Clinical summary

# Percutaneous transcatheter valve replacement in individuals with mitral regurgitation unsuitable for surgery or transcatheter edge-to-edge repair: a prospective, multicountry, single-arm trial

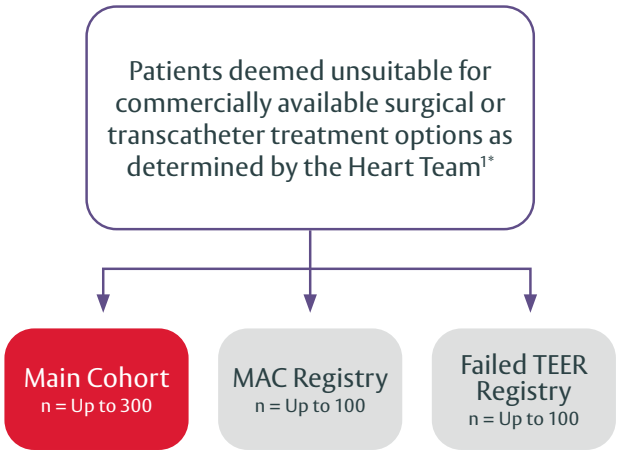
THE ENCIRCLE TRIAL

## Objectives

The ENCIRCLE trial is a prospective, single-arm, multi-center, pivotal trial to establish the safety and effectiveness of the SAPIEN M3 system in subjects with symptomatic MR ≥3+ for whom commercially available surgical or transcatheter treatment options are deemed unsuitable due to clinical, anatomical, or technical considerations.[1]

## Methods

- 56 sites in the United States, Canada, Israel, the Netherlands, the United Kingdom, and Australia[2]
- Primary endpoint was a non-hierarchical composite of all-cause mortality or HF hospitalization at 1 year[1]
- Secondary endpoints included the following at 1 year compared to baseline[1]:
  - Improvement in MR
  - Improvement in NYHA functional class
  - Improvement in KCCQ-OS score
  - Decrease in LVEDVi




## Key outcomes

- The **primary endpoint** of a non-hierarchical composite of all-cause mortality or heart failure hospitalization was achieved at 1 year with results **significantly better than the performance goal**[†] (25.2% vs 45%)[2]
- **<1% all-cause mortality** at 30 days[2]
- **96% of patients achieved MR ≤1+** at 1 year[2]
- Patients treated with the SAPIEN M3 system had **significant improvements in health status** at 1 year[2]

*Refer to Clinical Study Protocol for full enrollment criteria.
†Performance goal is based on the medical therapy arms of two trials with a similar subject population (MITRA-FR, COAPT).

Edwards

# Baseline characteristics

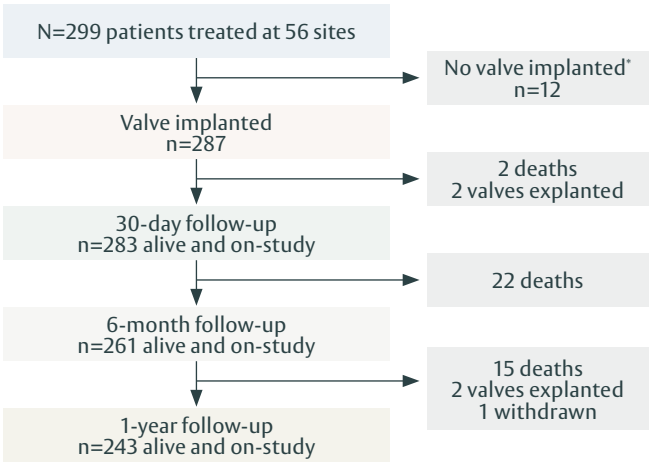
| Baseline Characteristics[2] | N=299 |
|---|---|
| Age (years) | 77.0 |
| Male | 51% |
| STS score, mitral valve replacement | 6.6% |
| MV mean gradient (mmHg) | 3.5 |
| LVEF | 49.5% |
| Congestive heart failure | 75% |
| Prior CABG | 30% |
| Prior TIA or stroke | 19% |
| Prior mitral repair | 9% |
| PPM or ICD | 36% |
| Hypertension | 84% |
| Atrial fibrillation | 70% |
| NYHA class III/IV | 71% |
| MR etiology | |
| FMR | 58% |
| DMR | 35% |
| Mixed | 6% |

