A Prospective, Multicenter, Non-Randomized, Single-Arm, Open-Label Clinical Study to Demonstrate the Safety and Performance of the Leaflex* Performer

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The purpose of this study is to demonstrate the safety and performance of the Leaflex* when used for aortic valve repair in patients with symptomatic severe aortic stenosis. The main performance objective is to demonstrate an acute increase in...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Cardiac valve disorders
Study type	Interventional

Summary

ID

NL-OMON55148

Source
ToetsingOnline

Brief title
The Leaflex* Standalone Study

Condition

- Cardiac valve disorders

Synonym
Aortic Stenosis, narrowing of the aortic valve

Research involving
Human

Sponsors and support

Primary sponsor: Pi-Cardia Ltd.
Source(s) of monetary or material Support: Pi-Cardia

Intervention

Keyword: Aortic Stenosis, Transcatheter heart valve intervention

Outcome measures

Primary outcome

Primary performance endpoint - change in AVA measured by echocardiography before treatment with the Leaflex* (within 7 days prior to index procedure) and after treatment with the Leaflex* (within 3 days post index procedure).

Main safety endpoints:

* Composite rates of all-cause mortality and stroke (according to VARC-2 definitions48) through 30 days post the procedure.

* Worsening of aortic regurgitation (AR) by >1 grade assessed by echocardiography at 30 days post the procedure compared to before treatment with the Leaflex* (within 7 days prior to treatment) and to after treatment with the Leaflex* (within three days post treatment).

* Assessment of all adverse events from enrollment up to 12 months post procedure.

Secondary outcome

Secondary performance endpoints:

* Post Leaflex* AVA, AVAi and peak and mean pressure gradients measured by echocardiography after treatment with the Leaflex* (within 3 days post index procedure).

* Intra-procedural change of invasive transvalvular pressure gradients, computed as difference in mean and in peak-to-peak pressure gradients across the aortic valve immediately prior to treatment with the Leaflex* and immediately following treatment with the Leaflex*.

* Change in AVA and in peak and mean pressure gradients, measured by echocardiography, from before treatment with the Leaflex* (within 7 days prior to index procedure) and from after treatment with the Leaflex* (within 3 days post index procedure) to 1, 3, 6, 9 and 12 months post procedure.

* Change in 6MWT from baseline to 1, 6 and 12 months post procedure.

* Change in quality of life from baseline to 1, 6 and 12 months post procedure.

Note: AVA and AVAi shall be computed by echocardiography as Effective Orifice Area (EOA) and Effective Orifice Area Index (EOAi).

Study description

Background summary

Aortic valve stenosis (the blood flow from the heart to the body is reduced because the passage through the aortic valve is reduced) causes symptoms such as shortness of breath.

Standard treatment for aortic stenosis is surgical valve repair or Transcatheter Aortic Valve Implantation (TAVI). However there remains a population of patients that require some treatment of their aortic stenosis but are not candidates for surgical repair or TAVI due to either co-morbidities, age or short life expectancy. Currently, these patients are left with the option of Balloon Aortic Valvuloplasty (BAV) or standard medical treatment.

The use of BAV is limited, mainly due to the very short durability of its therapeutic effect: early recoil or restenosis which occur with within 6*12 months in most patients, and mid- and long-term outcomes which are similar to the natural history of aortic stenosis.

The Leaflex* is a 16Fr catheter, introduced trans-femorally, designed to create scoring lines on the aortic surface of the aortic valve leaflets and score the calcific deposits within the leaflets that restrict leaflet motion and cause the clinical symptoms of aortic stenosis. The Leaflex* treatment is intended to increase leaflet pliability and mobility, and consequently increase the aortic valve area.

Study objective

The purpose of this study is to demonstrate the safety and performance of the Leaflex* when used for aortic valve repair in patients with symptomatic severe aortic stenosis. The main performance objective is to demonstrate an acute increase in aortic valve area (AVA).

Study design

Prospective, Multicenter, Non-Randomized, Single-Arm, Open-Label, interventional Clinical Study

Intervention

all patients undergo a trans-femoral catheter treatment of the aortic heart valve.

Study burden and risks

The primary risks and discomforts that may be associated with the use of the Leaflex are expected to be similar to complications associated with other trans-catheter aortic valve interventions. The blood examination before the Leaflex procedure is standard prior to any trans-catheter aortic valve interventions.

The burden and risk associated with the screening procedure is similar to the procedures performed prior to TAVI and is limited to:
* Echo (TTE) - unless a TTE performed within 60 days of screening is available
* Cardiac gated CT scan with and without contrast - unless a CT scan performed within 6 months of screening is available.

The burden and risks associated with study specific examinations during follow-up includes examinations that patients with aortic stenosis would typically undergo, althought the frequency of the follow-up visits (standard after 1 and 12 months) is increased (study 1, 3, 6, 9, and 12 months) and includes:

Echography heart (TTE)
Electrocardiography (ECG)

Physical examination
Medical evaluation
Neurological examination (in case of known/suspected TIA/CVA)
6 minute walk * test en 2 quality of life questionnaires (baseline, 1, 6 ,12 months)
5-meter walk-test (baseline)
Modified Physical Performance Test (PPT) (baseline)

Contacts

Public
Pi-Cardia Ltd.

Fikes Street 5
Rehovot 7632805
IL
Scientific
Pi-Cardia Ltd.

Fikes Street 5
Rehovot 7632805
IL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Male and female age >18 years.
2. Patient with severe aortic stenosis.
3. Senile degenerative severe aortic valve stenosis with echocardiography

derived criteria: mean gradient > 40 mmHg OR jet velocity > 4.0 m/s OR AVA * 1.0 cm2 OR AVA index (AVAi) * 0.6 cm2/m2.
4. NYHA Functional Class * 2 OR exercise test that demonstrates a limited exercise capacity, abnormal BP response, or arrhythmia.
5. Not recommended by the heart team for immediate treatment with surgical or transcatheter aortic valve replacement.

Exclusion criteria

1. Aortic valve is unicuspid, bicuspid, or non-calcified.
2. Severe aortic regurgitation (>2+).
3. An exceptional aortic valve leaflet Calcium morphology, as determined by the CT Core Lab.
4. Pre-existing mechanical or bioprosthetic aortic or mitral valve.
5. Iliofemoral vessel characteristics that would preclude safe placement of the introducer sheath.
6. Coronary disease that, in the opinion of the heart team, should be treated; or treatment of coronary disease * 1 month prior to index procedure.
7. Aortic balloon valvuloplasty * 3 months prior to index procedure.
8. CVA or TIA * 12 months prior to index procedure.
9. History of a myocardial infarction (MI) * 6 weeks prior to index procedure.
10. Previous or current bacterial endocarditis.
11. Ongoing severe infection or sepsis.
12. Life expectancy * 12 months post index procedure due to morbidity other than aortic valve related.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	10

Type:	Anticipated

Medical products/devices used

Generic name:	Leaflex Performer
Registration:	No

Ethics review

Approved WMO Date:	25-09-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-12-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-04-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-05-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
CCMO	NL73895.078.20