SAPIEN 3: Evaluation of a Balloon-Expandable Transcatheter Aortic Valve in High-Risk and Inoperable Patients With Aortic Stenosis – One-Year Outcomes

Howard C. Herrmann, MD
on behalf of The PARTNER II Trial Investigators
# Disclosure Statement of Financial Interest

**Howard C. Herrmann, MD**

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Grant/Research Support</td>
<td>• Abbott Vascular, Boston Sci, Cardiokinetx, Edwards Lifesciences, Gore, Medtronic, Mitraspan, Siemens, St. Jude Medical</td>
</tr>
<tr>
<td>• SAB (Equity)</td>
<td>• MicroInterventional Devices</td>
</tr>
<tr>
<td>• Honoraria</td>
<td>• Edwards Lifesciences</td>
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Background

• The initial PARTNER Trial for high-risk (HR) and inoperable (INOP) patients demonstrated the early promise of TAVR with first generation devices.

• At 1 year, mortality was 24% in HR (equivalent to SAVR) and 31% in INOP patients.

• 30-Day outcomes with the SAPIEN 3 (S3) TAVR system were presented at ACC 2015 demonstrating very low rates of adverse events.

• This presentation reports the study results in HR and INOP patients at 1 year.
The PARTNER II S3 Trial
Study Design

ASSESSMENT by Heart Valve Team

Intermediate Risk Operable (PII S3i)

ASSESSMENT: Optimal Valve Delivery Access

- Transfemoral (TF)
  - TF TAVR SAPIEN 3

- Transapical / Transaortic (TA/TAo)
  - TAA TAVR SAPIEN 3

High-Risk Operable / Inoperable (PII S3HR)

ASSESSMENT: Optimal Valve Delivery Access

- Transfemoral (TF)
  - TF TAVR SAPIEN 3

- Transapical / Transaortic (TA/TAo)
  - TAA TAVR SAPIEN 3

2 Single Arm Non-Randomized Historical-Controlled Studies

n = 1076 Patients

n = 583 Patients

1 Year
SAPIEN 3 Transcatheter Heart Valve

Distinguishing Features

- Bovine pericardial tissue
- Outer sealing skirt to reduce PVL
- Low frame height
- Enhanced frame geometry for low delivery profile
Key Inclusion Criteria

- Risk determined by STS score and Heart Team:
  - **High-Risk**: STS score > 8 or Heart Team determination
  - **Inoperable**: Risk of death or serious morbidity > 50% (assessed by a cardiologist and 2 cardiac surgeons)

- Severe aortic stenosis determined by echocardiography:
  - Valve area < 0.8 cm² or valve area index < 0.5 cm²/m² and mean gradient > 40mmHg or peak velocity > 4 m/s
The PARTNER II S3 Trial
Participating Sites

Co-Principal Investigators
Susheel Kodali
Columbia University, NY

Vinod Thourani
Emory University, GA

583 Patients Enrolled at
29 US Participating Sites
<table>
<thead>
<tr>
<th>Top 10 Enrollment Sites</th>
<th>Location</th>
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</thead>
<tbody>
<tr>
<td>Cedars-Sinai Medical Ctr.</td>
<td>(Los Angeles, CA) 73</td>
</tr>
<tr>
<td>Columbia University Medical Ctr.</td>
<td>(New York, NY) 65</td>
</tr>
<tr>
<td>Emory University</td>
<td>(Atlanta, GA) 63</td>
</tr>
<tr>
<td>University of Pennsylvania</td>
<td>(Philadelphia, PA) 43</td>
</tr>
<tr>
<td>Heart Hospital Baylor Plano</td>
<td>(Plano, TX) 30</td>
</tr>
<tr>
<td>Ochsner Hospital</td>
<td>(New Orleans, LA) 26</td>
</tr>
<tr>
<td>University of Texas, Houston</td>
<td>(Houston, TX) 25</td>
</tr>
<tr>
<td>Stanford University Medical Ctr.</td>
<td>(Palo Alto, CA) 24</td>
</tr>
<tr>
<td>Newark Beth Israel Medical Ctr.</td>
<td>(Newark, NJ) 21</td>
</tr>
<tr>
<td>Washington Hospital Ctr.</td>
<td>(Washington, DC) 19</td>
</tr>
</tbody>
</table>
Study Flow
30 Day and 1 Year Patient Status

