InvEstigation of the safety and perforMance of the NVT ALLEGRA THV System with a new delivery system in Patients with severe calcified aortIc stenosis or failed suRgical aortic bioprosthEsis

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Confirm the technical performance of the new IMPERIA Delivery System and evaluate the safety and efficacy of the entire ALLEGRA THV System.

Ethical review	Approved WMO
Status	Completed
Health condition type	Cardiac valve disorders
Study type	Interventional

Summary

ID

NL-OMON53564

Source
ToetsingOnline

Brief title
EMPIRE Study

Condition

- Cardiac valve disorders

Synonym
severe calcified aortic stenosis or failed surgical aortic bioprosthesis

Research involving
Human

Sponsors and support

Primary sponsor: NVT GmbH
Source(s) of monetary or material Support: NVT GmbH

Intervention

Keyword: Cardiology, delivery system, surgical aortic bioprosthesis, Transcatheter Heart Valve

Outcome measures

Primary outcome

Device success at 7 days, defined as

• Absence of procedural mortality AND

• Correct positioning of a single device in the proper anatomical location

(site-reported) AND

• Intended performance of the prosthetic heart valve (as determined by an

independent Echo Core Lab at discharge from index procedure or 7 days post

implant, whichever comes first)

• Indexed Effective Orifice Area (iEOA) > 0.85 cm2/m2 for BMI < 30kg/m2 and

iEOA > 0.70 cm2/m2 for BMI >= 30kg/m2

• Mean aortic valve gradient <20 mmHg or peak velocity <3 m/s

• No moderate or severe prosthetic valve regurgitation

Secondary outcome

1. All-cause mortality (discharge, 30 days, 6 and 12 months)

2. Cardiovascular mortality (discharge, 30 days, 6 and 12 months)

3. All stroke (discharge, 30 days, 6 and 12 months)

4. Transient ischemic attack (TIA)

5. Procedural success, defined as:

• Successful vascular access, delivery and deployment of the ALLEGRA THV

including re-positioning if required and successful retrieval of the

IMPERIA Delivery System (site-reported)

• Correct position of the ALLEGRA THV (site- reported)

• Only one ALLEGRA THV implanted in proper anatomical position (site-reported)

6. Echocardiographic performance assessment of the ALLEGRA THV (discharge, 30

days, and 12 months), as determined by an independent Echo

Core Lab)

• Effective orifice area (EOA)

• Transvalvular mean and peak pressure gradient

• Trans- and paravalvular regurgitation

7. NYHA classification (30 days, 6 months, and 12 months)

8. Safety profile according to VARC-21

• Early safety

• Time-related valve safety

9. Quality of life (KCCQ-12) (30 days, 6 months, and 12 months)

10. New pacemaker implantation (discharge, 30 days, 6 months and 12 months)

11. Delivery System-related AEs (discharge)

Study description

Background summary

Degenerative aortic valve stenosis is the most common heart disease in adults in western industrialized countries and TAVI has emerged as an alternative treatment for patients with aortic stenosis (AS) who are at high, intermediate or low risk for surgery with convincing long-term efficacy. In fact, TAVI has

developed as a standardized interventional procedure with a predictable risk and consequently, the number of implanted TAVI prosthesis has rapidly increased over the last decade.
After several randomized clinical studies showed non-inferiority or superiority of TAVI over surgical aortic valve replacement (SAVR), the latest 2020 ACC/AHA Valvular Heart Disease guidelines recommend TAVI as alternative treatment to SAVR in patients aged 65 years or older who are candidates for bioprostheses independent of the surgical risk as assessed by the heart team, but considering age, clinical and anatomical factors, and patient preferences. In recent years, the numbers of failing surgical aortic bioprostheses have been increasing and these high-risk patients also require for minimally invasive treatment options obvious..
Despite excellent outcomes in most cases, complications such as device malpositioning, coronary obstruction, para-valvular regurgitation and conduction system disturbances do occur after TAVI. Iterative design features in second generation TAVI systems allow more precise valve placement and can help to address some of these serious complications.
NVT has developed the new IMPERIA Delivery System so that the ALLEGRA THV can be re-sheathed and re-captured before it is fully released from the delivery catheter. In this way, the ALLEGRA THV can be repositioned if the initial position of the THV is not optimal, thus enabling precise final positioning and reducing the risks associated with suboptimal positioning.
There are additional technical factors making the ALLEGRA THV System especially suited for this purpose. The IMPERIA Delivery System and the ALLEGRA THV stent frame incorporate radio-opaque markers. The marker band on the IMPERIA Delivery System allows an assessment of implantation depth whilst 6 markers placed 12mm from the inflow on the ALLEGRA THV stent frame delineate the upper margin of the internal skirt and the level of the new valve closure line as well as facilitating the achievement of optimal co-axiality of the ALLEGRA THV prior to implantation.

