Triple-site biventricular stimulation in the optimisation of cardiac resynchronisation therapy.

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

Summary

ID

NL-OMON41981

Source
ToetsingOnline

Brief title
Triumph-CRT

Condition

- Heart failures

Synonym
heart failure, pump failure

Research involving
Human

Sponsors and support

Primary sponsor: Sorin Group Nederland N.V.
Source(s) of monetary or material Support: Sorin Group

Intervention

Keyword: CRT, heart failure, multi-site pacing

Outcome measures

Primary outcome

The primary objective of this study is to demonstrate that individually optimized, triple-site biventricular pacing is superior to standard biventricular pacing in reversing ventricular modeling as demonstrated by Echo Left Ventricle End-Systolic Volume (LVESV) at twelve months in patients with non LBBB morphology without increasing the risk of serious procedure and/or device related events at thirty days.

For the primary objective the primary efficacy endpoint is used, change in LVESV at 12 months post-implant, comparing both groups in a superiority context with an expected change of 12% between both groups.

The echo measures will be validated by an independent core lab, which will be blinded to the randomization assignments.

The primary efficacy endpoint will be evaluated in a superiority format, with statistical hypothesis tests formally defined in sections below.

For the primary safety endpoint, a patient*s clinical status will be evaluated considering the incidence of serious procedure and/or device related events assessed from the time of enrollment, during implant, through discharge and up

to thirty days follow-up.

Secondary outcome

The main secondary objectives of this study are:

- Evaluate reverse ventricular remodeling response based on echocardiographic measures at six and twelve months follow-up
- Assess clinical outcome using NYHA classification, at thirty days, six and twelve months after treatment compared to the baseline evaluation.

- Evaluate mortality and serious heart failure (HF) events during the procedure through discharge and at the different follow-up time-points.

- Evaluate serious device related complications at six and twelve months post-procedure.

The main secondary objectives will be based on the secondary endpoints as described in section 8.1.2.

Change in LV volumes and LV ejection fraction will be evaluated as part of reverse remodeling response, based on echocardiographic measurements:

o LVESV at 6 months

o LVEDV at 6 and 12 months

o LVEF at 6 and 12 months

Analysis will be done for patients were echocardiographic data are available at baseline and six and/or twelve month follow-up.

The echo measures will be validated by an independent core lab.

A patient*s clinical status will be evaluated considering:

o NYHA functional class improvement - The evaluation of the NYHA classification consists of reporting the percentage of patients who improved at least one NYHA class at each follow-up post-implant.
o Death from any cause - The reporting of deaths occurred consists of the percentage of dead patients, the causes of death, the time to death and survival curves.
o HF-related hospitalizations, as defined in section 15.4.
o The incidence of serious device related events assessed at six and twelve months.

A safety assessment will be performed, including all reported events collected for all enrolled patients.

Study description

Background summary

Cardiac resynchronization is a recommended therapy for patients with advanced heart failure, under optimized medical treatment with reduced left ventricular

ejection fraction and prolonged QRS. It reduces morbidity and mortality, and induces reverse left ventricular remodeling. Implantation of a standard biventricular therapy is today a Class I indication in LBBB patients under optimized medical therapy.

Nevertheless, still 30% of the population do not respond to standard biventricular implantation. Alternative RV stimulation sites (septal) have not showed substantial benefit over classical RV apical.

An individual patient meta-analysis showed benefit from CRT when QRS duration exceeds a threshold value of 140 ms. The importance of QRS morphology over QRS duration is supported by results of recent large scale randomized trials showing the absence of clear benefit of standard biventricular implantation in populations of non-LBBB patients, although significant numbers of individuals do take advantage. Similar individual benefit has also been shown even in narrow QRS patients at the condition that preexisting mechanical dyssynchrony was recorded prior to implantation.

Nevertheless, the present status of biventricular therapy (dyssynchrony identification and implantation process) does not take into account mechanical approach, and as a consequence, in the most recent international guidelines4,5, non-LBBB patients have been *downgraded* from Class I to Class IIa for QRS > 150 ms and to Class IIb for QRS between 120 and 150 ms. Patients with narrow QRS are not candidates for the therapy.

The frequent failure of CRT in non-LBBB patients is suspected to be due to more complex and heterogeneous forms of electrical/mechanical dyssynchronies needing more complex and individualized pacing configurations to be corrected.

Study objective

The primary objective of this study is to demonstrate that individually optimized, triple-site biventricular pacing is superior to standard biventricular pacing in reversing ventricular modeling as demonstrated by Echo Left Ventricle End-Systolic Volume (LVESV) at twelve months in patients with non LBBB morphology without increasing the risk of serious procedure and/or device related events at thirty days.

For the primary objective the primary efficacy endpoint is used, change in LVESV at 12 months post-implant, comparing both groups in a superiority context with an expected change of 12% between both groups.

The echo measures will be validated by an independent core lab, which will be blinded to the randomization assignments.

The primary efficacy endpoint will be evaluated in a superiority format, with statistical hypothesis tests formally defined in sections below.

For the primary safety endpoint, a patient*s clinical status will be evaluated considering the incidence of serious procedure and/or device related events assessed from the time of enrollment, during implant, through discharge and up to thirty days follow-up.

Study design

This is a multicenter, international, prospective, randomized, superiority, open label study.

The efficacy endpoint for this study is the change in LVESV at twelve months post-implant between individually optimized, triple-site biventricular pacing and standard biventricular pacing.
LVESV is a standard marker of CRT effectiveness1. Echocardiographic data collected at twelve months follow-up will document the evolution of LVESV as compared to baseline in order to assess reverse ventricular remodeling. The echo measures will be validated by an independent core lab.

The safety endpoint for this study is the rate of all serious procedure and/or device related events reported at thirty days post-implant. Events will be reviewed and adjudicated by an independent Clinical Events Committee.

Intervention

Group 1 : implantation triple site biventricular ICD
Group 2: implantation dual site biventricular ICD

Study burden and risks

No additional 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

Heart failure NYHA II, III, ambulatory IV
LVEF <35%
QRS >140 ms
Non-typical LBBB morphology

Exclusion criteria

Unstable heart failure
Permanent AF
Unstable angina, MI, CABG, PTCI in last 90 days
Renal failure GFR <30ml/min/1.37m2

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-04-2015
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	Triple Site Biventricular Implantable Cardioverter Defibrillator
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	31-08-2015
Application type:	First submission
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
ClinicalTrials.gov	NCT02350842
CCMO	NL52374.075.15