Transcatheter tricuspid valve replacement in patients with symptomatic severe tricuspid regurgitation.

THE TRISCEND II PIVOTAL TRIAL

Outcomes by baseline tricuspid regurgitation severity

Objectives

The TRISCEND II pivotal trial is the first prospective, multicenter, randomized controlled trial to evaluate transcatheter tricuspid valve replacement (TTVR) with the Edwards EVOQUE system in conjunction with optimal medical therapy (OMT) against OMT alone in a 2:1 randomization in patients with ≥ severe symptomatic tricuspid regurgitation (TR).[1] To assess whether baseline TR severity influenced treatment outcomes following TTVR, a sub-analysis was conducted.[2]

Patient Population Baseline Characteristics[1]

Baseline Characteristics	TTVR n=259*	OMT alone n=133
Mean age, years	79.3	79.1
Female	74.9%	76.7%
NYHA class III-V	73.0%	69.2%
Atrial fibrillation	96.1%	92.5%
Chronic kidney disease	54.1%	59.4%
Pacemaker/ICD	38.2%	39.8%
Ascites	18.5%	21.8%
KCCQ-OS (mean)	52.8	50.6
Secondary TR etiology	74.1%	71.4%

Primary Safety and Effectiveness endpoint

Primary safety and effectiveness endpoint was a hierarchical composite assessed at 1 year:[1]

- **All-cause mortality,**
- **RVAD implantation or heart transplant,**
- **Tricuspid valve surgery or percutaneous tricuspid intervention,**
- **Annualized rate of HF hospitalizations,**
- **KCCQ-OS improvement Δ ≥10 points,**
- **NYHA improvement Δ ≥1 functional class,**
- **6MWD improvement Δ ≥30 meters**

The same endpoint definition was used when patients were stratified by baseline TR severity.[2]

Key Outcomes

- At 1 year, **TTVR was superior to OMT alone,** regardless of baseline TR severity.[1-2]
- Patients with the **most severe TR at baseline treated with TTVR experienced a hard endpoint benefit** at18 months vs control group patients.[2]
- Patients treated with TTVR had greater improvements in health status[1], with the magnitude of improvement consistently greater in patients with the most severe TR at baseline compared to OMT alone.[2]
- At 1 year, TR elimination was achieved in 95% of patients treated withTTVR compared to < 3% with OMT alone.[1-2]

*Of the 267 patients randomized to TTVR, 8 exited prior to procedure

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Patient stratification by baseline TR severity

Patients were stratified into two cohorts, severe TR and massive/torrential TR, based on TR severity at baseline using a 5-grade echocardiographic classification system[3]. Patient demographics and comorbidities were well balanced between TTVR and OMT alone groups and between TR severity cohorts.

Outcomes assessed at 1 year
Primary safety and effectiveness endpoint, TR reduction, quality of life, functional status, and exercise capacity.

Outcomes assessed at 18 months*
Heart failure hospitalization (HFH) and all-cause mortality (ACM).

All-Cause Mortality and Heart Failure Hospitalization Outcomes

TTVR Patients with the most severe TR at baseline experienced a lower rate of ACM or HFH at 18 months (Figure 1A). These findings were primarily due to **a lower rate of HFH** (Figure 1B). ACM was similar in the Severe TR group for TTVR (13.6%) and OMT alone (13.5%; P = .980). In the Massive/Torrential TR group, ACM was 17.9% for TTVR and 23.6% for OMT alone (P = .338).