Study objective

Confirm the technical performance of the new IMPERIA Delivery System and evaluate the safety and efficacy of the entire ALLEGRA THV System.

Study design

Prospective, multi-center, single-arm, interventional pivotal study with 12 months follow-up.

Intervention

107 symptomatic patients who are candidates for an intervention on severe calcified and stenotic aortic valves or failing surgical bioprosthetic aortic valves as assessed by the heart team, the CSC and meeting all eligibility

criteria will be enrolled (ITT-cohort). Each site must treat 3 roll-in patients with the new ALLEGRA THV System first prior being allowed to recruit patients in the ITT-cohort of the EMPIRE study. Roll-in patients undergo same procedures per protocol as patients in the ITT-cohort..

Study burden and risks

The potential anticipated complications, risks and side effects associated with use of the IMPERIA DS will be similar to those associated with any routine TAVI procedure. It is not
anticipated that the IMPERIA Delivery System (DS) and Loading System add any new risks beyond what is currently seen for the first-generation ALLEGRA DS and Loading System
when implanting the ALLEGRA THV, which include, but may not be limited to:
* Acute coronary closure
* Acute kidney injury
* Acute myocardial infarction
* Acute renal failure
* Allergic reactions/intolerances (e.g. to contrast media)
* Aortic root injury (dissection, perforation)
* Arrhythmias including ventricular tachycardia or fibrillation extending to cardiac arrest
* Atrioventricular conduction disorders (AV-block, LBBB)
* Bleeding (hemorrhage)
* Cardiac tamponade
* Cardiogenic shock
* Cerebrovascular events such as TIA, Stroke
* Death
* Device embolization / migration
* Emergent cardiac surgery
* Endocarditis
* Exacerbation of heart failure
* Hemolysis
* Hemorrhage requiring transfusion
* Hypertension or hypotension
* Infection
* Mitral valve injury
* Non-structural prosthetic valve dysfunction: paravalvular or/and central regurgitation
* Prosthetic valve thrombosis
* Structural prosthetic valve damage (e. g. cusps tear, suture line disruption, stent fracture,
calcification)
* Thromboembolism
* Vascular injury (dissection, perforation)
The risks of long-term anticoagulation and/or antiplatelet therapy should be considered.

Potential risks related to study participation are expected to be like those associated with any other routine TAVI procedure. Only patients who were referred for a transfemoral TAVI procedure may participate in this clinical study and protocol-required examinations and assessments (outlined in section 10.1) indicate that the EMPIRE TAVI procedure does not differ from routine TAVI procedure. All patients who are assigned for a transfemoral TAVI procedure undergo a standard diagnostic program which includes at least a transthoracic echocardiography, aortic root- / coronary angiogram, angiogram of the iliofemoral vessels, cardiac CT. Blood samples are taken pre- and postoperatively for monitoring purpose. A transfemoral TAVI is routinely performed either in intubation anesthesia or using a local anesthesia in combination with a mild sedation.
Radiation exposure by fluoroscopic imaging and the burden of applied contrast media is a side effect of each standard TAVI procedure and may not significantly differ in the EMPIRE study.
The postoperative care does not differ between TAVI patients and EMPIRE study participants. Immediately after procedure TAVI patients are routinely monitored at the intensive care unit for a few days until they are hemodynamically stable. TTE will be performed at discharge to verify prosthesis function. Blood samples are controlled to monitor the status and exclude any serious adverse events.
Patients who will participate in this study will not be exposed to a burden of any additional invasive examinations. The pre- and postoperative care is identical with a standard TAVI procedure.
The transfemoral TAVI procedure is associated with risks attributed to the interventional catheterization. These risks are well known, identified and elaborated in section 13.7.

