VANTAGE Trial: Evaluation of TAVR using the NAVITOR* valve in a global investigation

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- The objective of the proposed clinical trial is to evaluate the safety and effectiveness of the Navitor Transcatheter Aortic Heart Valve in patients with severe, symptomatic aortic stenosis who are at intermediate or low risk of surgical mortality…

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

Summary

ID

NL-OMON51939

Source
ToetsingOnline

Brief title
VANTAGE

Condition

- Cardiac valve disorders

Synonym
Aortic valve replacement, Heartfailure

Research involving
Human

Sponsors and support

Primary sponsor: Abbott Medical Nederland
Source(s) of monetary or material Support: Abbott

Intervention

Keyword: Aortic Stenosis, Aortic Valve, TAVR

Outcome measures

Primary outcome

The primary safety endpoint is a composite of all-cause mortality or disabling stroke at 12 months.

The primary effectiveness endpoint is moderate or greater paravalvular leak (PVL) at 30 days post index Navitor implantation procedure.

Secondary outcome

The rate of the following key outcomes will be assessed as descriptive endpoints for the study:

1. Non-hierarchical composite of all-cause mortality, fatal stroke/stroke with disability, type 3/type 4 bleeding, stage 3/stage 4 acute kidney injury, major vascular complications, or major access-related non-vascular complications at 30 days

2. Non-hierarchical composite of all-cause mortality or all stroke at 12 months

3. Procedural success defined as successful vascular access, delivery and deployment of the Navitor Valve; retrieval of the delivery system and correct positioning of a single Navitor Valve in the proper anatomical location and the absence of procedural mortality

4. Mortality (all-cause, cardiovascular, and valve-related) at 30 days and 12 months

5. Stroke (All stroke, fatal stroke, stroke with disability, and stroke without disability) at 30 days and 12 months

6. Transient ischemic attack (TIA) at 30 days and 12 months

7. Bleeding (type 4, type 3, and type 2) at 30 days

8. Major vascular complications at 30 days

9. Major access-related non-vascular complications at 30 days

10. Major cardiac structural complications at 30 days

11. Acute kidney injury (stage 4, stage 3, and stage 2) at 30 days

12. Permanent pacemaker insertion at 30 days and 12 months

13. Myocardial infarction at 30 days and 12 months

14. Coronary obstruction requiring intervention at 30 days and 12 months

15. Changes in functional status from baseline to follow-up assessments at 30 days and 12 months (e.g., New York Heart Association (NYHA) functional classification, six-minute walk test, quality of life measure: Kansas City Cardiomyopathy Questionnaire (KCCQ))

16. Rehospitalization (procedure-related or valve-related hospitalization, and other cardiovascular hospitalization) at 30 days and 12 months

17. Paravalvular leak (none/trace, mild, moderate or severe) at discharge, 30 days, 12 months and annually (when collected) through 10 years

18. Changes in echocardiographic parameters from baseline to follow-up at 30 days, 12 months and annually (when collected) through 10 years (e.g., mean effective orifice area, mean transvalvular gradient)

19. Aortic valve reintervention at 30 days, 12 months, and annually through 10 years

20. Prosthetic valve endocarditis at 12 months and annually through 10 years

21. Structural valve deterioration at 12 months and annually through 10 years

22. Non-structural valve dysfunction at 12 months and annually through 10 years

23. Successful coronary access as needed at 12 months and annually through 10

years

24. Clinically significant prosthetic valve thrombosis at 12 months and

annually through 10 years

Study description

Background summary

Aortic stenosis is the most common primary valve disease that can be treated surgically or through catheter intervention. Once the stenosis gets worse, a patient may experience chest pain and shortness of breath. Often this is treated with a replacement of the aortic valve. Since 2002, the replacement of an aortic valve via a catheter has been possible. Not all patients are eligible for a heart valve replacement through a catheter.

The primary goals of aortic valve replacement are to reduce the risk of mortality, which can be as high as 25% per year if left untreated, and to relieve clinical symptoms such as angina pectoris and dyspnoea.
In 2012, the TAVI technique was recognized in the ESC / EACTS guidelines for the treatment of valvular heart disease with a class I indication for patients unsuitable for surgery and a class IIA indication for patients at high surgical risk. In 2014, comparable Class I indications for TAVI were included in the ACC / AHA guidelines for valvular heart disease. In 2017, the AHA / ASC ACC / AHA guidelines for valvular heart disease were revised to include a Class IIA indication for TAVI as a reasonable alternative for patients considered moderate surgical risk.

