LANDMARK Trial: A prospective, multinational, multicentre, open-label, randomised, noninferiority trial to compare safety and effectiveness of Meril*s Myval Transcatheter Heart Valve (THV) series vs. Contemporary Valves (Edwards* Sapien THV series and Medtronic*s Evolut THV series) in patients with severe symptomatic native aortic valve stenosis.

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

Summary

ID

NL-OMON56440

Source
ToetsingOnline

Brief title
Landmark

Condition

- Cardiac valve disorders

Synonym
Severe aortic stenosis

Research involving
Human

Sponsors and support

Primary sponsor: Meril Life Sciences Pvt. Ltd.
Source(s) of monetary or material Support: Industrie

Intervention

Keyword: Severic aortic valve stenosis, TAVR

Outcome measures

Primary outcome

Primary study parameters/outcome of the study:

It is the composite of following (at 30 days) VARC-3 defined criteria:

- All-cause mortality

- All stroke

- Bleeding (Type 3 and 4)

- Acute kidney injury (stage 2, 3 and 4)

- Major vascular complications

- Moderate or severe prosthetic valve regurgitation

- Conduction system disturbances resulting in a new permanent pacemaker

implantation

Secondary outcome

1- It is the composite of following [at 1-year] (VARC-3 defined criteria):

- All-cause mortality

- All stroke

- Bleeding (Type 3 and 4)

- Acute kidney injury (stage 2, 3 and 4)

- Major vascular complications

- Moderate or severe prosthetic valve regurgitation

- Conduction system disturbances resulting in a new permanent pacemaker

implantation

2- All-cause mortality (VARC-3 defined criteria) (till 10-year)

3- All stroke (VARC-3 defined criteria till 5-year

4. Acute Kidney Injury (AKI)(stage 2, 3 and 4) (VARC-3 defined criteria) (

till 1-year)

5. Bleeding (Type 3 and 4) (VARC-3 defined criteria) (till 5-year)

6. Moderate or severe prosthetic valve regurgitation (VARC-3 defined criteria)

(10-year)

7. New permanent pacemaker implantation (VARC-3 defined criteria) (till 10-year)

8. Conduction disturbances and arrhythmias (VARC-3 defined criteria(till

5-year)

9. Technical success (VARC-3 defined criteria) [Time Frame: Post-procedure]

10 Device success (VARC-3 criteria)

11 Safety at 30 days (VARC-3 criteria)

12 Clinical efficacy at 30 days (VARC-2 criteria)

13. Valve related long-term clinical efficacy (VARC-3 defined criteria) (till

10 years)

14. Vascular and access related complications (VARC-3 defined criteria) (till

1-year)

15. Major vascular complications (VARC-3 defined criteria) (till 1-year)

16. Myocardial Infarction (VARC-3 defined criteria) (till 5-year)

17. Functional improvement from baseline as measured per

- NYHA class

- 6 minute walking test

18 - Echocardiographic parameters (till 10 years)

19- Bioprosthetic valve deterioration (VARC-3 defined criteria (5-year)

20. Patient-prosthesis mismatch (VARC-2 defined criteria) (till 1-year)

21 Days Length of index hospital stay

22 Re-hospitalization (VARC-3 defined criteria) (5-year)

23. Health status as evaluated by Quality of Life questionnaires

24. Valve thrombosis (VARC-2 defined criteria) (till 5-year)

25. Coronary obstruction requiring intervention (VARC-3 defined criteria)

26. Valve malpositioning (VARC-3 defined criteria

27. Conversion to open surgery (VARC-3 defined criteria)

28. Unplanned use of mechanical circulatory support (cardiopulmonary bypass (CPB), extracorporeal membrane oxygenation (ECMO), transcatheter pumps or intra-aortic balloon pump (IABP) (VARC-3 defined criteria)

29. Implantation of multiple (>1) transcatheter valves during the index

hospitalization (VARC-3 defined criteria)

30. Cardiac structural complications (VARC-3 defined criteria) (till 5 years)

31. Ventricular septal perforation (VARC-2 defined criteria0

32. New onset of atrial fibrillation or atrial flutter (VARC-3 defined

criteria) (till5-year)

33. Endocarditis (VARC-3 defined criteria) (till 5-year]

Study description

Background summary

Aortic stenosis (AS) is one of the most prevalent diseases in the elderly patient population (>65 years of age). The estimated prevalence of the disease varies from 2% to 7% in the elderly population. The disease has a significant impact on patient morbidity and mortality as well as healthcare expenditures. Transcatheter aortic valve implantation (TAVI) has been introduced to treat patients with severe symptomatic aortic stenosis

Study objective

LANDMARK Trial is designed to compare safety and effectiveness of Meril*s Myval Transcatheter Heart Valve (THV) series vs. Contemporary Valves (Edwards* Sapien THV series and Medtronic*s Evolut THV series) in patients with severe symptomatic native aortic valve stenosis

Study design

This is a prospective, randomised, multinational, multicentric, open-label non-inferiority trial to compare clinical outcomes of Myval THV Series vs.

Contemporary Valves in severe symptomatic native aortic valve stenosis patients via transfemoral approach. The trial includes a total of 768 subjects across the globe.
A non-randomised nested registry will be conducted to include patients requiring extra-large size (30.5 mm and 32 mm) of Myval THV (XL Nested Registry)

Intervention

1 group (384 patients) will be treated with the Myval transcatheter heartvalve.
1 group (384 patients) will be treated with the Edwards Sapien or Medtronic Evolut heartvalve.
For the nested registry approximately 100 patients will be recruited from approximately 30 participating centres in the LANDMARK trial.

Study burden and risks

Based on current experience we do not expect extra risks.

Contacts

Public
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IN
Scientific
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IN

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

As per local Heart Team assessment, patient is eligible for TAVI and the patient is
suitable for implantation with all three study devices.

Exclusion criteria

Any condition, which in the Investigator*s opinion, would preclude safe participation of
patient in the study.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-11-2020
Enrollment:	422
Type:	Actual

Medical products/devices used

Generic name:	Transcatheter heart valve
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	14-10-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-12-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-03-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-08-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-10-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-12-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	16-02-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-06-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-07-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-11-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-06-2024
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
Other	NCT0427526 ClinicalTrial.gov
CCMO	NL73302.100.20