Tiara* Transcatheter Mitral Valve Replacement Study

Published: 06-03-2019
Last updated: 11-04-2024

To evaluate the safety and performance of the Neovasc Tiara MitralTranscatheter Heart Valve with the Tiara Transapical Delivery System.Data collected in this clinical study will include 30-day safety and performance ofthe device and delivery system...

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

Summary

ID

NL-OMON49193

Source
ToetsingOnline

Brief title
TIARA-II 047-CPT-003

Condition

- Cardiac valve disorders

Synonym
severe mitral regurgitation

Research involving
Human

Sponsors and support

Primary sponsor: Neovasc Medical Inc.
Source(s) of monetary or material Support: Manufacturer of the study device

Intervention

Keyword: Effectiveness, Safety

Outcome measures

Primary outcome

• Safety: Freedom from all-cause mortality and major adverse events defined as disabling stroke, myocardial infarction (peri-procedural or spontaneous), renal failure requiring dialysis, life-threatening bleeding, and cardiac surgical

or transcatheter reintervention at 30 days from the implant procedure.

• Device performance: The reduction of MR to optimal or acceptable at 30 days. MR reduction is considered optimal when post-procedure MR is reduced to trace or absent. MR reduction is considered acceptable when post-procedure MR is reduced by at least 1 class or grade from baseline and to no more than moderate (2+) in severity.

Secondary outcome

• Freedom from all-cause mortality and major adverse events defined as disabling stroke, myocardial infarction (peri-procedural or spontaneous), renal failure requiring dialysis, life-threatening bleeding, and cardiac surgical or transcatheter reintervention at 90 days, 180 days, one (1) year and annually to five (5) years from the implant procedure.

• Individual components of the primary safety endpoint (major adverse events of all-cause mortality, disabling stroke, myocardial infarction [peri-procedural or spontaneous], renal failure requiring dialysis, life-threatening bleeding, and

cardiac surgical or transcatheter reintervention) at 30 days from the implant procedure, 90 days, 180 days, 1 year, and annually to 5 years from the implant procedure.

• Technical success (measured at exit from the procedure room). All of the following must be present:

o Absence of procedural mortality; and

o Successful access, delivery, and retrieval of the device delivery system; and

o Successful deployment and correct positioning of the first intended device; and

o Freedom from emergency surgery or reintervention related to the device or access procedure.

• Procedural success (measured at 30 days). All of the following must be present:

o Device success (either optimal or acceptable); and

o Absence of major device or procedure related serious adverse events (SAEs), including:

* Death

* Stroke

* Life-threatening bleeding (MVARC scale)

* Major vascular complications

* Major cardiac structural complications

* Stage 2 or 3 acute kidney injury (includes new dialysis)

* Myocardial infarction or coronary ischemia requiring PCI or

CABG

* Any valve-related dysfunction, migration, thrombosis, or

other complication requiring surgery or repeat intervention

• Incidence of mitral valvular insufficiency of >= moderate at post-procedure,

discharge, 30 days, 90 days, 180 days, 1 year, and annually to 5 years as

compared to baseline.

• Device migration defined as any movement of any valve structure(s)

compared with the final implant location, resulting in hemodynamic or

pathoanatomic

consequences (e.g., mitral paravalvular leak or left ventricular

outflow tract obstruction).

• Device fracture (adjudicated as affecting valve performance or not affecting

valve performance).

• Device success defined as (measured at each assessment interval).

All of the following must be present:

o Absence of procedural mortality or stroke; and

o Proper placement and positioning of the device; and

o Freedom from unplanned surgical or interventional procedures

related to the device or access procedure; and

o Continued intended safety and performance of the device,

including:

* No evidence of structural or functional failure

* No specific device-related technical failure issues and

complications

* Reduction of MR to either optimal or acceptable levels*

without significant mitral stenosis (i.e., post-procedure

EROA is >=1.5 cm2 with a transmitral gradient <5 mm Hg),and with no greater than

mild (1+) paravalvular MR (and

without associated hemolysis)

• Performance (as assessed at 30 days, 90 days, 180 days, and once annually

for 5 years as compared to baseline):

o Clinical performance as measured by NYHA Functional Class,

6 Minute Walk Test (6MWT), and the Kansas City Cardiomyopathy

Questionnaire (KCCQ).

o Hemodynamic performance as assessed by echocardiography:

mean MV gradient, mitral regurgitation, effective orifice area (EOA)

of the MV, LV systolic and diastolic dimensions as well as volume.