The devices under investigation in this clinical trial are the Navitor Transcatheter Aortic Valve and the Navitor Loading System. Both are approved and marketed for implantation in patients with high surgical risk. The FlexNav* Delivery System is also used in the study and is approved and commercially available. The Navitor valve, FlexNav positioning system and Navitor charging system are used according to the instructions for use.

Since protocol version B, the Navitor Titan valve and the associated loading system can also be used, both are only available for use in this study and are not commercially available.

Study objective

- The objective of the proposed clinical trial is to evaluate the safety and effectiveness of the Navitor Transcatheter Aortic Heart Valve in patients with severe, symptomatic aortic stenosis who are at intermediate or low risk of surgical mortality.

- This trial will also evaluate the safety and effectiveness of the Navitor valve in a valve-in-valve application.

- Obtain CE mark for the Navitor valve and Navitor loading system for patients who are considered moderate or low surgical risk.

Study design

The VANTAGE clinical trial is a prospective, single-arm, multi-center, international, pre-market investigation designed in accordance with ISO standard 14155:2020.

Intervention

TAVI procedure with implantation of Navitor valve

Study burden and risks

Compared to a standard TAVI implantation, the additional study procedures involve only low risks.
Follow-up visits also follow the standard of care or will be performed as replacement of a standard care visit..
A TAVI is less invasive compared to a surgical valve replacement.

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. Subject who is judged by a heart team, including a cardiac surgeon, to be appropriate for transcatheter heart valve intervention therapy, and is deemed to be at intermediate or low risk for open surgical aortic valve replacement (i.e., heart team estimates risk of surgical mortality < 7% at 30 days, considering the Society of Thoracic Surgeons (STS) risk score, overall clinical status, and other clinical co-morbidities unmeasured by the risk calculator. #, F
2. New York Heart Association (NYHA) Functional Classification of II, III, or IV . #
3. Subject is of legal age for consent in the host country
4. Subject has been informed of the nature of the trial, agrees to its provisions and has provided written informed consent as approved by the Ethics Committee (EC) of the respective clinical site.
5. Able and willing to return for required follow-up visits and assessments
6. Degenerative aortic valve stenosis with echo-derived criteria, defined as: aortic valve area (AVA) of <= 1.0 cm2 (or indexed EOA <= 0.6 cm2/m2) AND either mean gradient >=40 mmHg or peak jet velocity >= 4.0 m/s or doppler velocity index (DVI) <=0.25. The echocardiogram supporting the qualifying AVA baseline measurement must be performed within 90 days prior to informed consent). #
7. Aortic annulus diameter of 19*30 mm and ascending aorta diameter of 26-44 mm for the specified valve size listed in the IFU, as measured by CT (systolic phase) conducted within 12 months prior to informed consent.

Eligibility criteria labeled with *#* are not applicable for the ViV cohort.
Sites in Switzerland will not participate in the ViV enrollment.
F: In France and Switzerland, if a subject is deemed low surgical risk, the

subject must be at age 75 or over to be included in this trial.

Exclusion criteria

1. Pregnant or nursing subjects and those who plan pregnancy during the clinical investigation follow-up period. A pregnancy test is required for all women of childbearing potential. 2. Need for emergency surgery for any reason 3. Life expectancy is less than 2 years in the opinion of the Investigator 4. Presence of other anatomic or comorbid conditions, or other medical, social, or psychological conditions that, in the investigator*s opinion, could limit the subject*s ability to participate in the clinical trial or to comply with follow up requirements, or impact the scientific soundness of the clinical trial results 5. Incapacitated individuals, defined as persons who are mentally ill, mentally handicapped, individuals with severe dementia or individuals without legal authority 6. Individuals who are unable to read or write 7. Currently participating in an investigational drug or device study that has not reached the primary endpoint or may confound the results of this trial 8. Evidence of an acute myocardial infarction [defined as:ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI) with acute ischemia symptoms and troponin elevation] within 30 days prior to index procedure 9. Untreated clinically significant coronary artery disease requiring revascularization 10. Any percutaneous coronary or peripheral interventional procedure performed within 30 days prior (except pacemaker or implantable cardioverter defibrillator (ICD) implant) to index procedure or planned within 30 days following the index procedure. 11. Blood dyscrasias as defined: leukopenia (WBC<3000 mm3), acute anemia (Hb < 9 g/dL), thrombocytopenia (platelet count <50,000 cells/mm^3); history of bleeding diathesis or coagulopathy 12. Refuses blood products 13. Cardiogenic shock manifested by low cardiac output, vasopressor dependence, or mechanical hemodynamic support 14. Hemodynamic instability requiring inotropic support or mechanical heart assistance 15. Hypertrophic cardiomyopathy with obstruction 16. Active peptic ulcer or upper GI bleeding within 3 months prior to index procedure that would preclude anti-coagulation 17. Known intolerance, hypersensitivity, or contraindication, including subjects that meet any of the following conditions: a. Subjects who cannot take any antiplatelets or anticoagulants #, b. Subjects who have sensitivity to contrast media which cannot be adequately premedicated, c. Subjects who have known hypersensitivity to nitinol (nickel or titanium), or d. Subjects who have clinical contraindication that precludes contrast CT imaging # Note: Subjects who can take either an antiplatelet or anticoagulant therapy post-procedure will be eligible. 18. Recent (within 6 months prior to index procedure date) cerebrovascular accident (CVA) or a transient ischemic attack (TIA) 19. Renal insufficiency (creatinine > 3.0 mg/dL or eGFR <30 ml/min/1.73m2) and/or end stage renal disease requiring chronic dialysis 20. Active bacterial endocarditis within 6 months prior to the index procedure 21. A positive

