A First-in-Human Study to Assess Safety and Performance of the Cardiac Implants Percutaneous Ring Annuloplasty System in the Treatment of Patients with Functional Tricuspid Regurgitation

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The objective of this study is to evaluate the safety and performance of the DaVingi* TR System for the treatment of patients with functional tricuspid regurgitation within its intended use.The study will:• Evaluate the safety and feasibility of...

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

Summary

ID

NL-OMON55204

Source
ToetsingOnline

Brief title
Percutaneous Ring Annuloplasty System FIH Study

Condition

- Cardiac valve disorders

Synonym
functional tricuspid regurgitation (TR)

Research involving
Human

Sponsors and support

Primary sponsor: Cardiac Implants LLC.
Source(s) of monetary or material Support: Cardiac Implants LLC.;sponsor van de studie.

Intervention

Keyword: Functional Tricuspid Regurgitation, Percutaneous Ring Annuloplasty System

Outcome measures

Primary outcome

Safety endpoints

- Implant Device SADE: the incidence and severity of device-related serious adverse device effects (SADE) from time of index implant procedure through 30 days post-implant.

- Adjustment Device SADE: the incidence and severity of device-related serious adverse device effects (SADE) from time of index adjustment procedure through 30 days post-adjustment.

Performance Endpoints

- Implant Device Technical Success: Rate of successful delivery, deployment and implantation of a DaVingi* TR ring onto the tricuspid annulus, defined as
(a) number of stakes embedded in tissue at the end of the procedure (by fluoroscopic and/or echocardiographic assessment)
(b) the ring is in stable position on the atrial side of the tricuspid valve as evidence by post-procedure cine CT showing concordant motion of the stakes with the plane of the tricuspid annulus.

Note: Implant Device Technical Success shall be assessed at the time of the index procedure after all DaVingi* TR ring devices have been used at the annulus

- Adjustment Device Technical Success: Rate of successful adjustment of the DaVingi* TR ring at the tricuspid annulus (i.e., level of annular contraction desired by physician is achieved).

The co-primary performance endpoint will also be reported for each individual component of the endpoint.

Secondary outcome

Safety Endpoints

• Incidence of device-related major adverse cardiac events (MACE)5 through 30 days post-implant and through 365 days post-index adjustment procedure.

• Rate of procedure-related serious adverse events (SAE) through 30 days post-implant and through 365 days-post index adjustment procedure.

Performance Endpoints

• Implant Procedural Success: Implant Device Technical Success met and no SADE(s) within 24 hours post index implant procedure.

• Adjustment Procedural Success: Adjustment Device Technical Success met and no SADE(s) within 24 hours post index adjustment procedure.

• Ability to maintain improvement in TR: at 30, 90, 180- and 365-days post-index adjustment procedure, relative to baseline.

• Change in Quality of Life assessment: by KCCQ at 90, 180- and 365-days years post-index adjustment procedure, relative to baseline.

• Change in 6MWT: at 90, 180, and 365 days post-index adjustment procedure, relative to baseline.

• Number of heart failure hospitalizations: through 365 days post-index adjustment procedure, as compared to 365-day interval prior to enrollment.

• The need for re-intervention for TR: at 30, 90, 180- and 365-days post-index adjustment procedure.

• Changes in NYHA Class: at 30, 90, 180- and 365-days post-index adjustment procedure, relative to baseline.

Study description

Background summary

Functional TR (tricuspic regurgitation) is primarily due to tricuspid annular dilation and right ventricular (RV) enlargement and dysfunction; it occurs most often secondary to left-sided heart disease, especially in the setting of mitral valve pathology.

The tricuspid valve has three leaflets (anterior, posterior, and septal). The anterior leaflet is largest in surface area and is almost always staked by a single papillary muscle; affected most by annular dilation, functional TR occurs when annular dilation reduces coaptation of the anterior leaflet. RV enlargement can result in papillary muscle displacement, another mechanism of functional TR.

Repair of the leaking tricuspid valve curently involves a surgical procedure to fix a ring around the atrial side of the annulus of the tricuspid valve. The surgical treatment can have significant risk for patients with other comorbidities.