• Patient success (measured at 1 year). All of the following must be present:

o Device success (either optimal or acceptable), and

o Patient returned to the pre-procedural setting; and

o No rehospitalizations or reinterventions for mitral regurgitation; and

o Improvement from baseline in symptoms (e.g., NYHA improvement

by >=1 functional class); and

o Improvement from baseline in functional status (e.g., 6MWT

improvement by >=50 meters); and

o Improvement from baseline in quality-of-life (e.g., Kansas City

Cardiomyopathy Questionnaire improvement by >=10)

Study description

Background summary

More than 50% of patients with severe MR who are potential candidates for surgery are denied this opportunity, most often due to comorbid conditions, advanced age, or impaired LV function. Transcatheter Mitral Valve Replacement (TMVR), may be a treatment option in the future for this patient population.
As of 30 October 2017, there have been a total of 37 patients implanted with Tiara mitral valves. While long term outcomes are not available for all patients,
the longest patient follow-up is over 3 years, with excellent valve function and New York Heart Association (NYHA) Class II.
Therefore, this study is moving forward with a prospective trial of 115 subjects,
with centralized screening, careful monitoring by both a Data and Safety Monitoring Board (DSMB) and Clinical Events Committee (CEC), and annual reports, if required, for continued assessment of safety and performance.

Study objective

To evaluate the safety and performance of the Neovasc Tiara Mitral Transcatheter Heart Valve with the Tiara Transapical Delivery System.
Data collected in this clinical study will include 30-day safety and performance of
the device and delivery system as well as up to 5-year clinical outcomes.

Study design

The TIARA-II study is an international, multicenter, single-arm, prospective, nonrandomized,
safety and performance clinical study. This study is designed
utilizing Mitral Valve Academic Research Consortium (MVARC) clinical trial design principles and endpoint definitions and ISO 5840-3.

Intervention

Tiara Mitral Valve transcatheter implantation is achieved transapically using a delivery system inserted through the apex of the heart. Deployment of the device is controlled by a single thumbwheel on the handle of the Tiara Delivery System and is guided by a combination of fluoroscopic and echocardiographic imaging (TEE). The patient is expected to remain hemodynamically stable throughout the procedure.
In all stages of valve deployment until the final step of deploying the ventricular

tabs, it is possible to recapture the partially deployed valve into the delivery catheter, reposition and complete the implant procedure, or alternatively, at the discretion of the operator, withdraw the catheter and unimplanted valve from the patient.

Study burden and risks

Severe mitral regurgitation is associated with high morbidity and mortality with impaired quality of life. Symptoms include fatigue, palpitations, dyspnea, anginal pain with ordinary physical activity and/or may be present at rest to the point that if any physical activity is undertaken, discomfort is increased. Surgical mitral valve repair or replacement is the treatment of choice. Many patients, due either to comorbidities or to reduced ejection fraction, are at high risk for a surgical approach and are therefore not suitable surgical candidates. The development of a transcatheter approach which can be accomplished on the beating heart without cardiopulmonary bypass may offer an important advance, with the possibility of reduction in both mortality and morbidity. The risks of the mitral implantation with the novel Tiara valve are therefore justified given the potential benefit of this scientific advance.

Contacts

Public
Neovasc Medical Inc.

Mayfield Place Canada
Richmond, BC V6V 2E4
US
Scientific
Neovasc Medical Inc.

