Transcatheter Mitral Valve Replacement with the Medtronic Intrepid* TMVR Transfemoral System in patients with severe symptomatic mitral regurgitation - APOLLO-EU Trial

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Evaluate the safety and efficacy of Medtronic Intrepid* TMVR TF System in patients with moderate-to-severe or severe symptomatic mitral regurgitation who, or moderate symptomatic mitral regurgitation combined with mitral stenosis in the presence of...

Ethical review	Approved WMO
Status	Recruitment started
Health condition type	Cardiac valve disorders
Study type	Interventional research applied for the first time in human subjects

Summary

ID

NL-OMON56063

Source
ToetsingOnline

Brief title
APOLLO-EU trial

Condition

- Cardiac valve disorders

Synonym
leaking heart valve mitral regurgitation

Research involving
Human

Sponsors and support

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

Intervention

- Medical device

Keyword: severe symptomatic mitral regurgitation, Transcatheter Mitral Valve Replacement

Explanation

N.a.

Outcome measures

Primary outcome

Primary Objective;
Evaluate one-month efficacy and one-year safety of the Medtronic Intrepid* TMVR
TF System

Primary endpoint:
Safety: all-cause mortality at 1-year post-procedure
Efficacy: defined as subjects with none/trace or mild regurgitation at 30 days
post-procedure as assessed by the Echocardiography Core Laboratory

Secondary outcome

Secondary objective:
Evaluate procedure-related safety and one-year efficacy of the Medtronic
Intrepid* TMVR TF System.

Secondary endpoints:
Safety
• all-cause mortality at 30 days
• Disabling stroke at 30 days
• Acute Kidney Injury (stage 3 or with renal replacement) at 30 days
• Reoperation or reintervention at 30 days
• Major access site vascular complications at 30 days

Efficacy:
• Degree of mitral valve regurgitation at 1 year as assessed by the
Echocardiography Core Laboratory
• Change in NYHA functional class at 1 year
• Change in Quality of Life (QoL) at 1 year as assessed by KCCQ

• Cardiovascular hospitalizations through 1 year</p>

Study description

Background summary

Please see section 4.1 of the protocol.

Study objective

Evaluate the safety and efficacy of Medtronic Intrepid* TMVR TF System in patients with moderate-to-severe or severe symptomatic mitral regurgitation who, or moderate symptomatic mitral regurgitation combined with mitral stenosis in the presence of MAC who, by agreement of the local site multidisciplinary heart team experienced in mitral valve therapies, are unsuitable for treatment with approved transcatheter repair or surgical mitral valve intervention.

Study design

The trial is designed as a prospective, single-arm, multi-center, interventional, pre-market trial to evaluate the safety and efficacy of transcatheter mitral valve replacement in patients with moderate-to-severe or severe symptomatic mitral regurgitation who, by agreement of the local site multidisciplinary
heart team experienced in mitral valve therapies, are unsuitable for treatment with approved transcatheter repair or surgical mitral valve intervention.

All required evaluations, post consent and before the investigation procedure (screening, baseline, and pre-index follow-up time points), as listed in Table 3 of the CIP, are considered interventional and may be outside the standard of care for a given subject.

The trial is expected to be conducted at approximately 50 study sites located in EMEA. Up to 400 subjects will be attempted in the trial to ensure 100 Roll-In subjects and up to 300 analysis subjects.
It is estimated that up to 400 IntrepidTM TMVR TF Systems will be implanted within this trial.
To ensure a widespread distribution of data and minimize study site bias in trial results, no site will implant more than 20% of total attempted subjects at any individual site.
Enrollment will be competitive across study sites; therefore, there is no set minimum number of subjects to be enrolled per site.
The study methods include the following measures to minimize potential sources of bias:

• Subjects will be screened to confirm eligibility with pre-defined inclusion and exclusion criteria prior to enrollment.
• An external, independent Clinical Events Committee (CEC) will review and adjudicate, at a minimum but not limited to all deaths and endpoint related adverse events. Safety study endpoint results will be based on CEC adjudications.
• All sites will follow a standardized protocol for acquisition of echocardiographic study endpoint data.
• An external, independent echocardiography Core Laboratory will evaluate all echocardiograms. Echocardiographic study endpoint results will be based on Core Lab assessments.

Intervention

The enrollment period is estimated to be approximately 2-3 years, and subjects will be followed for up to 10 years post-procedure; therefore, the expected trial duration is approximately 12-13 years.
A schedule of events is outlined in Table 3 of the protocol. Upon completion of the final protocol visit (discontinuation), subject participation will be considered complete and the subject should then be followed per the local standard of care for their condition.