PII S3 HR / INOP

n = 583

15 Deaths

n = 568
At 30 Days

71 Additional Deaths
5 Withdrew Consent

485 / 492 or 98.6%
Follow-up at 1 year
Baseline & Procedural Characteristics

Median STS = 8.4%
Average Age = 82yrs

N = 583

TF 84%
TA 6%
T Ao 10%

1.9% 34.3% 38.9% 24.9%

20 mm 23 mm 26 mm 29 mm

Male 58%
Female 42%
## Baseline Patient Characteristics

### Demographics

<table>
<thead>
<tr>
<th>Characteristic (%)</th>
<th>Overall (n=583)</th>
<th>HR (n=384, 66%)</th>
<th>INOP (n=199, 34%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>82</td>
<td>83</td>
<td>80</td>
<td>0.001</td>
</tr>
<tr>
<td>Female gender</td>
<td>42</td>
<td>40</td>
<td>46</td>
<td>0.14</td>
</tr>
<tr>
<td>STS Score (median)</td>
<td>8.4</td>
<td>8.6</td>
<td>7.4</td>
<td>0.002</td>
</tr>
<tr>
<td>NYHA Class 3/4</td>
<td>90</td>
<td>90</td>
<td>91</td>
<td>0.82</td>
</tr>
<tr>
<td>DM</td>
<td>35</td>
<td>33</td>
<td>37</td>
<td>0.42</td>
</tr>
<tr>
<td>COPD - O₂ Dependent</td>
<td>27</td>
<td>17</td>
<td>42</td>
<td>0.0001</td>
</tr>
<tr>
<td>CKD - Creat. ≥ 2mg/dL</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>0.81</td>
</tr>
<tr>
<td>Hostile Chest</td>
<td>10</td>
<td>3</td>
<td>24</td>
<td>0.0001</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>44</td>
<td>42</td>
<td>48</td>
<td>0.16</td>
</tr>
<tr>
<td>Permanent Pacemaker</td>
<td>16</td>
<td>17</td>
<td>15</td>
<td>0.42</td>
</tr>
<tr>
<td>Frailty</td>
<td>31</td>
<td>26</td>
<td>41</td>
<td>0.0002</td>
</tr>
</tbody>
</table>
Survival (All-Cause) S3 HR / INOP by Cohort at 1 Year

<table>
<thead>
<tr>
<th>Numbers at Risk</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>583</td>
</tr>
<tr>
<td>HR</td>
<td>384</td>
</tr>
<tr>
<td>INOP</td>
<td>199</td>
</tr>
</tbody>
</table>

p (log rank) = 0.14

87.3% HR
85.6% Overall
82.3% INOP
## Survival (All-Cause)

### S3 HR / INOP by Access at 1 Year

<table>
<thead>
<tr>
<th>Numbers at Risk</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>583</td>
</tr>
<tr>
<td>TF</td>
<td>491</td>
</tr>
<tr>
<td>TA / TAo</td>
<td>92</td>
</tr>
</tbody>
</table>

\[p \text{ (log rank)} = 0.0006\]
# Survival (All-Cause)

**S3 HR / INOP Transfemoral Access at 1 Year**

Survival (%)

<table>
<thead>
<tr>
<th>Numbers at Risk</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TF HR</strong></td>
<td>324</td>
</tr>
<tr>
<td><strong>TF INOP</strong></td>
<td>167</td>
</tr>
</tbody>
</table>

$p$ (log rank) = 0.1665

89.3% TF HR
84.3% TF INOP
Disabling Strokes
Modified Rankin Score ≥ 2, CEC Adjudicated

There was no difference between TF and TA / TAo.

There was no difference between HR and INOP.

<table>
<thead>
<tr>
<th>Stroke (%)</th>
<th>Numbers at Risk</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>583</td>
</tr>
</tbody>
</table>
### Other Clinical Outcomes

**S3 HR / INOP – 30 Days and 1 Year**

<table>
<thead>
<tr>
<th>Clinical Outcomes (%)</th>
<th>30 Days</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-Cause Mortality</td>
<td>2.2</td>
<td>14.4</td>
</tr>
<tr>
<td>Cardiac Mortality</td>
<td>1.4</td>
<td>8.1</td>
</tr>
<tr>
<td>All Stroke</td>
<td>1.4</td>
<td>4.3</td>
</tr>
<tr>
<td>Disabling Stroke</td>
<td>0.9</td>
<td>2.4</td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>8.0</td>
<td>17.1</td>
</tr>
<tr>
<td>New Permanent Pacemaker</td>
<td>13.3</td>
<td>16.9</td>
</tr>
<tr>
<td>Surgical AVR</td>
<td>0.2</td>
<td>0.6</td>
</tr>
<tr>
<td>Structural Valve Deterioration</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Valve Thrombosis</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
NYHA Class
Survivor Analysis

