kg in weight at time of enrollment, has cardiac anatomy conducive to RV coil placement, and is allowed to participate in study per local law and requirements. Subjects from 12 years of age until adult also have a separate indication for pacing or CRT or are anticipated to develop one
3.Subject provides written authorization and/or consent per institution and geographical requirements.
4.Subject is geographically stable and willing and able to complete the study procedures and visits for the duration of the follow-up.
5. Subject is willing to undergo implant defibrillation testing if requested

*CRT-D indications in the U.S. are based on Class I and II indications per current AHA/ACC/HFSA Guideline

Exclusion criteria

1.Subject has contraindication for screw-in active fixation transvenous lead placement (e.g., mechanical right heart valve).
2.Subject is contraindicated for <=1 mg dexamethasone acetate
3.Subject has a life expectancy of less than 12 months
4.For subject undergoing defibrillation testing the following medical conditions exclude them:
o Pre-existing or suspected pneumothorax
o Current intracardiac left atrial or LV thrombus
o Severe aortic stenosis
Severe proximal three-vessel or left main coronary artery disease without revascularization
o Unstable angina
o Recent stroke or transient ischemic attack (within the last 6 months)
o Known inadequate external defibrillation
o Any other known medical condition not listed that precludes their participation in the opinion of the investigator
5.Subject is enrolled or planning to enroll in a concurrent clinical study that may confound the results of this study, without documented pre-approval from a Medtronic study manager
6.Subject with any exclusion criteria as required by local law (e.g., age or other)
7.Subject is pregnant or breastfeeding, or subject is of childbearing potential and not on a reliable form of birth regulation method or abstinence**
8.Subject with an existing pacemaker (including transvenous and transcatheter pacing system), ICD (transvenous) or CRT-D (transvenous) device or leads
9.Subject with previous subcutaneous ICD (S-ICD), extravascular ICD (EV ICD) or Implantable Cardiac Monitor explanted within 30 days before implant.
10.Subject with any evidence of active bacterial infection or undergoing treatment for a bacterial infection within the last 30 days
11.Recent (or planned) cardiovascular intervention within 30 days before or after implant, such as cardiac surgery, cardiac ablation, Percutaneous Coronary Intervention (PCI), or temporary cardiac pacing for >12 hours
12.Subjects with end stage renal disease
13.Subjects with NYHA IV classification
14.Subjects with a transplanted heart or on the waiting list for a heart transplant
15.Subjects with previously extracted leads
16.Subjects with Left Ventricular Assist Device
17.Subjects that are vulnerable adults

**If required by local law, individuals who are of child-bearing potential must undergo a pregnancy test within seven days prior to study procedures

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-12-2024
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	Model 093000 lead (Next Generation ICD Lead)
Registration:	No

Ethics review

Approved WMO

Date:	08-10-2024
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL85887.000.24