## Complex patient population at baseline with multiple comorbidities[2]

- 75% of patients had congestive heart failure and 70% had atrial fibrillation
- Mild to moderate MAC present in 24% of the Main Cohort patients
- Over 25% of patients had >1 reason for TEER unsuitability

# Results

**Trial Profile[2]**

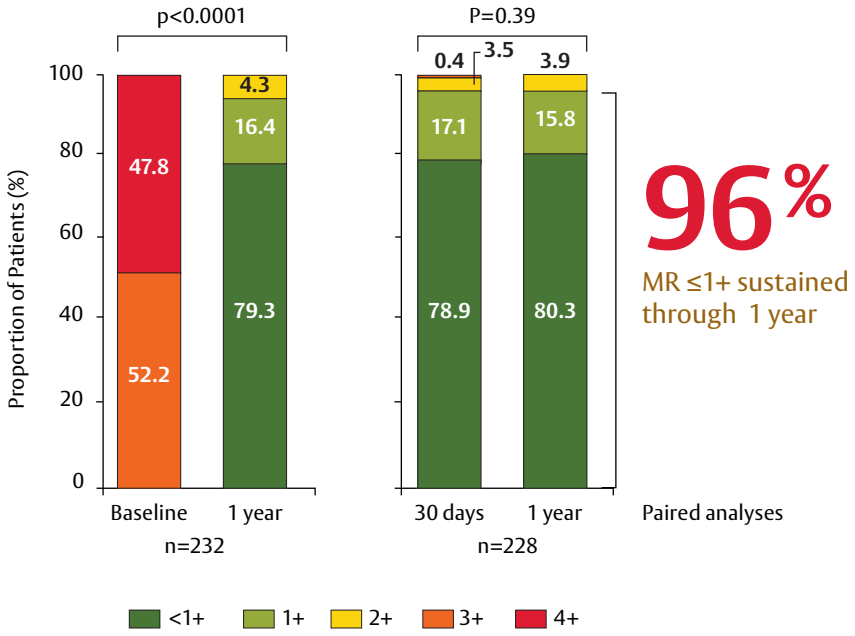



| Procedural Information[2] | SAPIEN M3 system N=299 |
|---|---|
| Procedure time (min)†,‡ | 127.0 ± 47.1 |
| Device time (min)¶ | 102.8 ± 42.6 |
| Dock deployment time (min)** | 65.9 ± 35.0 |
| Valve implant time (min)†† | 12.1 ± 14.3 |
| Procedure aborted | 4.0% |
| Conversion to surgery | 0.0% |
| PVL closure | 5.0% |
| ASD closure | |
| Routine closure | 12.4% |
| Clinically significant closure | 5.0% |
| Discharged home | 96.3% |
| Index hospital stay | 2.0 days |

*Encircling difficulties, n=5; Low dock, n=5; Mobile echodensity, n=1; Unable to gain medial commissure access, n=1.
†Data on file. Sample sizes for procedure time measurements varied across groups.
‡Defined as the time from femoral vein access puncture to guide sheath removal.
¶Defined as the time from guide sheath insertion to removal.
**Defined as the time from dock delivery system insertion to removal.
††Defined as the time from Commander delivery system insertion to removal.

