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

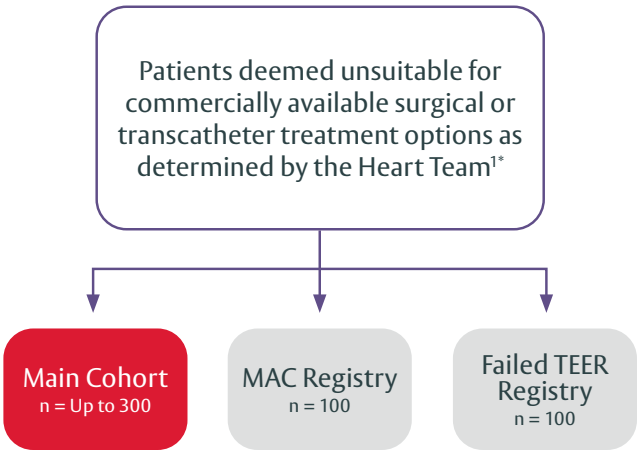
THE ENCIRCLE TRIAL

Objectives[1]

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.

Methods

- 56 sites in the United States, Canada, Israel, the Netherlands, the United Kingdom, and Australia[2,3]
- 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 overall score
  - Decrease in LVEDVi



Key Outcomes[2,3]

- 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%)
- **<1% all-cause mortality** at 30 days
- **96% achieved MR 0/1+ at 1 year**
- Patients treated with the SAPIEN M3 system had **significant improvements in health status,** including an 18-point increase in KCCQ-OS score at 1 year

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

Edwards

Results[2,3]

Baseline Characteristics	N=299
Age (years)	77.0
Male	51%
STS score, mitral valve replacement	6.6%
MV mean gradient (mmHg)	3.4
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	58.3%
DMR	35.4%
Mixed	6.4%

Complex Patient Population at Baseline with Multiple Comorbidities

- 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

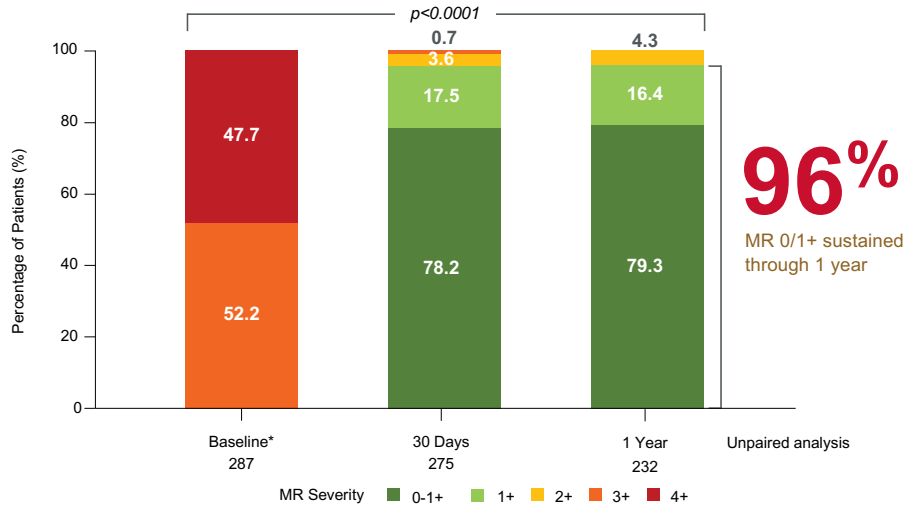
Procedural Information	SAPIEN M3 system N=299
Procedure time (min)[*†]	127.0 ± 47.1
Device time (min)[‡]	102.8 ± 42.6
Dock deployment time (min)[§]	65.9 ± 35.0
Valve deployment time (min)[Δ]	12.1 ± 14.3
Procedure aborted	4.0%
Conversion to surgery	0.0%
PVL closure	5.0%
ASD closure	
• Clinically significant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

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%
Valve embolization	0.0%	0.0%
Hemolysis requiring intervention[¶]	4.3%	7.1%

[*]Data on file. Sample sizes for procedure time measurements varied across groups.
[†]Defined as the time from femoral vein access 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.
[Δ]Defined as the time from Commander delivery system insertion to removal.
[◊]Major bleeding or above includes bleeding with MVARC primary bleeding scale of major, extensive, life-threatening or fatal.
[¶]Hemolysis requiring intervention: hemolysis requiring blood transfusion or mitral reintervention.

