The ENCIRCLE Trial; SAPIEN M3 System TransCatheter MItral Valve ReplaCement via TransseptaL AccEss

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To establish the safety and effectiveness of the SAPIEN M3 System in subjects with symptomatic, at least 3+ mitral regurgitation (MR) for whom commercially available surgical or transcatheter treatment options are not preferred/appropriate due to...

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

Summary

ID

NL-OMON51198

Source
ToetsingOnline

Brief title
The ENCIRCLE Trial

Condition

- Cardiac valve disorders

Synonym
Symptomatic Mitral regurgitation

Research involving
Human

Sponsors and support

Primary sponsor: Edwards Lifesciences LLC
Source(s) of monetary or material Support: Edwards Lifesciences

Intervention

Keyword: Safety and Effectiveness Trial, TransCatheter Mitral Valve ReplaCement, Transseptal Mitral Valve ReplaCement

Outcome measures

Primary outcome

All-cause mortality or Heart failure rehospitalization at 1 year post-index

procedure

Secondary outcome

• Improvement of heartfailure - in New York Heart Association (NYHA) functional

class at 1 year compared to baseline

• Improvement of quality of life - in Kansas City Cardiomyopathy Questionnaire

(KCCQ) overall score at 1 year compared to baseline

• Improvement in mitralis regurgitation at 1 year compared to baseline

• Decrease in left ventricular end-diastolic volume index (LVEDVi) at 1 year

compared to baseline

• Major iatrogenic atrial septal defect (ASD) through discharge

• Clinically significant transcatheter mitral valve replacement (TMVR)-related

left ventricular outflow tract (LVOT) obstruction

• Stroke

• Mitral valve reintervention

• Days alive out of hospital at 1 year (all hospitalizations) from index

procedure

• Cardiovascular rehospitalization

• Improvement in 6-minute walk test

• mitralis regurgitation <=1+

• Paravalvular regurgitation

• Left ventricular end-diastolic diameter (LVEDD) by echo compared to baseline

• LVEDVi by echo compared to baseline

Study description

Background summary

Mitral regurgitation (MR) is the most frequent valve disease in the US and the second most common form of valvular heart disease requiring surgery in Europe. Treatment options for chronic MR include surgical valve repair or replacement, guideline-directed medical therapy (GDMT), cardiac resynchronization therapy (CRT) and transcatheter valve repair. Surgical valve repair techniques include annuloplasty, leaflet resection, leaflet suturing and chordal transfer and shortening. Annuloplasty and mitral valve replacement (MVR) are the most common surgical procedures. GDMT includes treatment with angiotensin-converting enzyme inhibitors (ACEI) (or angiotensin receptor blockers, ARB), beta-blockers, diuretics and aldosterone antagonists. Transcatheter valve repair techniques can include leaflet plication, annuloplasty and chordae tendineae implantation. To establish the safety and effectiveness of the SAPIEN M3 System in subjects with symptomatic, at least 3+ mitral regurgitation (MR) for whom commercially available surgical or transcatheter treatment options are not preferred/appropriate due to clinical, anatomic or technical considerations.

Study objective

To establish the safety and effectiveness of the SAPIEN M3 System in subjects with symptomatic, at least 3+ mitral regurgitation (MR) for whom commercially available surgical or transcatheter treatment options are not preferred/appropriate due to clinical, anatomic or technical considerations

Study design

This is a non-randomized, prospective, multi-center safety and device success study. Up to three hundred (300) patients are planned to be implanted at up to 75 participating investigational centers in Europe, United States, Canada and Australia. Up to 100 additional subjects who have had an attempted but failed transcatheter edge-to-edge repair (TEER) procedure will be treated in a separate registry. Up to 100 additional subjects with mitral annular calcification (MAC) will be treated in a separate registry.

Patient participation will last for a minimum of 5 years. Patients will be assessed at the following intervals: baseline, hospital discharge, 30 days, 6 months, 1 year and annually thereafter through 5 years.

Intervention

All study subjects will receive a non-CE marked heartvalve.

Study burden and risks

The additional burden for the participating patients will concern the six-minute walking tests and the questionnaires about their quality of life. The usual risks of a TransCatheter MItral Valve ReplaCement also apply here.

Contacts

Public
Edwards Lifesciences LLC

One Edwards Way .
Irvine CA 92614
US
Scientific
Edwards Lifesciences LLC

One Edwards Way .
Irvine CA 92614
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. 18 years of age or older
2. MR >= 3+ as assessed by the Echo Core Lab (See MAC Registry)
3. NYHA functional class >= II
4. Per the Heart Team, commercially available surgical or transcatheter treatment options are deemed unsuitable due to clinical, anatomic or technical considerations.
5. Subject*s heart failure management has been optimized based on subject characteristics and applicable guidelines, and stable for at least 30 days prior to enrollment (See Failed TEER Registry)
Note: Subjects who require significant changes to heart failure medication after enrollment but prior to the procedure must re-stabilize for 30 days to be eligible.
6. The subject or subject*s legal representative has been informed of the nature of the study, agrees to its provisions and has provided written informed consent.

