Neo Randomized Heart Failure Study

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The purpose of this clinical inestigation is to verify the efficacy and safety of the CVRx Neo baroreflex Activation Therapy System in subjects with heartfailure.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON38346

Source
ToetsingOnline

Brief title
Neo HF

Condition

- Heart failures

Synonym
heartfailure; decompensatio cordis

Research involving
Human

Sponsors and support

Primary sponsor: CVRx Inc
Source(s) of monetary or material Support: CVRx Inc

Intervention

Keyword: baroreflex, heart failure

Outcome measures

Primary outcome

3.1.1 Primary Efficacy Objective

To determine whether Baroreflex Activation Therapy with the Neo system produces a change in Left Ventricular Ejection Fraction (LVEF) from screening through 6 months of follow-up for subjects treated with Neo therapy relative to standard of care.

3.1.2 Primary Safety Objective

To describe the safety of Baroreflex Activation Therapy utilizing the Neo system by estimating the rate of all system- and procedure-related complications through the 6-month visit.

Secondary outcome

The following secondary endpoints will be compared between the randomized groups:

1. Six-Minute Hall Walk

2. NYHA Classification

3. Quality of Life, as measured by the Minnesota Living With Heart Failure Questionnaire

4. NT-pro BNP

5. Creatinine

6. Central pressure and hemodynamic parameters

7. Electrocardiographic parameters and indices of rhythm status derived from 24-hour Holter recordings

8. Additional echocardiographic parameters.

Study description

Background summary

Despite advances in incidence and control of cardiovascular disease, heart failure (HF) persists as a significant public health problem. It has been estimated that over 6.5 million people in Europe suffer from HF. Prevalence of HF is expected to increase in coming decades as the average age of the population continues to rise.
HF is generally characterized by diminished exercise tolerance, elevated left ventricular filling pressure, fluid retention, predominance of sympathetic influence on autonomic tone, and neurohormonal activation. Rather than being a well-defined disease, HF is a complex syndrome with a spectrum of etiologies.
Baroreceptor activation therapy (BAT) is emerging as a therapeutic option in the treatment of cardiovascular disease. BAT is CE marked for the treatment of hypertension and has been shown to maintain long-term therapeutic effects. BAT is applied through electrical stimulation of carotid baroreceptors, whose associated nerve traffic modulates the body*s chief hemodynamic regulatory mechanism, the baroreflex. Although the baroreflex is commonly associated with blood pressure control, its influence on circulatory regulation is more complex and pervasive. Importantly, the effector mechanisms of the baroreflex are directly applicable to heart failure.
A wealth of historic studies on the baroreflex and more recent clinical and pre-clinical studies of BAT demonstrate that activation of the baroreflex exerts significant impact on the autonomic nervous system, the heart, the vasculature, and the renin-angiotensin-aldosterone system (RAAS) in the setting of hypertension and heart failure. Via these pathways, changes induced by BAT directly address the pathophysiology responsible for HF and its associated symptoms.

Study objective

The purpose of this clinical inestigation is to verify the efficacy and safety of the CVRx Neo baroreflex Activation Therapy System in subjects with heartfailure.

Study design

The Neo Randomized Heart Failure Study will be conducted as a prospective, randomized, study describing the safety and efficacy of the Neo system in the heart failure subjects with a left ventricular ejection fraction <= 35%.
The first 10 subjects will be implanted with a device, followed by 140 subjects

randomized in a 1:1 ratio to receive a device plus medical management or to receive medical management alone. To account for screen failures, up to 300 subjects will be enrolled at up to 30 clinical sites in Europe and Canada. For those receiving a device, therapy will initially be programmed OFF, until two weeks following device implantation, at which point therapy will be turned ON. Study visits will occur at 1, 2, 3, 4, 5, 6, 9 and 12 months post-activation, and semi-annually thereafter. For those randomized to the medical management arm, study visits will occur at 3, 6, and 12 months post-activation, where activation is the intended activation date set prior to randomization.