COVID-19 test within 30 days prior to the index procedure 22. Liver failure (Child-Pugh class B or C) 23. Subjects with atrial fibrillation who are not on anticoagulants or who are not implanted with a left atrial appendage occlusion (LAAO) device 24. Symptomatic carotid or vertebral artery disease, significant carotid or vertebral artery disease requiring intervention, or successful treatment of carotid or vertebral stenosis within 30 days prior to index procedure 25. Severe pulmonary hypertension with pulmonary systolic pressure greater than two-thirds of systemic pressure 26. Severe lung disease (FEV1 < 50% predicted) or currently on home oxygen 27. Hostile chest or conditions or complications from prior surgery that would make the subject be considered high surgical risk (i.e., mediastinitis, radiation damage, abnormal chest wall, porcelain aorta, adhesion of aorta or internal mammary artery (IMA) to sternum, etc.) * 28. Significant frailty as determined by the heart team (after objective assessment of frailty parameters) that would indicate high or extreme surgical risk # 29. Mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation 3-4+) # 30. Aortic valve is a congenital unicuspid or congenital bicuspid valve as verified by echocardiography or CT # 31. Non-calcified aortic valve *# 32. Severe ventricular dysfunction with LVEF <30% as measured by resting echocardiogram 33. Pre-existing prosthetic heart valve or other implant (such as prosthetic ring or transcatheter edge-to-edge repair (TEER) clip) in any valve position. * (Note: Subjects with a bio-prosthetic aortic valve may be included in the Valve-in-Valve cohort 34. Severe circumferential mitral annular calcification (MAC) which is continuous with calcium in the left ventricular outflow tract (LVOT) # 35. Prohibitive left ventricular outflow tract calcification # 36. Severe (greater than or equal to 3+) mitral regurgitation or severe mitral stenosis with pulmonary compromise 37. Severe tricuspid regurgitation or severe right ventricle dysfunction 38. Echocardiographic or multi-slice computed tomography (MSCT) evidence of intracardiac mass, thrombus or vegetation 39. Significant aortic disease, including abdominal aortic or thoracic aneurysm defined as maximal luminal diameter 5.5cm or greater or ascending aortic aneurysm defined as maximal luminal diameter 5cm or greater. 40. Marked aortic tortuosity (hyperacute bend) or severe *unfolding* and tortuosity of the thoracic aorta (applicable for transfemoral access only) 41. Aortic arch atheroma (thick [> 5 mm], protruding or ulcerated) 42. Significant narrowing (calcification and surface irregularities) of the abdominal or thoracic aorta 43. Aortic root angulation > 70° 44. Undue risk of coronary obstruction (e.g., low coronary ostia, narrow Sinus of Valsalva anatomy that would prevent adequate coronary perfusion, or bulky aortic valve leaflets in close proximity to coronary ostia) 45. Access vessel characteristics that would preclude safe insertion of the FlexNav Delivery System such as severe obstructive calcification, protruding thrombus or severe tortuosity 46. Minimum access vessel diameter of <5.0mm for small FlexNav Delivery System and <5.5 mm for large FlexNav Delivery System 47. Ascending aorta anatomy that would preclude safe delivery of the valve to the native aortic annulus 48. Egocentricity ratio of the annulus <0.73 * Criterion not applicable for ViV cohort

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-04-2022
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	NAVITOR System
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	02-11-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-03-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-11-2023
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-10-2024
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	NCT04788888
CCMO	NL76500.000.21