# Significant and sustained MR reduction[2]

## Figure 1: MR Severity

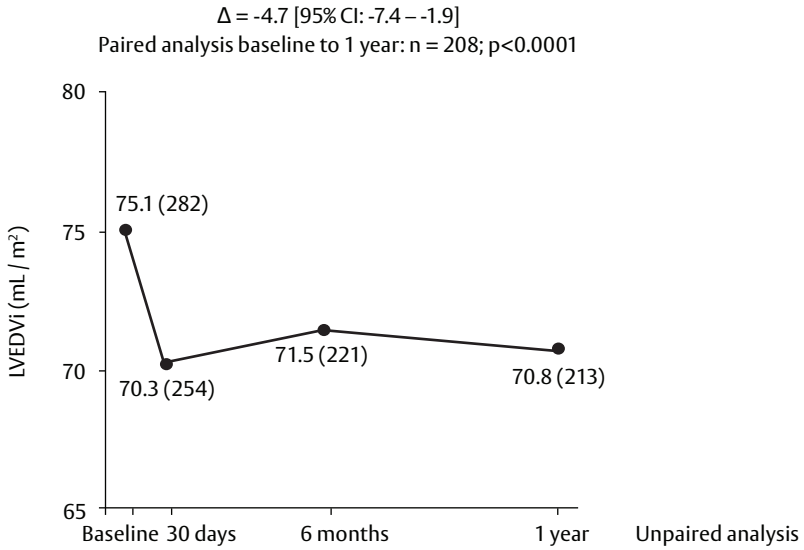



**96%**

MR ≤1+ sustained through 1 year

# Favourable left ventricular remodelling, with a significant reduction in LVEDVi[2,3]

## Figure 2: LVEDVi by Core Lab*




*By Core Lab, MedStar Health (Washington).

# Achieved primary endpoint, a non-hierarchical composite of all-cause mortality or HFH, delivering results significantly better than the performance goal[2*]

## Figure 3: All-cause Mortality or HFH


Event rates are Kaplan-Meier estimates.

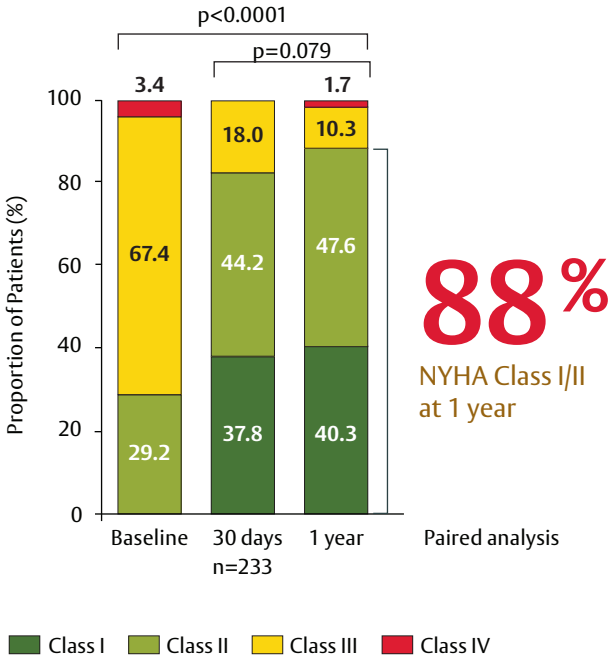
# Proven safety profile in comorbid, MR ≥3+ patients[2]

| Safety Outcomes† | 30 Days | 1 Year |
|---|---|---|
| All-cause mortality | 0.7% | 13.9% |
| • Cardiovascular mortality | 0.7% | 8.9% |
| Stroke | 2.7% | 9.3% |
| • Disabling stroke | 1.7% | 3.9% |
| • Non-disabling stroke | 1.0% | 5.5% |
| New Afib | 7.9% | 11.5% |
| New PPM | 2.6% | 5.5% |
| Major bleeding or above, MVARC‡ | 8.7% | 18.5% |
| HF hospitalization | 4.0% | 16.7% |
| Mitral valve reintervention | 2.3% | 6.4% |
| Clinically significant valve thrombosis¶ | 2.3% | 6.7% |
| Valve embolization | 0.0% | 0.0% |
| Hemolysis requiring intervention** | 4.3% | 7.1% |

*Performance goal is based on the medical therapy arms of two trials with a similar subject population (MITRA-FR, COAPT).
†Data are Kaplan-Meier estimates %.
‡Major bleeding or above includes bleeding with MVARC primary bleeding scale of major, extensive, life-threatening or fatal.
¶Clinically significant valve thrombosis includes leaflet thickening with impaired leaflet motion with mitral valve stenosis (increase in mean mitral valve gradient ≥5 mm Hg) and clinical signs or symptoms of mitral valve stenosis.
**Hemolysis requiring blood transfusion or mitral reintervention.