Baseline
30.2% Class 4
59.9% Class 3
10.0% Class 2
0.0% Class 1

30 Days
11.3% Class 4
42.0% Class 3
13.3% Class 2
7.7% Class 1

1 Year
6.8% Class 4
34.1% Class 3
58.2% Class 2

p < 0.0001
p = NS

# of Patients
583
550
440

Baseline 30 Days 1 Year

Class 4
Class 3
Class 2
Class 1

p = NS
p < 0.0001

583 patients
550 patients
440 patients
<table>
<thead>
<tr>
<th># of Patients</th>
<th>mmHg</th>
<th>cm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>568</td>
<td>544</td>
<td>532</td>
</tr>
<tr>
<td>544</td>
<td>510</td>
<td>379</td>
</tr>
<tr>
<td></td>
<td></td>
<td>357</td>
</tr>
</tbody>
</table>
Paravalvular Regurgitation
Paired Analysis

Comparison of severity of paravalvular regurgitation between 30 days and 1 year post-operation:

- **30 Days**:
  - Severe: 2.5%
  - Moderate: 33.2%
  - Mild: 64.3%
  - None/Trace: 100%

- **1 Year**:
  - Severe: 2.7%
  - Moderate: 29.1%
  - Mild: 68.1%
  - None/Trace: 99%

The number of patients for both time points is 364.

Statistical significance:

\[ p = 0.99 \]
### 1 Year KM Survival by 30-Day PVL

#### Numbers at Risk

<table>
<thead>
<tr>
<th>Numbers at Risk</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>None / Trace</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td></td>
</tr>
<tr>
<td>Mod / Severe</td>
<td></td>
</tr>
</tbody>
</table>

- **None / Trace**: 351, 339, 321, 309, 219
- **Mild**: 191, 186, 177, 168, 110
- **Mod / Severe**: 16, 15, 12, 11, 9

**Overall**: Log-Rank p-value = 0.0058

**M / S vs N / T**: Log-Rank p-value = 0.0015

**M / S vs Mild**: Log-Rank p-value = 0.0058

---

**No statistical difference between None/Trace and Mild.**

- **88.0% N / T**
- **85.9% Mild**
- **61.9% M / S**
PARTNER I and II Trials
TF Patients

All-Cause Mortality at 1 Year
Edwards SAPIEN Valves (As Treated Patients)

- P1B (TF): 30.7%
- P1A (TF): 21.4%
- P2B (TF): 23.7%
- P2B XT (TF): 22.5%
- S3 Inoperable (TF): 15.7%
- S3HR (TF): 10.7%
- S3 CE HR (TF): 8.4%

TF Patients | SAPIEN | SXT | SAPIEN 3
--- | --- | --- | ---
175 | 240 | 271 | 282
101 | 324 | 96

High-Risk
Inoperable
Conclusions

• In high-risk and inoperable patients, the low rate of 30-day complications with the SAPIEN 3 TAVR system resulted in improved 1-year survival.
  
  – Overall Survival: 85.6%
  – High-Risk Survival: 87.3%
  – High-Risk TF Survival: 89.3%

• Between 30 days and 1 year, the rates of both disabling stroke and significant paravalvular AR remained low and stable, with no significant differences between TF and alternative access.

• There was no association observed between the occurrence of Mild PVL and mortality at 1 year.

• Hemodynamic valve performance and early symptomatic improvement were sustained at 1 year.
Implications

- The combination of new *design features* of SAPIEN 3, *procedural improvements, operator experience and improved patient selection* have all contributed to a low rate of important adverse events (including stroke) and a high rate of 1-year survival in high-risk and inoperable patients with severe AS.

- These excellent 1 year follow-up data with SAPIEN 3 support the use of *TAVR as the preferred therapy* in high-risk and inoperable patients with aortic stenosis.

- The 1 year outcomes of the Intermediate Risk cohort will be available at ACC 2016.