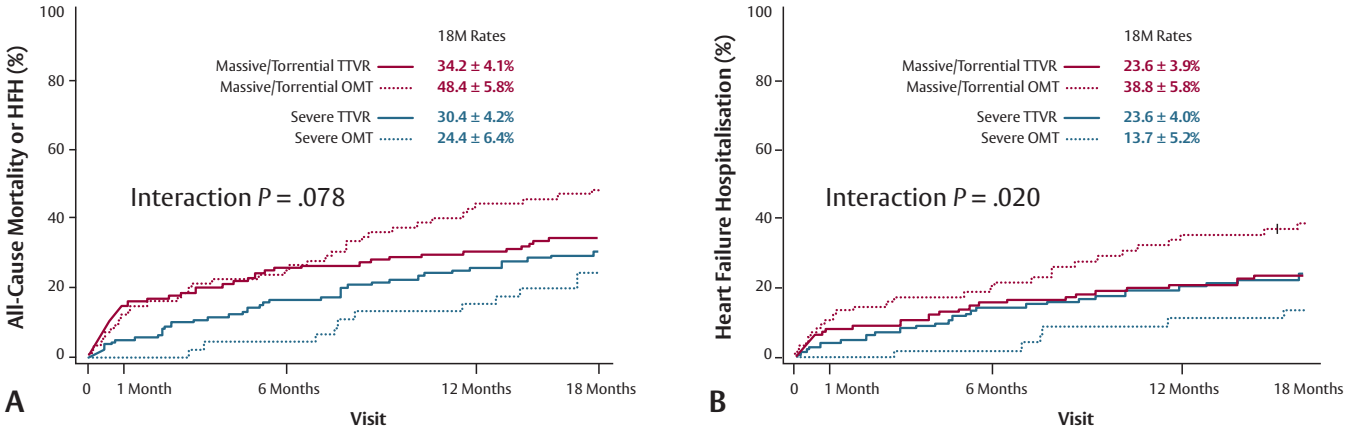


Figure 1: Kaplan-Meier estimates at 18 months stratified by baseline TR severity for (A) ACM or HFH (Massive/Torrential TR: TTVR 34.2 ± 4.1% vs. OMT alone 48.4 ± 5.8%; P = .045; NNT 7; Severe TR: TTVR 30.4 ± 4.2% vs. OMT alone 24.4 ± 6.4%; P = .438); **and (B) HFH alone** (Massive/Torrential TR: TTVR, 23.6 ± 3.9% vs. OMT alone, 38.8 ± 5.8%, P = .030; NNT 7; Severe TR: TTVR 23.6 ± 4.0% vs. OMT alone13.7 ± 5.2, P = .134). For further details on statistical analyses please see reference 2.

‡ 53 patients in the control group crossed over to TTVR after their 1-year visit (n=22 in the Severe TR group; n=31 in the Massive/Torrential TR group).

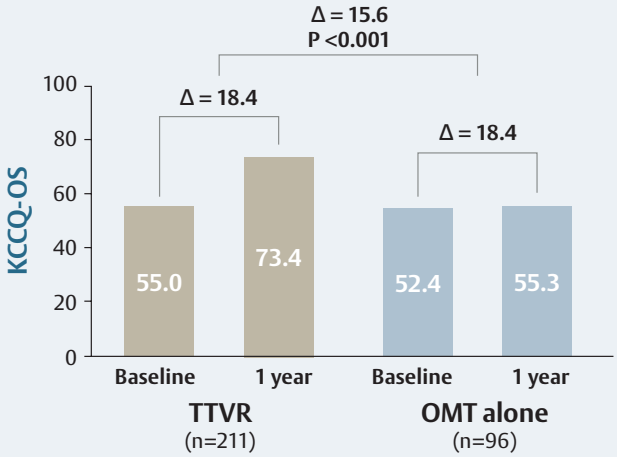
* Analyses of 18-month outcomes were not pre-specified in the trial protocol. ACM and HFH data were collected through routine adverse event reporting by the sites, and these events were CEC-adjudicated.

Clinical, Functional, and Quality-of-Life Outcomes

Clinically **meaningful improvements with TTVR at 1 year**[1], with magnitude of improvement consistently **greater in patients with the most severe TR** at baseline[2].

Full cohort[1,*] **Patients stratified by baseline TR severity**[2]

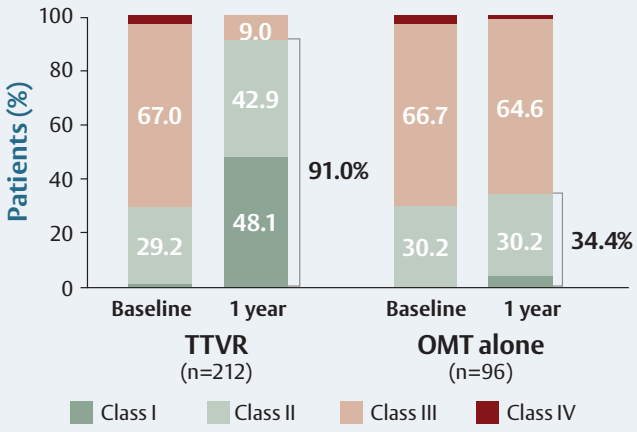
Figure 2. KCCQ-OS Improvement



Severe TR	+14.6 points vs 7.4 (*P* = .066[a])
Massive / Torrential TR	+22.2 points vs -0.7 (*P* < .001[a])

Reported values correspond to TTVR vs OMT alone

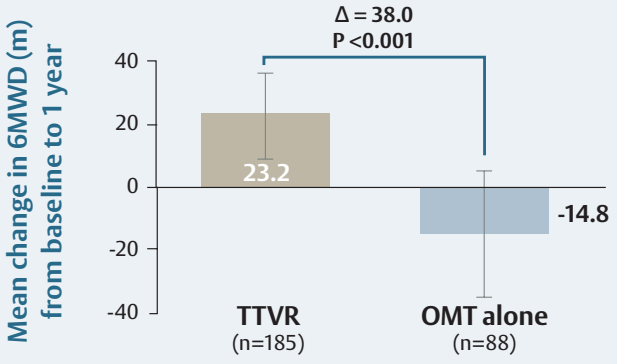
Figure 3. NYHA Functional Class Improvement



Severe TR	88.6% vs 33.3%
Massive / Torrential TR	93.5% vs 35.2%

Reported values correspond to TTVR vs OMT alone

Figure 4. 6MWD Improvement



Severe TR	+10.6 meters vs -27.2 (*P* = .021[a])
Massive / Torrential TR	+35.2 meters vs -5.4 (*P* = .030[a])