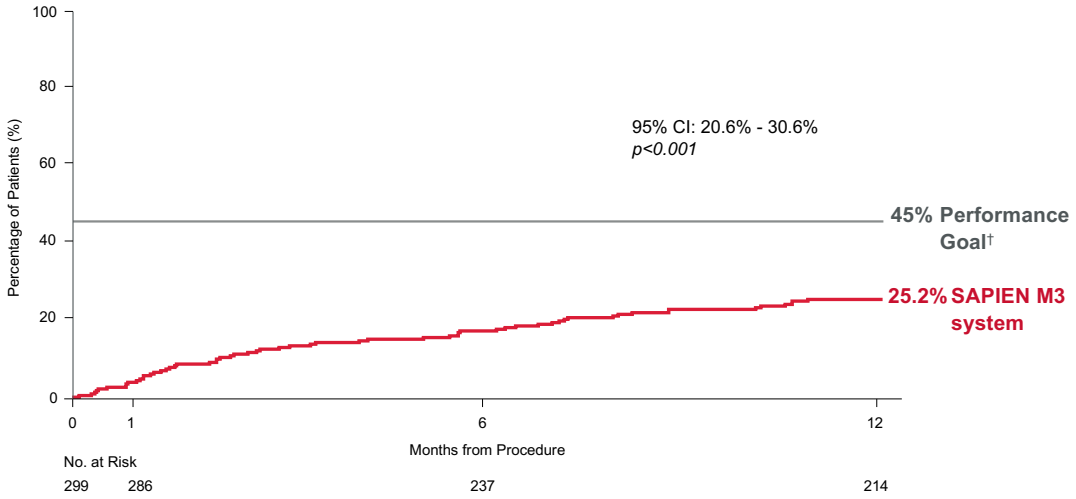
Results *(continued)*[2,3]

Figure 1: MR Severity through 1 Year



*The worst case among TEE and TTE was used as the baseline; TTE was used for all other visits.

Figure 2: All-Cause Mortality or HF Hospitalization



†Based on the medical therapy arms of two trials with a similar subject population (MITRA-FR, COAPT).

Results *(continued)*[2,3]

Figure 3: NYHA Functional Class

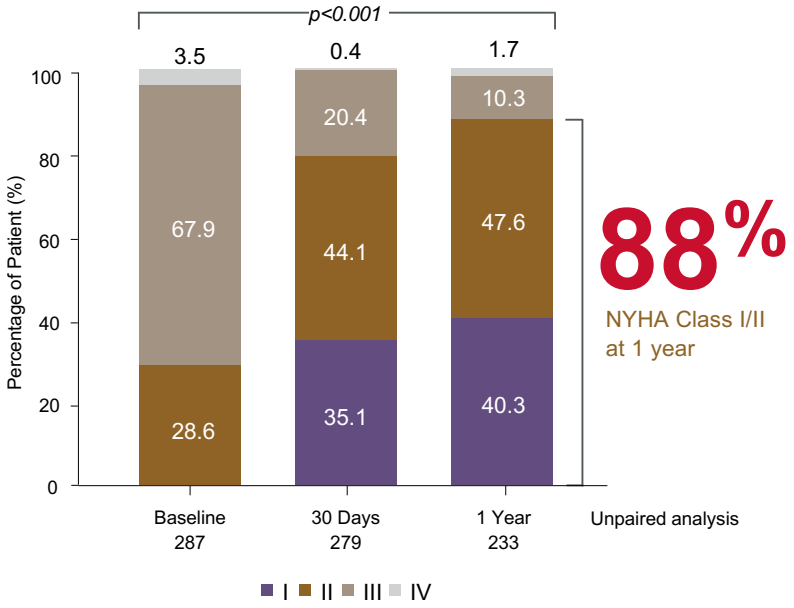
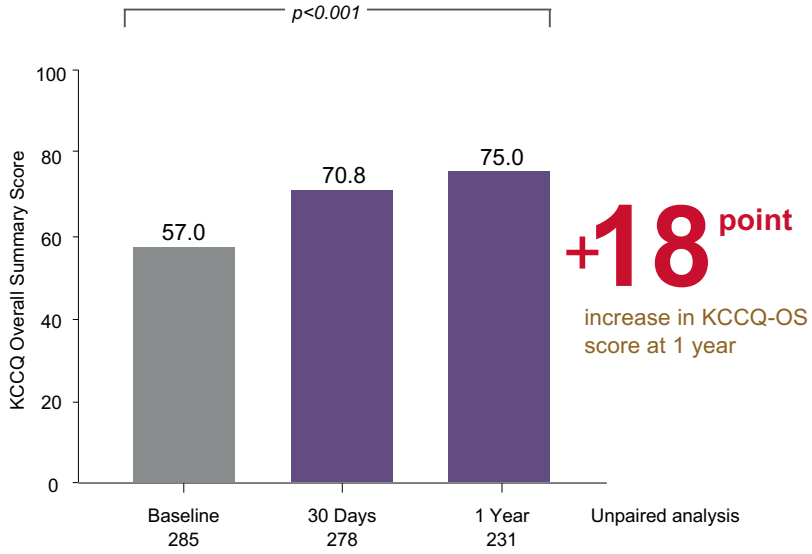


Figure 4: KCCQ Overall Summary Score



Conclusion[2,3]

Results from the pivotal trial demonstrate that the primary endpoint (composite of all-cause mortality or heart failure hospitalization) and secondary endpoints were achieved, accompanied by significant MR reductions and improvements in health status, confirming the efficacy and proven safety profile of the SAPIEN M3 system in symptomatic patients with MR ≥3+.

Abbreviations

Afib = *Atrial fibrillation*

ASD = *Atrial septal defect*

CABG = *Coronary artery bypass graft*

DMR = *Degenerative mitral regurgitation*

FMR = *Functional mitral regurgitation*

HF = *Heart failure*

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*

TEE = *Transesophageal echocardiography*

TEER = *Transcatheter edge-to-edge repair*

TMVR = *Transcatheter mitral valve replacement*

TTE = *Transthoracic echocardiogram*

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. *The Lancet.* 2025.
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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