Study burden and risks

This trial will enroll only subjects with moderate-to-severe or severe symptomatic mitral regurgitation who by agreement of the local site multidisciplinary heart team experienced in mitral valve therapies are unsuitable for treatment with approved transcatheter repair or surgical mitral valve intervention. This TMVR procedure may provide an alternative mitral valve replacement for subjects for whom conventional surgery or approved transcatheter repair is not an option. Transfemoral access may also mitigate procedural complications compared to transapical access from the TMVR procedure.

The clinical experience, to date, has demonstrated successful implantation of the Intrepid* TMVR TF System, proper TMVR function, and elimination of mitral regurgitation, warranting continued study in additional subjects, as proposed in this trial. The potential benefit of a less invasive transfemoral procedure, for those that are unsuitable for treatment with approved transcatheter repair, to reduce their mitral regurgitation is considered to outweigh the risks from an MVR surgical procedure.

The investigational plan is specifically designed to manage and minimize risks through careful subject selection, thorough training of investigators, adherence to the pre-determined time points to assess subject clinical status and regular clinical monitoring visits by Sponsor appointed monitoring

personnel.

Study subjects will be exposed to the procedural and device risks associated with TMVR, as well as the study specific risks listed in section 11.1. of the CIP. However, evidence from the scientific literature indicates subjects with moderate-to-severe or severe mitral regurgitation who do not receive therapy are exposed to the serious risks associated with their disease including worsening heart failure, irreversible ventricular functional impairment, and death. While most risks are being minimized, there are some residual risks, as further described in the risk management report. Those residual risks were considered to have been to an acceptable level for the intended application and current phase of the device.

While the Intrepid* TMVR TF System is a novel device, based on the results of the Pilot and Mitral Early Feasibility studies and the benefits observed by relieving mitral regurgitation in other transcatheter mitral valve repair and replacement trials, it is expected that these benefits will be conferred to the study subjects in the APOLLO-EU Trial, and that the benefit of mitral regurgitation reduction will outweigh the risks of intervention.

Contacts

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Trial sites

Trial sites in the Netherlands

Catharina-ziekenhuis

Target size: 8

Erasmus MC, Universitair Medisch Centrum Rotterdam
Target size: 8

St. Antonius Ziekenhuis
Target size: 8

Listed location countries

Denmark, Israel, Switzerland, Italy, Netherlands, Spain, United Kingdom, Germany, France

Eligibility criteria

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

Inclusion criteria

- Subject has moderate-to-severe or severe symptomatic mitral regurgitation as defined by the American Society of Echocardiography 2017 Guidelines and Standards - Recommendations for Non-invasive Evaluation of Native Valvular Regurgitation,or subject has moderate symptomatic mitral regurgitation combined with mitral stenosis with the presence of MAC
- Local site multidisciplinary heart team experienced in mitral valve therapies agrees that patient is unsuitable for treatment with approved transcatheter repair or conventional mitral valve surgery
- Subject and the treating physician agree that the subject will return for all required post-procedure follow-up visits
- Subject meets the legal minimum age to provide informed consent based on local regulatory requirements
- Subjects anatomically suitable for the Medtronic Intrepid* TMVR TF System

Exclusion criteria

- Estimated life expectancy of less than 24 months
- Currently surgically implanted mitral valve
- Prior transcatheter mitral valve procedure with device currently implanted
- Anatomic contraindications
- Anatomically prohibitive mitral annular calcification (MAC)
- Aortic valve disease requiring intervention or previous intervention within 90 days of enrollment
- LVEF < 25% (measured by resting transthoracic echocardiogram).

- Left ventricular end diastolic diameter (LVEDD) > 75mm
- Need for emergent or urgent surgery
- Hemodynamic instability
- History of bleeding diathesis or coagulopathy
- End stage renal disease
- Liver failure
- Frailty

Study design

Design

Study phase:	N/A
Study type:	Interventional research applied for the first time in human subjects
Intervention model:	Single
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment started
Start date (anticipated):	23-02-2024
Enrollment:	24
Duration:	120 months (per patient)
Type:	Actual

WORLD

Recruitment status:	Recruitment started
Start date (anticipated):	22-12-2023
Enrollment:	400
Type:	Actual

Medical products/devices used

Product type:	Medical device

Generic name:	Intrepid™ Transcatheter Mitral Valve Replacementtransfemoral system
Registration:	No

IPD sharing statement

Plan to share IPD: No

Plan description
N.a.

Ethics review

Approved WMO Date:	15-03-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-07-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-11-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-07-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-11-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	07-05-2025
Application type:	Amendment
Review commission:	METC Erasmus MC

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	NCT05496998
CCMO	NL81992.000.22
Research portal	NL-007646