Cardionomic Cardiac Pulmonary Nerve Stimulation Pilot Study

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

Summary

ID

NL-OMON51129

Source
ToetsingOnline

Brief title
CPNS Pilot Study

Condition

- Heart failures

Synonym
Acute congestive heart failure

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Acute Decompensated Heart Failure, Contractility, Neurostimulation, Right Pulmonary Artery

Outcome measures

Primary outcome

All analyses will be descriptive with no inferential statistical test.

1. Safety Measures through 6-months:

The following measures will be characterized in all enrolled subjects:

• Death

• Serious Adverse Events

• Procedure-related Adverse Events

• System-related Adverse Events

• Therapy-related Adverse Events

2. Performance Measures:

The following measures will be characterized in the Treatment Analysis Set:

• Characterize the change in pressures (e.g., RV dP/dt, RV, SBP, DBP, PA, etc) and heart rate during Therapy OFF and Therapy ON start of therapy and daily assessments

• Characterize the change in cardiac output (via the Fick method) from start of therapy to end of therapy (only calculated in subset of subjects with an arterial line and SpO2 may be used as a surrogate for SaO2)Characterize the change in pressures through the therapy duration

• Characterize the change in mixed venous oxygenation saturation during Therapy OFF and Therapy ON at start of therapy and daily assessments

• Characterize the change in mixed venous oxygenation saturation through the therapy duration

• Characterize echocardiogram assessments during therapy OFF and therapy ON at 48 hours post baseline/randomization

The following measures will be characterized in the modified Intent-to-Treat (mITT) set separately by the Lead-In Phase and the Randomized Phase:• Discharge and follow-up oral medications:

• Medical treatment provided throughout hospitalization (e.g., medication usage, mechanical support, etc)

• Change in NT-proBNP, serum creatinine, BUN and troponin throughout hospitalization

• Change in dyspnea throughout hospitalization compared to enrollment

• Patient Global Assessment throughout hospitalization

• Change in KCCQ-12 from enrollment to 30-days post hospital discharge

• Hospital readmission rates within 30 days post hospital discharge

• Length of hospital stay

• Echocardiogram assessments at baseline and 48 hours post baseline/randomization

• In-hospital mortality

Secondary outcome

Not applicable, all study parameters are described in section above

Study description

Background summary

Heart failure affects an estimated 26 million people worldwide, resulting in more than 1 million hospital admissions each year in both the United States and Europe. Heart failure is a progressive and complex condition that results from the reduced contractility of the heart. Patients who enroll may experience the following symptoms: shortness of breath, tiredness and weakness, swelling in the legs, ankles and feet, or fast and irregular heartbeat

Current treatments for acute decompensated heart failure have remained unchanged for many years and consist mainly of administering drugs to relieve symptoms.

Previous research has shown that stimulation of the cardiopulmonary nerve by the CPNS system can increase the contractility of the heart without increasing the heart rate. The aim of this study is to further investigate the safety and operation of the CPNS system.

Study objective

The objective of the study is to assess the safety and performance of the Cardionomic cardiopulmonary nerve stimulation (CPNS) system in patients with acute decompensated heart failure. The intent of the study is descriptive in nature, without a formal hypothesis testing.

Study design

The CPNS Pilot Study is a prospective, two-phased, multi-center and multinational study.

The study is designed with two phases: the Lead-In Phase and the Randomized Phase.

The purpose of the Lead-In Phase is to gain first experience with the CPNS System in ADHF patients. Up to 30 subjects will be enrolled to refine study methods and develop practical experience.
The Randomized Phase will follow and includes up to 60 subjects 2:1 randomized to characterize outcome differences between treatment and control groups.

All patients will be followed through 6 months post discharge.

Intervention

Patients in phase 1 or patients in phase 2 who are randomised to the CPNS treatment receive the CPNS system implanted:

The CPNS System is a neuromodulation system used to treat ADHF, the sudden or slow deterioration of chronic heart failure. The CPNS System is intended to provide acute (<= 5 days) endovascular stimulation of the cardiac autonomic nerves in the right pulmonary artery in hospitalized ADHF patients.

The system consists of an acute transient neuromodulation pacing catheter (CN2 catheter) placed into the right pulmonary artery through venous access and a modified external stimulator. Through electrical stimulation of the terminal sympathetic nerve branches in the cardiopulmonary plexus, this can provide an inotropic and / or lusitropic therapeutic effect.

The procedure to place the catheter takes place in the cath lab and takes approximately 2 to 3 hours, including the testing to test correct placement. The system will be removed during a +/- 1 hour intervention after a maximum treatment of 5 days.

Detailed description of the implant and explant procedures can be found in the study protocol and the instructions for use.

Patients randomized to the control arm in phase 2 receive standard treatment for their heart failure (standard of care) without a CPNS system.

Study burden and risks

There are risks associated with performing the CPNS catheter implantation, the use of anesthesia, and the CPNS therapy itself. The risks associated with the implantation procedure of a CPNS catheter are comparable to those of a standard cardiac catheterization procedure. These risks are listed below. In addition, the CPNS treatment can also have side effects that we do not yet know.