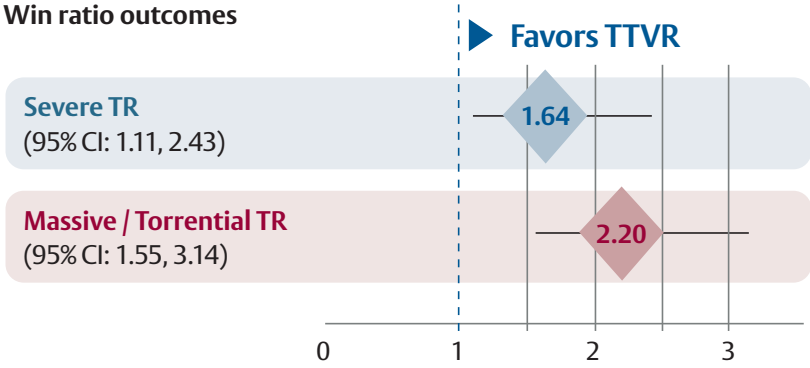
Reported values correspond to TTVR vs OMT alone

*Data on file at Edwards Lifesciences. Graphs show paired analysis. [a]Kruskal-Wallis test.

Primary Safety and Effectiveness Endpoint

At 1 year, **TTVR was superior to OMT alone** regardless of baseline TR severity.[2]

Win ratio outcomes



The win ratio analysis demonstrated that **TTVR provides a greater likelihood of clinical benefit† at 1 year vs OMT alone** for both the Severe TR (P = 0.008) and Massive/Torrential TR (P<0.001) cohorts.

Tricuspid Regurgitation Reduction

Consistent TR elimination with TTVR, regardless of baseline TR severity.[1-2]

Patients with **TR ≤ mild** at 1 year, for both TR severity groups

>95% TTVR

<3% OMT alone

Procedural Outcomes[1,*]

- **100% performed via percutaneous femoral vein access**
- **High procedural success (95%) and 1.2% conversion to surgery**
- **93% discharged home**

Procedural Characteristics	n=259[Δ]
Device implanted as intended	95.4%[‡]
Device time, median (IQR), min	56.5 (41.0, 75.0)
Length of stay, median (IQR), days	3.0 (2.0, 6.0)

30-day Safety Outcomes[1]

CEC-Adjudicated Safety Events	TTVR n=259*
Cardiovascular mortality	3.1%
Myocardial infarction	0.8%
Stroke	0.4%
Severe bleeding	10.4%
Non-elective tricuspid re-intervention	0.8%
New pacemaker/CIED implants in pacemaker-naïve patients	24.7%

* Data on file at Edwards Lifesciences. Graphs show paired analysis.

† The primary endpoint was a hierarchical composite that included death, durable right ventricular assist device/heart transplantation, tricuspid valve intervention, annualized HFH, and pre-specified improvements in quality of life, functional status, and exercise capacity.

Δ Of the 267 patients randomized to TTVR, 8 exited prior to procedure.

‡ 12 patients (4.6%) did not receive device due to challenging imaging or anatomy

§ Fatal, life-threatening, extensive, or major bleeding, as defined by Mitral Valve Academic Research Consortium (MVARC; Stone et al. 2015).

Conclusion

- TRISCEND II is the first randomized controlled trial studying tricuspid valve replacement in conjunction with optimal medical therapy compared to medical therapy alone.[1]
- Results from the TRISCEND II trial establish TTVR as an effective therapy with a proven safety profile for patients with symptomatic ≥ severe TR.[1]
- Regardless of baseline TR severity, treatment with TTVR demonstrated **superior clincial benefits and consistent TR elimination** vs OMT alone.[1-2]
- For patients with the most severe TR, treatment with TTVR demonstrated **a hard endpoint benefit** vs OMT alone, with a number needed to treat of 7 at 18 months.[2]
- For patients treated with TTVR, **KCCQ-OS scores and symptoms improved compared to the OMT cohort.**[1] The magnitude of improvement was consistently **greater in patients with baseline massive/torrential TR.**[2]

Reference:
1. Hahn R.T et al., *N Engl J Med.* 2025;392(2):115-126;
2. Lurz P, et al. *Eur Heart J.* 2025. doi:10.1093/eurheartj/ehaf676;
3. Hahn RT, Zamorano JL. *Eur Heart J Cardiovasc Imaging* 2017;18(12):1342-1343.

Acronyms:
6MWD = Six-minute walk distance
ACM = All-cause mortality
CEC = Clinical events committee
CI = Confidence interval
CIED = Cardiac implantable electronic device
HF = Heart failure
HFH = Heart failure hospitalization
ICD = Implantable cardioverter defibrillator
IQR = Interquartile range
KCCQ-OS = Kansas City Cardiomyopathy Questionnaire – Overall Summary
MVARC = Mitral Valve Academic Research Consortium
NNT = Number needed to treat
NYHA = New York Heart Association
OMT = Optimal Medical Therapy
RVAD = Right ventricular assist device
TR = Tricuspid regurgitation
TTVR = Transcatheter tricuspid valve replacement

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