A study to evaluate the DC Devices, Inc. IASD* System II to REDUCE Elevated Left Atrial Pressure in Patients with Heart Failure

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The objective of this clinical study is to evaluate the safety and performance of the IASD System II in the treatment of heart failure patients with elevated left atrial pressure, who remain symptomatic despite appropriate medical management.

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

Summary

ID

NL-OMON45159

Source
ToetsingOnline

Brief title
REDUCE LAP-HF TRIAL

Condition

- Heart failures

Synonym
Heart Failure

Research involving
Human

Sponsors and support

Primary sponsor: Corvia Medical, Inc.

Source(s) of monetary or material Support: Corvia Medical;Inc.;sponsor of the study

Intervention

Keyword: Heart Failure, Medical device, Safety and performance

Outcome measures

Primary outcome

The primary safety endpoint is the percent of subjects who experience major adverse cardiac and cerebrovascular events (MACCE) defined as death, stroke, MI; or subjects who experience a systemic embolic event (excluding pulmonary thromboembolism); or subjects who require surgical implant removal within 6 months from day of implant.

The primary device performance endpoints are:

* The percent of subjects who have successful device implantation, defined as deployment at the intended location during the index procedure

* The percent of subjects with reduction of PCWP, and demonstration of left to right flow through the device at 6 months

Secondary outcome

1. Incidence of major adverse cardiac events through 6-months post implant

2. Incidence of all serious adverse events (SAEs) through 6-months post implant

3. All-cause, and heart failure related hospitalizations; and number of hospitalization days, ICU days, through 6 months

4. All-cause mortality, CV mortality and heart failure related mortality through 6 months

5. Changes in invasive and noninvasive hemodynamic measures (at rest and when

performed at baseline, also during exercise) assessed compared to baseline at 6 months by a core laboratory.

a. The percent of patients with reduction of PCWP below the baseline value at rest and during exercise;

b. Changes in pulmonary and systemic cardiac output; and in PA pressures

6. Changes in BNP and/or NT-pro-BNP assessed at 6 months compared to baseline

7. Changes in Investigator assessed NYHA classification assessed at 6 months compared to baseline

8. Changes in RA, LA, LV and RV dimensions, volume, and function as measured by echocardiography, assessed compared to baseline at 6 months by a core laboratory

9. Improvement in Quality of Life (QOL) as measure by Minnesota Living with Heart Failure Questionnaire (MLWHFQ) assessed at 6 months compared to baseline

10. Improvement in QOL as measured by EQ-5D-3L assessed compared to baseline at 6 months

11. Incidence of cerebrovascular events, through 6-months post implant

12. The percent of subjects with an improvement in exercise tolerance as assessed by 6MWT at 6 months compared to baseline

13. Incidence of newly acquired atrial arrhythmia, through 6-months post implant

14. Incidence of new onset or worsening of kidney dysfunction (defined as eGFR decrease of > 20 ml/min) through 6-months post implant

15. Implant embolization and clinically significant device migration, defined

as serious adverse event(s) probably related to device migration

Study description

Background summary

Heart failure is defined as a disorder of the heart pump function with associated symptoms. Symptoms can be very different, but include at least his fatigue and / or dyspnea.
Mortality is high and depending on the severity of the heart failure. Fifty percent of patients deceased within five years (with severe heart failure, within one year) after diagnosis.
The prevalence of heart failure among the population is 2-2.5%. Currently there are 200,000 patients with heart failure in the Netherlands. The prevalence increases sharply with increasing age.
With increasing aging population combined with improved medical techniques of cardiac and non-cardiac diseases, the prevalence of heart failure is increasing.
This study is evaluating a new device (Inter-atriale septum Device (IASD) System II) that is permanently implanted in the heart and is designed to reduce the increased pressure due to heart failure, by creating a small permanent opening between the two upper chambers in the heart. The relief of this pressure by the study device may reduce some or all of the symptoms a subject is experiencing.

Study objective

The objective of this clinical study is to evaluate the safety and performance of the IASD System II in the treatment of heart failure patients with elevated left atrial pressure, who remain symptomatic despite appropriate medical management.

Study design

A prospective, Non-randomized; Open label study. Up to 100 subjects at up to 30 investigational Sites will be enrolled in order to obtain 50 subjects with 6 month follow-up.

Intervention

Percutaneous implantation (permanent) of the IAS System II.