Subjects who had an attempted but failed TEER procedure may be considered for enrollment if they meet all eligibility criteria except inclusion 5, and do not meet the following modified exclusion criteria:
10. Hemodynamic instability requiring inotropic or mechanical support within 72 hours of procedure
13. Percutaneous cardiovascular intervention (other than TEER procedure), cardiovascular surgery, or carotid surgery within 30 days prior to the procedure

Exclusion criteria

Mitral/cardiac anatomy that would preclude appropriate delivery and deployment of the dock or valve, including but not limited to:
• Annular dimensions that could potentially increase the risk of paravalvular leak (as assessed by Computed Tomography [CT] core lab)
• Commissural jet or lateral commissural flail/prolapse that could potentially increase the risk of paravalvular leak
• Medial commissural flail or prolapse
• Calcification that would interfere with the SAPIEN M3 System during delivery or after implantation; if potential for interference is uncertain, see MAC Registry
• Interatrial septum or left atrium not suitable for transcatheter trans-septal access
• LVEDD >= 75 mm as assessed by Echo core lab
• Sub-valvular anatomy that is unsuitable for dock encircling as assessed by CT core lab

• Significant risk of LVOT obstruction as assessed by CT core lab
2. Inappropriate anatomy for femoral introduction and delivery of the SAPIEN M3 Dock and Valve
3. Presence of any device that will contact or interfere with the SAPIEN M3 System during delivery or after implantation
4. LVEF < 25% as assessed by Echo core lab
5. Severe right ventricular dysfunction as assessed by Echo core lab
6. Need for aortic, tricuspid or pulmonic valve intervention within the next 12 months
7. History of heart transplant
8. Cardiac imaging evidence of intracardiac mass, thrombus or vegetation
9. Active bacterial endocarditis within 180 days of the procedure
10. Hemodynamic instability requiring inotropic or mechanical support within 30 days of the procedure
11. Myocardial infarction within 30 days of the procedure
12. Clinically significant untreated coronary artery disease requiring revascularization
13. Any percutaneous cardiovascular intervention, cardiovascular surgery, or carotid surgery within 30 days of the procedure; TEER procedures are excluded regardless of timeframe (See Failed TEER Registry).
14. Stroke or transient ischemic attack within 90 days of the procedure
15. Irreversible, severe pulmonary hypertension (e.g., pulmonary artery systolic pressure >= 2/3 systemic pressure)
16. Chronic obstructive pulmonary disease (COPD) requiring home oxygen therapy or chronic outpatient oral steroid use
17. Renal insufficiency (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m2) or receiving renal replacement therapy
18. Liver disease (cirrhosis of the liver [Child-Pugh class B or C])
19. Planned surgery within the next 12 months
20. Inability to tolerate or a medical condition precluding treatment with antithrombotic (antiplatelet, anticoagulant) therapy, including heparin administration during the procedure
21. Active infection requiring current antibiotic therapy (if temporary illness, subject may be a candidate 2 weeks after discontinuation of antibiotics)
22. Active SARS-CoV-2 infection (Coronavirus-19 [COVID-19]) or previously diagnosed with COVID-19 with sequelae that could confound endpoint assessments (as assessed by the Case Review Board)
23. Leukopenia (White Blood Cells < 3000 cells/mL), anemia (Hemoglobin < 9 g/dL), thrombocytopenia (platelet < 50,000 cells/mL), history of bleeding diathesis or coagulopathy, or hypercoagulable states
24. Refusal of blood products
25. Female who is pregnant or lactating
26. Estimated life expectancy <12 months due to non-cardiac conditions
27. Participating in another investigational drug or device study that has not reached its primary endpoint
28. Subject considered to be part of a vulnerable population

Subjects who had an attempted but failed TEER procedure may be considered for enrollment if they meet all eligibility criteria except inclusion 5, and do not meet the following modified exclusion criteria:
10. Hemodynamic instability requiring inotropic or mechanical support within 72 hours of procedure
13. Percutaneous cardiovascular intervention (other than TEER procedure), cardiovascular surgery, or carotid surgery within 30 days prior to the procedure
MAC Registry
Subjects with MAC where the impact on delivery and implantation of the SAPIEN M3 system is uncertain may be considered for enrollment if they meet the following modified inclusion criterion and all other eligibility criteria:
2. MR >= 3+, moderate MR and moderate MS, or severe MS as assessed by the Echo Core Lab

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):	21-12-2021
Enrollment:	24
Type:	Actual

Medical products/devices used

Generic name:	SAPIEN M3 System (mitral valve replacement)
Registration:	No

Ethics review

Approved WMO

Date:	17-05-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-10-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-06-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-08-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-02-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-04-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-02-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	18-12-2024
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	NCT04153292
CCMO	NL76081.078.21