Intervention

The Neo System is implanted during an operation procedure, which takes place in an operating room under general or local anesthesia. The electrode is wrapped around the carotic sinus at one side of the neck. The battery is subcutaneously placed below the clavicle. The electrode lead is extended through subcutaneously tunnels from the carotic sinus incision to the battery. The mean produre time is 1 - 2 hours.

Study burden and risks

The total burden for a patient in the Operation-group is 60 hours and for a patient in hte Medication group is the burden 20 hours during 2 years. The risks associated with participation are relatively small, an are similar to related surgical procedures involving the neck. These may include infections, bleedings, tissue damages and the occurrence of TIA or stroke. Regular measures are taken during the implant procedure to decrease the risks of infection, bleeding and tissue damage.

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

1.Age at least 21 years ;2.Bilateral carotid bifurcations that are easily interrogated by carotid duplex ultrasound and are below the level of the mandible. ;3.No ulcerative carotid arterial plaques or carotid atherosclerosis producing a 50% or greater reduction in linear diameter in the internal or the distal common carotid, as determined within 45 days prior to randomization. ;4.Left ventricular ejection fraction <= 35% within 45 days prior to randomization. ;5.NYHA Class III within 45 days prior to randomization. ;6.Have a six-minute hall walk test performance: 150m <= 6MW <= 450m within 45 days prior to randomization. ;7.On optimal, stable pharmacological therapy for at least 4 weeks prior to obtaining the baseline echocardiographic measurement, where optimal and stable are defined as follows: Optimal pharmacological therapy: Prescribed to a beta blocker, a diuretic, and an ACE inhibitor or ARB unless contraindicated or not tolerated. These drugs must be used in a manner consistent with their labeling. ;Stable pharmacological therapy: No more than a 50% increase or a 50% decrease of the dosage of any one medication, and post titration of all heart failure medications. ;8.Not currently being treated with dialysis. ;9.Heart rate is between 60 and 110 b/min via a clinic measurement. ;10. If female and of childbearing potential, must use a medically accepted method of birth control (e.g., barrier method with spermicide, oral contraceptive, or abstinence) and agree to continue use of this method for the duration of the study. Women of childbearing potential must have a negative pregnancy test within 14 days prior to randomization. ;11. An appropriate surgical candidate. ;12. Signed a CVRx-approved informed consent form for participation in this study.

Exclusion criteria

1. Known or suspected baroreflex failure or autonomic neuropathy.
2. Body mass index of greater than 40.
3. Significant uncontrolled symptomatic bradyarrhythmias.
4. If the subject has recently received a pacemaker or an ICD implant, the subject may not be

implanted until at least 90 days after the implant procedure. Patients with a CRT(D) implant may not be randomized untill 6 months after the activation of CRT therapy.
5. Solid organ or hematologic transplant.
6. Episode of NYHA class IV heart failure with acute pulmonary edema within 30 days prior to implant.
7. Myocardial infarction, unstable angina, syncope, cerebral vascular accident, SCD, or received defibrillation therapy within the 3 months prior to implant.
8. Prior surgery, radiation, or endovascular stent placement in the carotid sinus region, limiting the ability to place the carotid sinus lead.
9. Heart failure secondary to a reversible or treatable condition such as, cardiac structural valvular disease, acute myocarditis and pericardial constriction.
10. Heart failure secondary to right ventricular failure or right ventricular myocardial infarction.
11. Primary cardiomyopathy or infiltrative heart disease.
12. Asthma, severe COPD (e.g. FEV1<1.5 liter), or severe restrictive lung disease.
13. Non-cardiovascular condition limiting the ability to assess the six-minute hall walk test.
14. Co-morbid medical condition that would adversely affect participation in the study.
15. Life expectancy less than one year.
16. Clinically significant psychological condition that in the physician's opinion would prohibit the subject's ability to meet the protocol requirements.
17. Unable or unwilling to fulfill the protocol medication compliance, testing, and follow-up requirements.
18. Enrolled in another concurrent clinical trial, without prior approval of CVRx.
19. Known allergy to silicone or titanium.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Generic name:	Neo System
Registration:	No

Ethics review

Approved WMO Date:	14-03-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-06-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-12-2012
Application type:	Amendment
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
ClinicalTrials.gov	NCT01471860
CCMO	NL36523.068.11