Mayfield Place Canada
Richmond, BC V6V 2E4
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Age 18 years or older.
2. NYHA Class II to ambulatory Class IV.
3. Severe mitral regurgitation (reference Section 20)
4. High surgical risk for open mitral valve surgery as determined by the examining cardiac surgeon and the local institutional Heart Team (consisting of an interventional cardiologist and cardiac surgeon, at a minimum) based on an STS mitral valve replacement PROM >=8% and/or the Heart Team assessing the risk of operative mortality >=8% (modified from 2014 AHA/ACC Valvular Heart Disease Guidelines definition of high risk).
5. Subject meets the initial anatomical eligibility criteria for annulus size (site measurement of diameter <50 mm) for the available size(s) of the Tiara Mitral Valve based on CT scan or TTE and/or TEE.
6. The subject has been informed of the nature of the investigational device, required study follow-up procedures and visits and agrees to participate, and has provided written informed consent.

Exclusion criteria

1. Deemed too frail by objective frailty assessments or with severe comorbidities such that the subject is unlikely to benefit from the procedure as determined by the local institutional Heart Team.
2. Previous cardiac procedures:
a. PCI within 30 days of enrollment
b. Drug Eluting Stent implantation within 30 days of enrollment
c. Bare Metal Stent implantation within 30 days of enrollment
d. Coronary artery bypass graft (CABG) within 30 days of enrollment
e. Any surgical or transcatheter mitral valve replacement that would interfere

with the placement of the TiaraMitral Valve
f. TAVR within 30 days of enrollment
g. Mitral valve repair surgery within 30 days of enrollment
h. Cardiac transplant
i. CRT/ICD implant within 30 days of enrollment
3. Evidence of any myocardial infarction (MI) within 30 days of enrollment.
4. Cardiac structures:
a. Ventricular dysfunction with ejection fraction <= 25% within 30 days of enrollment
b. Left ventricular outflow tract (LVOT) obstruction
c. Evidence of left atrial and/or left ventricular thrombus (within 90 days of enrollment), vegetation or cardiac mass
d. Apex not amenable to transapical access as deemed by the examining cardiac surgeon(s)
e. Aortic, tricuspid or pulmonary valve disease requiring intervention
f. Presence of a hemodynamically significant intracardiac shunt
g. Clinically significant untreated coronary artery disease (CAD) requiring revascularization
5. Cerebrovascular accident (CVA) and/or transient ischemic attack (TIA) within 30 days of enrollment or Modified Rankin Scale >=4 disability.
6. Subjects who are on chronic dialysis or who have a serum creatinine value > 3.0 mg/dL (265.2 µmol) or eGFR < 35 ml/min within 30 days of enrollment.
7. Pregnant, currently breastfeeding, or planning pregnancy within next 12 months.
8. Documented bleeding or coagulation disorders which limit anticoagulant therapy.
9. Documented recent (within 90 days of enrollment) GI bleeding requiring medical intervention (e.g., blood transfusion).
10. Active infections requiring antibiotic therapy.
11. Known hypersensitivity or contraindication to:
a. Aspirin, or heparin, or clopidogrel (Plavix)
b. Allergy to contrast media which cannot be managed medically
c. Nitinol or its components (e.g., nickel or titanium)
12. Subject is unable to undergo transesophageal echocardiography (TEE) during the implantation procedure.
13. Subject is currently participating in another investigational drug or device clinical trial that may interfere with the results of either trial.
(Note: Patients
enrolled in a clinical trial involving products that are currently commercially available are eligible).
14. Need for emergent or urgent surgery for any reason or any planned cardiac surgery within the next 12 months.
15. Subjects with a life expectancy of less than 12 months due to noncardiac reasons.
16. Hypotension (systolic pressure <90 mm Hg) or requirement for inotropic support or mechanical hemodynamic support.

17. Subject is unable to complete study required screening procedures.

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):	29-05-2019
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	Neovasc Tiara Mitral Heart Valve and transapical Tiara Delivery System
Registration:	No

Ethics review

Approved WMO Date:	06-03-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	05-06-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	27-08-2020
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	NCT03039855
CCMO	NL66466.100.18