The AdaptResponse clinical study

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The AdaptResponse study is a prospective, randomized, controlled, interventional, single-blinded, multi-center, post-market, global Cardiac Resynchronization Therapy (CRT) in heart failure (HF) clinical study. The purpose of this clinical study is...

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

Summary

ID

NL-OMON53104

Source
ToetsingOnline

Brief title
AdaptResponse study

Condition

- Heart failures

Synonym
heart decompensation, Heartfailure

Research involving
Human

Sponsors and support

Primary sponsor: Medtronic Bakken Research Center
Source(s) of monetary or material Support: Industrie/bedrijf

Intervention

Keyword: AdaptivCRT(aCRT) Algorithm, Cardiac Resynchronization Therapy, Heart Failure

Outcome measures

Primary outcome

To test the hypothesis that AdaptivCRT® reduces the incidence of the combined endpoint of all-cause mortality and intervention for heart failure decompensation, compared to standard CRT therapy, in patients with a CRT indication, LBBB and normal AV conduction. Intervention for heart failure decompensation (HF event) is defined as an event requiring *invasive intervention (i.e. IV diuretics, ultrafiltration, or equivalent)* or inpatient hospitalization*.

Secondary outcome

•To test the hypothesis that aCRT ON reduces all-cause mortality compared to aCRT OFF.

•To test the hypothesis that aCRT ON reduces the rate of intervention for heart failure decompensation compared to aCRT OFF.

•To test the hypothesis that aCRT ON increases the proportion of patients that improve on the Clinical Composite Score (CCS) compared to aCRT OFF, at 6 months of follow-up.

•To test the hypothesis that aCRT ON reduces the incidence of AF compared to aCRT OFF.

•To test the hypothesis that the change in quality of life, measured by the KCCQ, in the aCRT ON group is better than the change in the aCRT OFF group.

•To test the hypothesis that the change in health outcome, measured by the EQ-5D, in the aCRT ON group is better than the change in the aCRT OFF group.

•To test the hypothesis that aCRT reduces the incidence of all-cause

re-admissions after a heart failure (HF) admission within 30-days of the index

event.

•To assess cost-effectiveness of CRT devices with the aCRT algorithm relative

to traditional CRT devices.

Study description

Background summary

CRT is an established therapy for patients with HF symptoms, left ventricular systolic dysfunction, and a wide QRS. However, the magnitude of clinical and hemodynamic benefit of CRT varies significantly among its recipients with no clinical improvement in approximately one third. Evidence from the Medtronic pre-market approval aCRT study has demonstrated that aCRT-optimized CRT is at least as effective as echo optimized BiV pacing in terms of CCS (73.6% improved in aCRT arm vs. 72.5% in echo optimized arm, with a non-inferiority margin of 12%, p=0.0007). Additionally, a comparison with a historical echocardiographic AV-optimized CRT cohort indicated that the aCRT algorithm increased the proportion of patients with an improved CCS by 11.9% (95% CI: 2.7% to 19.2%).Importantly, a post-hoc sub-analysis of the Adaptive CRT Clinical Study showed that in patients with sinus rhythm, normal AV conduction and LBBB, more aCRT patients improved in their CCS compared with the echo arm (80.7% vs. 68.4%, p=0.04). In this subgroup the aCRT patients received LV-only pacing 64.0% ± 32.8% of the time.Additionally, in an unpublished analysis on extended follow-up duration in patients with normal AV conduction, there was a lower risk of death or HF hospitalization (HR=0.71, 95% CI: 0.40-1.27, p=0.25) with aCRT. Also a greater proportion of aCRT patients improved in CCS at 6 (81% vs.69%, p=0.041) and 12 months (77% vs. 66%, p=0.076) than echocardiography-optimized control patients. Furthermore, over the longer term follow-up (20.2 + 5.9 months) the aCRT algorithm has been shown to reduce the risk of the incidence of 48 consecutive hours in AF (HR=0.54 [95% CI 0.31-0.93]; p=0.03) and aCRT patients without history of AF were less likely to develop persistent AF (HR=0.44 [95% CI 0.19-1.03]; p=0.05).Further investigation of clinical outcomes over longer follow-up is needed to support the benefit of aCRT. Therefore the AdaptResponse study is designed to test the hypothesis that the aCRT algorithm reduces the incidence of total mortality and heart failure decompensation events, increases the proportion of patients with an improved CCS and reduces the incidence of persistent or permanent AF in CRT

patients with normal AV conduction and LBBB.

Study objective

The AdaptResponse study is a prospective, randomized, controlled, interventional, single-blinded, multi-center, post-market, global Cardiac Resynchronization Therapy (CRT) in heart failure (HF) clinical study. The purpose of this clinical study is to test the hypothesis that market released CRT devices which contain the AdaptivCRT® (aCRT) algorithm have a superior outcome compared to standard CRT devices in CRT indicated patients with normal AV conduction and left bundle branch block (LBBB).

Study design

Following enrollment and baseline assessment, eligible subjects will be implanted with a CRT system containing the aCRT algorithm and randomized in a 1:1 fashion to either treatment (aCRT ON) or control (aCRT OFF) groups. Study subjects will be followed for a minimum of 24 months or until study closure, whichever comes first.

Intervention

Randomization to aCRT ON versus aCRT OFF (programming of the aCRT) and the 2 questionnaires

Study burden and risks

There is no additional risk for subjects participating in the study.

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

* Subject is indicated for a CRT device according to local guidelines.
* Subject has, minimally:
o Sinus Rhythm at time of enrollment.
o Left Bundle Branch Block (LBBB)
o Intrinsic, normal AV conduction
o Left ventricular ejection fraction less than or equal to 35%
o NYHA class II, III or IV

Exclusion criteria

* Subject is not expected to remain available for at least 2 years of follow-up visits.
* Subject has permanent atrial arrhythmias for which pharmacological therapy and/or
cardioversion have been unsuccessful or have not been attempted
* Subject is, or previously has been, receiving CRT.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-07-2015
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO Date:	12-06-2015
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	06-11-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-01-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-05-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-04-2022
Application type:	Amendment
Review commission:	METC NedMec

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	NCT02205359
CCMO	NL50365.041.14