Cardiac Implants is developing a percutaneous catheter-based device to repair tricuspid regurgitation. The device is designed to deliver a small, flexible, fabric covered ring around the atrial side of the annulus of the tricuspid

valve. Once implanted, the ring is left in place for 90 days until the ring and the stakes are embedded in new connective tissue grown due to normal foreign body reaction. This process is designed to secure the ring in place and allow safely adjusting the annulus of the valve using the ring*s internal adjustment cord under physiologic conditions and with echocardiographic guidance in order to diminish valve regurgitation.

The annuloplasty ring is a small multi-element ring, consisting of an outer fabric layer, a pre-set stake array and internal adjustment cord that can be adjusted at a later chronic stage after the outer layer of the ring and stakes are encapsulated in new tissue growth. Once implanted, the ring is designed to serve as a foundation for promoting new annular tissue growth, effectively growing a new adjustable annulus around the valve.
In this study, the ring will be delivered percutaneously or via surgical venotomy, to accommodate a 22F vascular sheath size using a right jugular vein access approach.

The Cardiac Implants progressive approach to valve annuloplasty repair is designed to enable a low risk and effective means for physicians to perform valve annuloplasty as a treatment for annular dilatation and valve regurgitation of heart valves.

Study objective

The objective of this study is to evaluate the safety and performance of the DaVingi* TR System for the treatment of patients with functional tricuspid regurgitation within its intended use.
The study will:
• Evaluate the safety and feasibility of delivery & implantation of annuloplasty ring.
• Evaluate the safety and feasibility of ring adjustment following healing period.
• Evaluate the effect of annuloplasty on tricuspid regurgitation.

Study design

The study is a prospective open label, multi center first-in-human study. Up to 30 subjects will be treated.

Intervention

The enrolled patient will undergo 2 interventions.
1) The index implant procedure. The initial percutane transkatheter implantation of the Cardiac Implants DaVingi* TR annuloplastyring.
2) The index adjustment procedure visit at 90 days post implantation. The percutane transkatheter adjustment of the implanted Cardiac Implants DaVingi*

TR annuloplastyring using the same technique as for the implantation.

Study burden and risks

Benefit (Protocol 5.2.1)
1. The Cardiac Implants DaVingi* TR System is expected to bear a significant lower risk than cardiac surgery.
2. Moreover, it may be the only option for a group of patients with additional comorbidities, in the presence of high risk for surgery (after maximizing the medical therapy (i.e. diuretics)) and deteriorating symptomatic disease state.
3. In addition, the investigational device is not preventing an implanted subject from being treated later with any know therapy (percutaneous or surgical) across the valve, such as: pacemaker lead implantation, ablation, surgical annuloplasty and valve replacement.

(Protocol 18.6) As noted in the protocol section, for purposes of this study, various events are not considered reportable adverse events because they are normally expected to occur in conjunction with treatment of tricuspid regurgitation or structural heart interventional procedures, or are associated with customary, standard care of subjects undergoing minimally invasive cardiovascular intervention.

(Protocol 18.10) Possible risks and adverse events that may be associated with the DaVingi* TR System are based on adverse events reports of similar cardiac implant devices and include, but are not limited to the following:
• Abnormal lab values (including electrolyte imbalance)
• Allergic reaction to antiplatelet agents, contrast medium, or anesthesia
• Anemia
• Bowel ischemia
• Cardiac arrhythmias including cardiac arrest, conduction system disturbances (e.g., atrioventricular node block, left-bundle branch block, asystole), which may require a permanent pacemaker
• Cardiac tamponade
• Cardiogenic shock
• Cardiorenal syndrome
• Coronary occlusion, obstruction, or vessel spasm (including acute coronary closure)
• Device or components embolization
• Emergent percutaneous coronary intervention (PCI)
• Emergent surgery (e.g., coronary artery bypass, heart valve replacement/ repair, valve explant)
• Heart failure
• Heart murmur
• Hemolysis
• Hypotension or hypertension
• Infection (including septicemia and endocarditis)
• Lungs injury/trauma

