A New Lifeline for Inoperable Aortic Stenosis Patients

- Superior survival
- Significantly improved cardiac function
- Dramatic reduction in symptoms
- Restored quality of life

References
1. Data on file, Edwards Lifesciences LLC.

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Definitive Results Through Rigorous Design

The PARTNER (Placement of AoRtic TraNscathetER Valves) Trial represents a paradigm shift in clinical investigation and interpretability. As the world’s first prospective, randomized, and controlled trial for transcatheter heart valves, the PARTNER Trial sets new standards in site selection, case screening, study management, multidisciplinary teamwork, and patient follow-up.1

The PARTNER Trial consists of two individually powered patient cohorts.

- In Cohort A, the safety and effectiveness of the Edwards SAPIEN Transcatheter Heart Valve (THV) was compared to surgical aortic valve replacement (sAVR) in high-risk patients with severe aortic stenosis. The results of Cohort A are forthcoming.1
- In Cohort B, the safety and effectiveness of the Edwards SAPIEN THV was compared to best medical management (standard therapy) in inoperable patients with severe aortic stenosis. Patient selection required at least two cardiothoracic surgeons and an interventional cardiologist to agree that patients were not suitable candidates for surgery.1

The Edwards SAPIEN THV Significantly Improves Survival

20% absolute reduction in mortality1

Despite expert care and frequent BAV (78.2%), standard therapy failed to alter the dismal natural course of disease1

24% absolute reduction in cardiovascular mortality at 1 year (P < .001)2

29% absolute reduction in all-cause mortality or hospitalization at 1 year (co-primary endpoint; P < .001)3

NNT = 5
Need to treat just 5 patients to save a life1

THE PARTNER TRIAL PROTOCOL1

Cohort A: n = 700
Cohort B: n = 358

Symptomatic Severe Aortic Stenosis

ASSESSMENT Operability

ASSESSMENT Transfemoral Access

1:1 Randomization

Transfemoral vs Standard Therapy

Not in Study

Mean age 83 y
NYHA Class III-IV 93%
COPD, O₂ dependent 23%
PVD 28%
Porcelain aorta 15%
Chest wall deformity 7%
CAD 71%
Frail 23%

COHORT B POPULATION PROFILE1

CO-PRIMARY ENDPOINT: ALL-CAUSE MORTALITY1,2

P < .001
Δ at 1 y = 20.0%
NNT = 5.0 pts

0 6 12 18 24
All-Cause Mortality, %

Standard Therapy

Edwards THV

50.7% 30.7%

0 20 40 60 80 100

Months

P < .001
Δ at 1 y = 20.0%
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THE PARTNER TRIAL PROTOCOL1

Cohort A
- n = 700
- Symptomatic Severe Aortic Stenosis
- Operability
  - Yes
  - No

Cohort B
- n = 358
- Symptomatic Severe Aortic Stenosis
- Transfemoral Access
  - Yes
  - No

1:1 Randomization
- Transfemoral
- Standard Therapy
- Not in Study

COHORT B POPULATION PROFILE1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
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NNT = 5
Need to treat just 5 patients to save a life1

[CO-PRIMARY ENDPOINT: ALL-CAUSE MORTALITY1]1

- Standard Therapy
  - 50.7%
  - NNT = 5.0 pts
- Edwards THV
  - 30.7%

[DEFINITION OF PATIENTS]1

- Definitive Results Through Rigorous Design
- COHORT B POPULATION PROFILE1

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association; PVD, peripheral vascular disease; BAV, balloon aortic valvuloplasty.
The Edwards SAPIEN THV Significantly Improves Hemodynamics and Sustains Valve Performance

- Reduced mean gradient ($P < .001$)\(^1\)
- Increased and sustained aortic valve area ($P < .001$)\(^2\)
- Increase in ejection fraction at 1 year ($P < .01$)\(^1\)
- Reduction in left ventricular mass index at 6 months and 1 year ($P < .0001$)\(^1\)
- Reduction in mitral regurgitation at 1 year ($P < .001$)\(^1\)

The Edwards SAPIEN THV Significantly Improves Patient Symptoms and Quality of Life (QOL)

- 75% of the Edwards SAPIEN THV patients in NYHA class I or II at 1 year\(^2\)
- Significant improvement observed as early as 30 days ($P < .001$)\(^1\)
- 25-point treatment effect in KCCQ score
- 20-point improvement in KCCQ score represents change of large clinical importance\(^3\)

KCCQ, Kansas City Cardiomyopathy Questionnaire; MCID, minimum clinically important difference.
The Edwards SAPIEN THV Significantly Improves Hemodynamics and Sustains Valve Performance

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Critical Insights

With standard therapy, predicted survival of inoperable patients with aortic stenosis is lower than with certain metastatic cancers

![5-Year Survival Rate, %]

<table>
<thead>
<tr>
<th>Condition</th>
<th>Survival Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>23</td>
</tr>
<tr>
<td>Lung</td>
<td>4</td>
</tr>
<tr>
<td>Colorectal</td>
<td>12</td>
</tr>
<tr>
<td>Prostate</td>
<td>30</td>
</tr>
<tr>
<td>Ovarian</td>
<td>28</td>
</tr>
<tr>
<td>Severe Inoperable Aortic Stenosis</td>
<td>3</td>
</tr>
</tbody>
</table>

*Using constant hazard ratio.

Based on 1-year results of Cohort B patients treated with the Edwards SAPIEN THV:

**Only need to treat 5 patients to save a life**

**3 out of 4 patients were asymptomatic or mildly symptomatic**

Increased experience and next-generation technology may lower the incidence of acute major complications:

- Vascular complications (16.2%)
- Bleeding episodes (16.8%)
- Strokes (5.0%)

“On the basis of a rate of death from any cause at 1 year that was 20 percentage points lower with TAVI than with standard therapy, balloon-expandable TAVI should be the new standard of care for patients with aortic stenosis who are not suitable candidates for surgery.”


“Rarely in medical research has so dramatic an improvement in survival been achieved in such a short time, with so few iterations.”

— Lars Svensson, MD, PhD, Cardiothoracic Surgeon, Cleveland Clinic, Cleveland, Ohio

“The dramatic improvement in quality of life scores in the Edwards SAPIEN THV group is equivalent to a 10-year reduction in age.”

— David J. Cohen, MD, PhD, Cardiologist and Director of Cardiovascular Research, St Luke’s Mid America Heart and Vascular Institute, Kansas City, Missouri
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![5-year survival rate chart]

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Establishing the New Standard of Care for Inoperable Aortic Stenosis

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