• Allergic reaction to the catheters, dye or medications used during or after the procedure
• Bleeding that may require blood transfusion
• Complications related to the fluid used to view your vessels under x-ray during the procedure (contrast agent)
• Complications at catheter insertion site (i.e., bruising, pooling of blood (hematoma), infection, numbness, bleeding)
• Nausea and/or vomiting
• Confusion or decreased awareness of surrounding environment (delirium)
• Bruising, blood clots or blood collection
• Collapsed lung
• Damage to blood cells, blood vessels, nerves, or the heart
• Damage to or narrowing of the heart valves
• Death

• Fluid or inflammation around the heart or lungs
• Electrical shock and/or burn
• Heart attack
• High or low blood pressure
• Immune response to device components
• Infection
• Internal bleeding
• Irregular or stopped heartbeat that may or may not require an electrical shock
• Kidney damage
• Obstruction of blood flow in the arteries or heart
• Pain or discomfort - during or after the procedure that may require treatment with pain medications
• Surgical intervention for device malfunction or removal
• Swelling or distension

There are additional risks that could possibly be associated with the test procedures performed for the clinical study. These potential risks are described below:
• There are risks related to the blood tests required for the study (e.g., excessive bleeding, fainting or light-headedness, pooling of blood (hematoma), infection, or requirement of multiple punctures to locate a vein to draw the sample).
• This study involves a small amount of radiation during the procedure angiograms. Radiation may slightly elevate the risk for cancer.

The full list of risks associated with general anesthesia, the procedure and treatment as well as the risk mitigation process is described in the study protocol (section 9).

Contacts

Public
Cardionomic Inc

Campus Drive 601 (Suite 12)
New Brighton, MN 55112
NL
Scientific
Cardionomic Inc

Campus Drive 601 (Suite 12)
New Brighton, MN 55112
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Subjects must meet all the following inclusion criteria to be eligible to participate in this study:
1. At least 18 years of age, or older if required by local law
2. Admitted to the hospital with a principal diagnosis of acute decompensated heart failure.
3. BMI adjusted BNP >= 500 pg/mL or NT-pro-BNP >= 2000 pg/mL; 4% reduction in BNP/NT-proBNP for every increase of 1 kg/m2 in BMI above a reference of 20kg/m2 (Refer to Appendix B: BNP/NT-proBNP corrected for BMI)
4. Left ventricular ejection fraction <= 45%; documented within previous 12 months
5. At least one sign or symptom of fluid overload
6. At least one of the following:
o Persistent inadequate diuretic response
o At least one sign or symptom of low perfusion

Exclusion criteria

1. First IV treatment upon presentation in hospital to randomization is > 48 hours
2. Received an inotrope during current hospitalization or anticipated to receive an inotrope in the 12 hours following enrollment
3. Requires mechanical support (e.g., mechanical circulatory support, ultrafiltration) or anticipated to receive mechanical support in the 12 hours following enrollment
4. Manually measured systolic blood pressure < 80 mmHg at screening
5. Manually measured systolic blood pressure > 130 mmHg at screening
6. Symptomatic hypotension

7. eGFR < 25 mL/min/1.73m2
8. Has an active infection
9. Has an active or passive implantable device that may interfere with CPNS therapy per physician discretion
10. Has a cardiac resynchronization therapy (CRT) device or a pacemaker
11. Has an implantable cardioverter defibrillator (ICD) and is pacemaker dependent or has had a sustained VT/VF episode in the previous 90 days (a subject can be enrolled if he/she meets this criterion, the physician deems it appropriate to suspend therapies during hospitalization and leads have been implanted for at least six months prior to the study procedure) 12. Permanent or persistent atrial fibrillation with uncontrolled ventricular response (ventricular rate > 125 BPM) at time of enrollment
13. Unstable angina or documented myocardial infarction within last 30 days
14. Prior heart transplant
15. History of severe mitral or aortic stenosis or regurgitation
16. History of pulmonary embolism within the last 6 months
17. History of hyper-coagulation disorders
18. History of more than one CABG procedure
19. History of severe pulmonary hypertension (pulmonary arterial systolic pressure >= 75 mmHg)
20. Diagnosis of primary pulmonary hypertension
21. Diagnosis of congenital heart disease
22. Participating in concurrent trial unless approved by Cardionomic study manager
23. Pregnant or childbearing age and not on reliable form of birth control
24. Allergy to nickel, fentanyl, midazolam, propofol, heparin, eggs, egg products, soybeans or soy products
25. Unwilling or unable to provide consent
26. Exclusion criteria by local law (e.g., age, prisoner, etc)

Study design

Design

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):	13-04-2021
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	Cardiac Pulmonary Nerve Stimulation System (CPNS)
Registration:	No

Ethics review

Approved WMO Date:	28-10-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-07-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NCT04814134
CCMO	NL75779.000.21