Study burden and risks

Heart Catheterization Risks
The main risks of a heart catheterization include but are not limited to:
* pain at the catheter insertion site,
* abnormal heart rate,
* excessive collection of blood at insertion site,
* fever after the procedure,
* significantly increased or decreased blood pressure sometimes requiring medication,
* blood loss sometimes requiring blood replacement,
* allergic reaction to the dye used to take pictures of the heart,
* temporary stoppage of breathing,
* reaction to the anesthesia medications,
* accidental creation of an abnormal passage between an artery and vein,
* obstruction of a blood vessel by an air bubble,
* blockage of a blood vessel by a blood clot,
* injury to a nerve at the insertion site,
* appearance of a bulge in a blood vessel,
* the tearing or poking of a hole through a blood vessel or heart.
These risks are uncommon. To reduce the likelihood of these risks, the study sponsor carefully selects and trains, and supports study doctors that have significant experience with similar types of procedures.

Study Device and Implantation Procedure Risks
The main risks of having the study device implanted are similar to the risks listed above for heart catheterization.
In addition, the following risks have been identified:
* small clots may form on the implant itself and be released into the blood circulation.
* stroke,
* heart failure,
* heart attack
* death
* study device embolization: the study device does not stay in place and floats away into another part of the heart or into a blood vessel..
* One or more of the study device arms rubs or pokes a hole into a blood vessel or part of the heart. If this happens, urgent surgery may be required to remove the device and repair the tear or hole.
* Study device fracture : break of one or more of the study device arms once it is in the heart
* Callous
* Blood clot
* Infection
* Allergic reaction to the study device
* Heart rhythm disturbances (for example, slow rate)
* Perforation of the blood vessel or part of the heart
* Fluid around the heart
* the heart failure does not improve during the study, or worsens.

To minimize those risks, the study doctor has been carefully trained on the study device placement; in addition:
* the study device is made of materials that were specifically selected because of their strength and resistance to wear
* the study doctor will give the patient appropriate medications before and after the procedure, and during the study follow up period to reduce this risk.
* the study doctor uses special imaging equipment during the procedure to see the study device and make sure it is placed in the correct position in the heart.
* the study device shape and materials were selected to hold it in place.
* if the device does move out of place during the implant procedure, your study doctor may use a catheter to retrieve and remove it. If the device moves out of place after the patient has been discharged from the hospital, the study device may need to be removed during open heart surgery.
* in the unlikely event that the study device breaks into several pieces, a piece of it could potentially break off and float away to another place in the patient's body. Depending on its final location, surgery may be required to remove the piece and the remaining broken device.

It is not expected that patients enrolled in this study will have these complications. Side effects are usually temporary and manageable.
If we learn of any new risks while this study is ongoing, the study doctor will make the patients aware of them as soon as possible.

Exercise Testing Risks
The risks related to the exercise stress test are fatigue, muscle soreness, irregular heartbeat, chest pain, sudden heart attack, stroke, or death. To minimize these risks trained medical professionals will be present during this procedure. In addition, the patient will have his heart rate monitored continuously throughout the testing. The patient will also have your blood pressure and your rate of perceived exertion monitored throughout the testing.

Echocardiogram Risks
In addition to the risks listed above, there are possible, although very rare, risks with echocardiograms. A potential risk of the echocardiogram when the tube is placed into the patient's esophagus is a tear or poking of your esophagus, the tube connecting the mouth to the stomach. This tear could cause bleeding or infection that is potentially life threatening, and in some cases may require surgery for repair. If the study doctor uses intra-cardiac echocardiogram during the implant procedure, potential risks are puncture of a blood vessel as it travels to the heart or puncture of the heart, both of which may be life threatening and may require urgent surgery to correct. To reduce the likelihood of these unlikely risks, specially trained doctors perform these procedures.

Blood Test Risks
There are some side effects that can happen when the patient has blood drawn.

This includes excessive bleeding, fainting or feeling light-headed, hematoma (blood pooling under the skin), infection (a slight risk any time the skin is broken).

Pregnant women
This treatment may have unforeseeable risks the embryo or foetus if the subject ispregnant at the moment of the procedure. Woman of childbearing age and fertile are not authorized to take part of this clinical trial.

Benefits
There is no guarantee that the subject will benefit from participation in this study.
Potential benefits to patients implanted with the study device include the following:
* Reduction in shortness of breath
* Reduction in the number of hospitalizations and/or hospital days
* Reduction in the number of emergency room visits
* Reduction in medications
* Improved exercise tolerance
* Improved quality of life
* Improved life expectancy

By participating in this study, the patient will help others by providing information that may be used to develop new treatments for patients with similar conditions.