• Major or minor bleeding that may or may not require transfusion or intervention (including life-threatening or disabling bleeding)
• Myocardial infarction
• Myocardial ischemia
• Native valve dysfunction including, but not limited to, fracture; pannus; leaflet wear, tear, prolapse, or retraction; poor valve coaptation; suture breaks or disruption; leaks; mal-sizing (ring-patient mismatch); malposition/misplacement; regurgitation; stenosis
• Pericardial effusion
• Peripheral ischemia
• Permanent disability
• Pulmonary edema
• Pulmonary effusion
• Renal failure
• Renal insufficiency or renal failure (including acute kidney injury)
• Reoperation (transcutaneous or surgical)
• Respiratory insufficiency or respiratory failure
• Ring partial attachment, late detachment or ring embolization
• Rupture/ perforation of the myocardium or a vessel
• Skin, endocardium or valve apparatus erosion
• Stroke, transient ischemic attack (TIA), or other neurological deficits such as encephalopathy
• SyncopeDyspnea
• Thrombosis/embolus (including ring or components thrombosis)
• Tricuspid valve regurgitation or injury
• Vascular access related complications (e.g., dissection, perforation, pain, bleeding, hematoma, pseudoaneurysm, irreversible nerve injury, compartment syndrome, arteriovenous fistula, stenosis) that may require vascular surgery
• Elevated liver enzymes

There are additional risks that could possibly be associated with the tests and procedures performed for the clinical study. These potential risks are described below:
• Risks related to the blood tests required for the study, e.g., excessive bleeding, fainting or light- headedness, hematoma, infection, or the requirement of multiple punctures to locate a vein to draw the sample.
• Risks related to central venous pressure measurement, e.g., infection, irregular heart-beats, collapsed lung, bleeding or death.
• Risks related to radiation; X-ray and CT imaging are required in addition to the routine care. The additional radiation dose for these tests is limited.
• Risks related to transesophageal echocardiography (TEE), e.g. some risks are associated with the medicine that might be used for sedation during TEE, including allergic reaction to medication, breathing difficulty, or nausea. TEE may also cause throat soreness, and rarely damage to the teeth or esophagus.

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. Moderate to Severe functional tricuspid regurgitation (FTR) as defined by ASE2.
2. Symptoms of right ventricular (RV) failure despite guideline directed medical therapy, NYHA Class II-IV.
3. Multidisciplinary heart team (minimum of three physicians, including Imaging and heart Failure cardiologists and cardiac surgery representatives) agree that percutaneous tricuspid annuloplasty is a reasonable treatment option and consider the subject to be a high risk for surgical annuloplasty.
4. >=18 years old at time of enrollment.
5. LVEF >= 30% within 45 days prior to index implant procedure.
6. PASP < 70 mmHg within 90 days prior to index implant procedure.
7. Right Ventricle TAPSE >= 13 mm within 45 days prior to index implant

procedure.
8. Tricuspid valve annular diameter >= 40 mm as measured by baseline TTE in the 4 chamber view within 45 days prior to index implant procedure.
9. Subject has provided written informed consent.
10. Subject agrees to comply with all required post-procedure follow-up visits, including device adjustment.

Exclusion criteria

1. Acutely decompensated heart failure (i.e. hemodynamically unstable or on IV inotropes).
2. Severe RV dysfunction per ASE guidelines3.
3. Primary tricuspid pathology (e.g. rheumatic, congenital, infective, etc.).
4. Previous tricuspid valve repair or replacement.
5. Transvalvular pacemaker or defibrillator lead is present.
6. Severe left-sided valve disease.
7. Right-sided intra-cardiac mass, thrombus or vegetation is present.
8. Inability to properly guide the index implant procedure using TEE (e.g. acoustic window not adequate).
9. MI or known unstable angina within the 30-days prior to the implant index procedure.
10. CVA within 3 months prior to index implant procedure.
11. Bleeding disorders, active peptic ulcer or GI bleed.
12. Contraindication to anticoagulation or antiplatelet medication, based on investigator*s opinion.
13. Chronic oral steroid or immunomodulator use (>= 6 months) or other condition that could impair healing response (e.g. cardiac sarcoidosis or other chronic inflammatory disease).
14. Any condition that, in the opinion of the investigator, may render the subject unable to complete the study (life expectancy < 1 year), or lead to difficulties for subject compliance with study requirements.
15. Subject is enrolled in another investigational study which has not completed the required primary endpoint follow-up period (Note: patients involved in a long-term surveillance phase of another study are eligible for this study).
16. Female patients who are pregnant or lactating.

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:	Percutaneous Ring Annuloplasty System
Registration:	No

Ethics review

Approved WMO Date:	17-02-2021
Application type:	First submission
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	NCT03700918
CCMO	NL74979.100.20