



Edwards SAPIEN 3 Transcatheter Heart Valve

# Evaluating Transcatheter Aortic Valve Replacement (TAVR) in Asymptomatic Severe Aortic Stenosis Patients

Trial Overview for Health Care Professionals

# Objective & Key Endpoints

## Background

For asymptomatic severe aortic stenosis patients, a strategy of clinical surveillance has been adopted with intervention planned once symptoms emerge or left ventricular (LV) systolic dysfunction develops. This strategy has some practical challenges: 1) interpreting symptoms may be difficult, particularly in elderly sedentary populations; 2) with AS progression being variable and unpredictable, rapid deterioration may occur; 3) late symptom reporting may result in irreversible myocardial damage with worsened prognosis, despite AVR; and 4) operative risk increases with patient age and LV dysfunction. Whether an early intervention will improve outcomes remains unknown and has never been studied in a randomized trial.

## Objective

The objective of the EARLY TAVR Trial is to establish the safety and effectiveness of the Edwards SAPIEN 3 transcatheter heart valve compared with clinical surveillance in asymptomatic patients with severe, calcific aortic stenosis.

Patients will be randomized 1:1 to receive either TAVR with the SAPIEN 3 valve (via the transfemoral approach) or clinical surveillance. Patients will be stratified by whether or not they are able to perform a treadmill stress test.

## Primary Endpoint:

*Safety and Effectiveness:* Composite endpoint of all-cause death, all stroke, and unplanned cardiovascular hospitalization through 2 years

## Secondary Endpoints:

- Composite of patient being 1) Alive, 2) Kansas City Cardiomyopathy Questionnaire (KCCQ) score  $\geq 75$  and 3) KCCQ decrease  $\leq 10$  points at 2 years
- Integrated measure of left ventricular (LV) health (LV global longitudinal strain, LV mass index, and left atrial (LA) volume index) at 2 years
- Change in LV ejection fraction (LVEF) at 2 years
- New onset atrial fibrillation through 2 years
- Death or disabling stroke through 2 years

# Key Inclusion Criteria

1. 65 years of age or older at randomization
2. Severe aortic stenosis defined as:
  - 1) Aortic valve area (AVA)  $\leq 1.0 \text{ cm}^2$  or AVA index  $\leq 0.6 \text{ cm}^2/\text{m}^2$  AND
  - 2) Peak jet velocity  $\geq 4.0 \text{ m/s}$  or mean gradient  $\geq 40 \text{ mmHg}$
3. Patient is asymptomatic defined as:
  - 1) Negative treadmill stress test, OR
  - 2) Per physician after thorough assessment of patient history if the patient is unable to perform a stress test
4. LV ejection fraction  $\geq 50\%$
5. Society of Thoracic Surgeons (STS) risk score  $\leq 10$

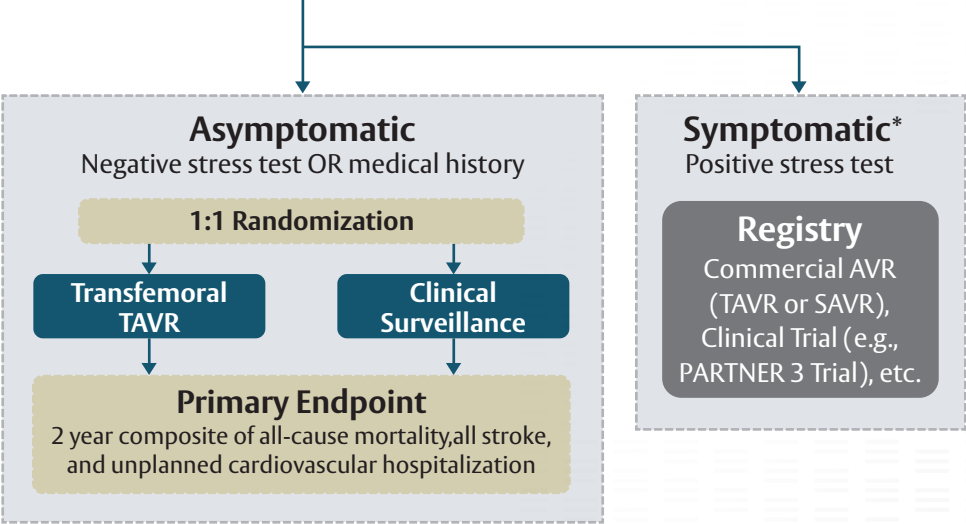
# Key Exclusion Criteria

1. Patient is symptomatic (e.g., NYHA Functional Class  $\geq 2$ , history of syncopal episode, or CCS angina score  $> 1$ , hospitalization for heart failure within the last 6 months)
2. Patient has any concomitant valvular, aortic, coronary artery disease requiring surgery making AVR a Class I indication
3. Evidence of an acute myocardial infarction  $\leq 30$  days before randomization
4. Aortic valve is unicuspid, bicuspid, or is non-calcified
5. Severe aortic regurgitation ( $> 3+$ )
6. Severe mitral regurgitation ( $> 3+$ ) or  $\geq$  moderate mitral stenosis
7. Pre-existing mechanical or bioprosthetic valve in any position (of note, mitral ring is not an exclusion)
8. Symptomatic carotid or vertebral artery disease or successful treatment of carotid stenosis within 30 days of randomization

# EARLY TAVR Trial Design

## Asymptomatic, Severe Aortic Stenosis

**Screening / Stress Test\***  
Inclusion/exclusion criteria, treadmill stress test



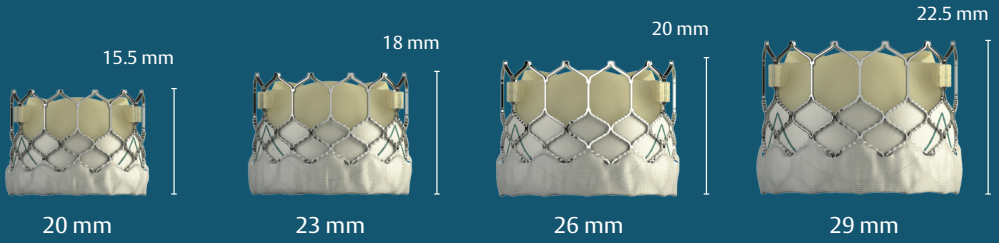
\* For some patients, interpreting symptoms may be difficult. According to a pooled analysis of large observational studies, as many as 49% of asymptomatic patients undergoing stress testing had an abnormal stress test. Aortic valve replacement is recommended for these patients.<sup>1</sup>



For more detailed information about the EARLY TAVR Trial, visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov)

# Products Under Clinical Investigation

## Edwards SAPIEN 3 Transcatheter Heart Valve





For more detailed information about the EARLY TAVR Trial, please visit:

[www.clinicaltrials.gov](http://www.clinicaltrials.gov)

Search: EARLY TAVR

<sup>1</sup> Genereux P. Natural history, diagnostic approaches and therapeutic strategies for patients with asymptomatic severe AS. JACC 2016; 2263-88

**INVESTIGATIONAL DEVICES. CAUTION: The Edwards SAPIEN 3 transcatheter heart valve is an investigational device when used in asymptomatic or low-risk patients. Limited by Federal (USA) law to investigational use only. These devices are not available for marketing or commercial sale in the United States for asymptomatic or low-risk patients. See Instructions for Use for full information, including indications, contraindications, warnings, precautions, and adverse events.**

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