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

Candidates for the study must meet ALL of the following inclusion criteria:
1. Chronic symptomatic Heart Failure (HF) documented by one or more of the following:
a. New York Heart Association (NYHA) Class II/III/ambulatory class IV symptoms (Paroxysmal nocturnal dyspnea, Orthopnea, Dyspnea on mild or moderate exertion) at screening visit; or signs (Any rales post cough, Chest x-ray demonstrating pulmonary congestion,) within past 12 months;
b. One hospital admission for which HF was a major component of the hospitalization within the 12 months prior to study entry (transient heart failure in the context of myocardial infarction does not qualify);
c. On-going management with recommended heart failure medications and comorbidities for several months according to the guidelines (2012 ESC Guidelines for diagnosis and Treatment of Acute and Chronic Heart Failure).
2. Age * 40 years old
3. Left ventricular ejection fraction (obtained by echocardiography) * 40%
4. Elevated left ventricular filling pressures with a gradient compared to CVP documented by :
a. PCWP (end expiratory) or LVEDP (end expiratory) at rest * 15 mmHg, and greater than CVP, OR
b. PCWP (end expiratory) during supine bike exercise * 25mm Hg, and CVP < 20 mm Hg
5. Subject has been informed of the nature of the study, agrees to its provisions and has provided written informed consent, approved by the EC
6. Subject is willing to comply with clinical investigation procedures and agrees to return for all required follow-up visits, tests, and exams
7. Trans-septal catheterization and femoral vein access is determined to be feasible

Exclusion criteria

Candidates for this study will be excluded if ANY of the following conditions are present:
1. MI and/or percutaneous cardiac intervention within past 3 months; CABG in past 3 months, or current indication for coronary revascularization
2. Cardiac Resynchronization Therapy initiated within the past 6 months
3. Severe heart failure defined as:
a. ACC/AHA/ESC Stage D heart failure, Non-ambulatory NYHA Class IV HF;
b. Cardiac Index < 2.0 L/min/m2
c. Requiring inotropic infusion (continuous or intermittent) within the past 6 months
d. Patient is on the cardiac transplant waiting list
4. Inability to perform 6 Minute Walk Test
5. Known significant coronary artery disease (stenosis >70%)
6. History of stroke, transient ischemic attack (TIA), deep vein thrombosis (DVT), or pulmonary emboli within the past 6 months
7. Known severe carotid artery stenosis (> 70%)
8. Presence of significant valve disease defined by echocardiography as:
a) Mitral valve regurgitation defined as grade >2+ MR
b) Tricuspid valve regurgitation defined as grade * 2+ TR;
c) Aortic valve disease defined as * 2+ AR or moderate AS
9. Hypertrophic cardiomyopathy, restrictive cardiomyopathy, constrictive pericarditis, cardiac Amyloidosis or other infiltrative cardiomyopathy (e.g. hemochromatosis, Sarcoidosis)
10. Subject is contraindicated to receive either dual antiplatelet therapy or warfarin analogue; or has a documented coagulopathy
11. Atrial fibrillation with resting HR > 100 BPM
12. Arterial Oxygen saturation < 95% on room air
13. Significant hepatic impairment defined as 3X upper limit of normal of transaminases, total bilirubin, or alkaline phosphatase
14. Right ventricular dysfunction, defined as
a. More than mild RV dysfunction as determined by TTE: OR
b. TAPSE < 1.4 cm: OR
c. RV volume * LV volume on echo estimate; OR
d. Echocardiographic or clinical evidence of congestive hepatopathy
15. Resting CVP > 14 mmHg
16. Evidence of pulmonary hypertension with PVR > 4 Woods Units (mm Hg/L/min)
17. Chronic pulmonary disease requiring home oxygen, OR hospitalization for exacerbation in the 6 months prior to study entry, OR significant chronic pulmonary disease defined either as FEV1 <1, or in the opinion of the investigator
18. Currently participating in an investigational drug or device study. Note: Trials requiring extended follow-up for products that were investigational but have since become commercially available are not considered investigational trials
19. Life expectancy less than 12 months for non-cardiovascular reasons
20. Echocardiographic evidence of intra-cardiac mass, thrombus or vegetation.
21. Known or suspected allergy to nickel
22. Fertile women
23. Currently requiring dialysis; or e-GFR <25ml/min
24. SABP >170 despite appropriate medical management
25. Subjects in whom trans-esophageal echocardiography (TEE) is contraindicated
26. Subjects with existing Atrial Septal Defects. Subjects with a Patent Foramen Ovale (PFO),

who have elevated filling pressure despite the PFO are allowed.
27. Subjects on immunosuppression or systemic steroid treatment (>10 mg prednisone/day)
28. Subjects who have diagnosed scleroderma
29. In the opinion of the investigator, the subject is not an appropriate candidate for the study

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-02-2014
Enrollment:	15
Type:	Actual

Medical products/devices used

Generic name:	IASD System II
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	24-01-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-06-2014

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-04-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-10-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-08-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NCT01913613
CCMO	NL46012.100.13