## Significant and sustained improvements in functional status[2]

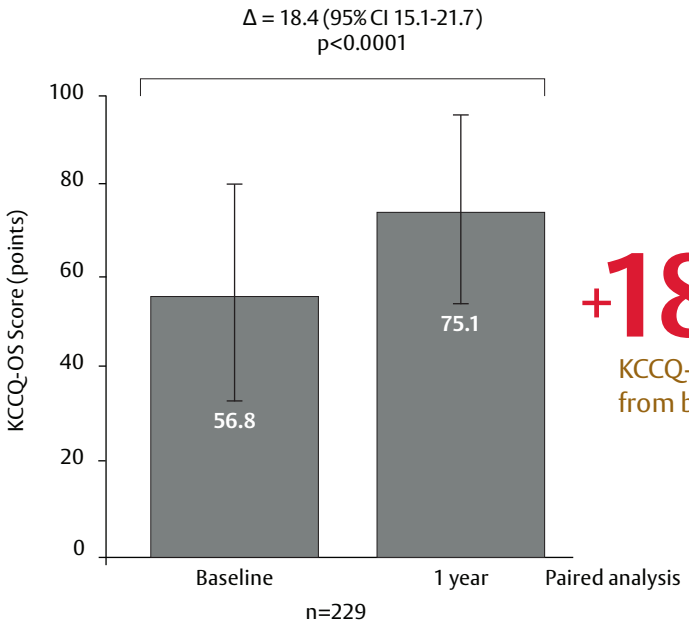
### Figure 4: NYHA Functional Class




**88%**
NYHA Class I/II
at 1 year

## Significant quality of life improvements[2]

### Figure 5: KCCQ Overall Summary Score

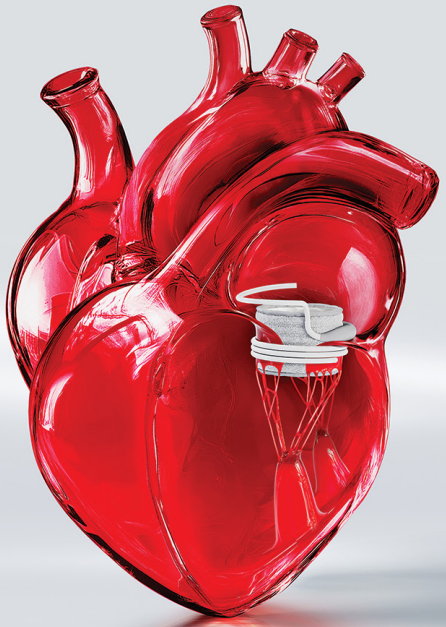



**+18 point**
KCCQ-OS score increase
from baseline to 1 year

## Conclusion

The SAPIEN M3 system is an effective TMVR therapy with a proven safety profile for a wide range of patients[2]:

- **Significant and sustained MR reduction**
- **Proven safety profile with low rates of all-cause mortality and HFH**
- **Significant quality of life improvements**



### Abbreviations

***Afib*** = *Atrial fibrillation*

***ASD*** = *Atrial septal defect*

***CABG*** = *Coronary artery bypass graft*

***DMR*** = *Degenerative mitral regurgitation*

***FMR*** = *Functional mitral regurgitation*

***HF*** = *Heart failure*

***HFH*** = *Heart failure hospitalization*

***HR*** = *Hazard ratio*

***ICD*** = *Implantable cardioverter-defibrillator*

***KCCQ-OS*** = *Kansas City Cardiomyopathy Questionnaire – Overall Summary*

***LVEDVi*** = *Left ventricular end-diastolic volume index*

***LVEF*** = *Left ventricular ejection fraction*

***MAC*** = *Mitral annular calcification*

***MR*** = *Mitral regurgitation*

***MV*** = *Mitral valve*

***MVARC*** = *Mitral Valve Academic Research Consortium*

***NYHA*** = *New York Heart Association*

***PPM*** = *Permanent pacemaker*

***PVL*** = *Paravalvular leak*

***STS*** = *Society of Thoracic Surgeons*

***TEER*** = *Transcatheter edge-to-edge repair*

***TIA*** = *Transient Ischemic Attack*

***TMVR*** = *Transcatheter mitral valve replacement*


1. The ENCIRCLE Trial. Clinicaltrials.gov Identifier: NCT04153292. Updated August 09, 2025. https://clinicaltrials.gov/study/NCT04153292
2. Guerrero M, et al. Percutaneous transcatheter valve replacement in individuals with mitral regurgitation unsuitable for surgery or transcatheter edge-to-edge repair: a prospective, multicountry, single-arm trial. Lancet. 2025 Nov 29;406(10519):2541-2550. doi: 10.1016/S0140-6736(25)02073-2
3. Daniels D. et al. Percutaneous Transcatheter Valve Replacement for Mitral Regurgitation: 1-Year Outcomes from the ENCIRCLE Trial. Presented at TCT 2025.





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