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

Inclusion Criteria:
Patients will be included if ALL of the following criteria are met:
1. Symptomatic severe calcific stenosis of a native aortic valve with an AVA <=1.0 cm2 (or AVA index <=0.6 cm2/m2), AND mean aortic pressure gradient >= 40mmHg OR maximal transaortic velocity >=4.0m/s OR Doppler velocity index <=0.25 on site-reported echocardiography OR symptomatic patients with degeneration of a surgical bioprosthetic valve (stenosis and/or insufficiency) on sitereported echocardiography
2. Local multi-disciplinary Heart Team and Central Screening Committee (CSC) agree on indication and eligibility for TAVI
3. Age >=18 years
4. Patient has signed the Patient Informed Consent Form
5. Patient is willing and able to comply with requirements of the study, including all follow-up visits

Exclusion criteria

Exclusion Criteria
General:
1. Mean aortic annulus diameter as measured by preprocedural CT or internal diameter of the bioprosthesis is <16.5 mm or >27 mm
2. Echocardiographic evidence of intracardiac thrombus or vegetation (site-reported)
3. Significant disease of the aorta that would preclude safe advancement of the ALLEGRA THV System
4. Severe ilio-femoral vessel disease that would preclude safe placement of an 18 Fr introducer sheath or make endovascular access impossible

5. Severe tricuspid regurgitation and/or failing right heart (site-reported)
6. Severe left ventricular dysfunction with ejection fraction (EF) <20% (site-reported)
7. Evidence of active endocarditis or other acute infections
8. Renal failure requiring continuous renal replacement therapy
9. Untreated clinically significant coronary artery disease requiring revascularization
10. Any percutaneous interventional procedure (e.g. PCI with stenting) within 14 days prior of the index procedure
11. Acute MI <=30 days prior to the index procedure
12. Symptomatic carotid or vertebral artery disease requiring intervention or carotid/vertebral intervention within the preceding 45 days
13. Cerebrovascular accident (CVA) or transient ischemic attack (TIA) <=6 months or prior CVA with moderate or severe disability (e.g. modified Rankin scale score >2)
14. History of bleeding diathesis or coagulopathy; acute blood dyscrasias as defined: thrombocytopenia (platelets <80,000/µl), acute anemia (hemoglobin <10 g/dl), leukopenia (WBC <3000/ µl)
15. Active peptic ulcer or gastrointestinal (GI) bleeding <=3 months
16. Severe (greater than 3+) mitral insufficiency (sitereported)
16a. Pre-existing prosthetic heart valve in any position other than aortic
17. Uncontrolled atrial fibrillation
18. Required emergency surgery for any reason
19. Known hypersensitivity to contrast media, which cannot be adequately pre-medicated or contraindication to anticoagulant or anti-platelet medication or to nitinol alloy or to bovine tissue
20. Life expectancy <=12 months due to other medical illness
21. Currently participating in another investigational drug or device study
22. Pregnancy or intend to become pregnant during study participation

Specific exclusions in patients with native aortic valve disease (site-reported):

23. Unicuspid or bicuspid aortic valve
24. Non-calcified aortic stenosis
25. Predominant aortic regurgitation > grade 3
26. Distance between native aortic valve basal plane and the orifice of the lowest coronary artery <8 mm

Specific exclusions in patients with degenerated surgical bioprosthetic aortic valves (valve-in-valve) (site-reported):

27. Low position of the coronary ostia, especially in combination with shallow sinuses (high risk of coronary occlusion)
28. Partially detached leaflets that may obstruct a coronary ostium
29. Para-valvular regurgitation of a surgical bioprosthesis (site-reported)

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	04-04-2023
Enrollment:	36
Type:	Actual

Medical products/devices used

Generic name:	ALLEGRA THV system with the ALLEGRA THV and the new IMPERIA Delivery System
Registration:	No

Ethics review

Approved WMO Date:	25-01-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-04-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-05-2023
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-07-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-09-2023
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
ClinicalTrials.gov	NCT05478161
CCMO	NL81924.000.22