Transcatheter Therapies For Aortic Valve Disease

March 2017

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Introduction

“I got into this field to ‘protect my turf.’ I must say, I have come full circle. . . .”
- Kent W. Jones

I got into this field to ‘protect my *patients.*’
- BKW Interpretation
“Among the great benefits of TAVR is how this has brought cardiologists and surgeons together working for our patients.”

- Kent W. Jones
Operative Rates for Severe Aortic Stenosis

Approximately half of patients with severe symptomatic AS do not undergo surgery.

Valvular Heart Disease
Who does and does not receive valve surgery?

- Healthy but elderly
- Palliation Candidate
- Technically Extreme

AVR

Low Risk

Medium Risk

High Risk

Extreme Risk

Nada

Low Risk

Medium Risk

High Risk

Extreme Risk
Risk Evolution

PARTNER 1 demonstrated TAVR to be:

- superior to standard therapy in patients who were not candidates for surgery
- equivalent to surgery in high-risk patients
### PARTNER INOPERABLE ENDPOINTS

**Benefit Despite Procedural Risk**

TAVR is a Management Strategy Including Surgical Rescue

<table>
<thead>
<tr>
<th>Outcome</th>
<th>30 Days n=179</th>
<th>1 Year n=179</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAVI</td>
<td>Standard Rx</td>
</tr>
<tr>
<td>Death (%)</td>
<td>5.0</td>
<td>2.8</td>
</tr>
<tr>
<td>Stroke or TIA (%)</td>
<td>6.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Death (all) or major stroke (%)</td>
<td><strong>8.4</strong></td>
<td><strong>3.9</strong></td>
</tr>
</tbody>
</table>

#### Graph

- **All-cause mortality (%)**
  - **Standard Rx**
    - **50.7%**
  - **TAVR**
    - **30.7%**

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Intermountain Heart Institute
PARTNER 2A Intermediate Risk
Participating Sites

2032 Randomized Pts: 49 at Intermountain Medical Center
### Transcatheter Heart Valve Device Evolution

<table>
<thead>
<tr>
<th>Partner 1</th>
<th>Partner 2</th>
<th>Partner 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve Technology</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sheath Compatibility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22-24F</td>
<td>16-20F</td>
<td>14-16F</td>
</tr>
<tr>
<td>Available Valve Sizes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23 mm</td>
<td>23 mm</td>
<td>20 mm</td>
</tr>
<tr>
<td>26 mm</td>
<td>26 mm</td>
<td>23 mm</td>
</tr>
<tr>
<td></td>
<td>29mm*</td>
<td>26 mm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>29 mm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>29 mm</td>
</tr>
</tbody>
</table>

*Note: The available valve size for Partner 3 includes an additional size, 29mm, not listed for Partner 1 and Partner 2.*
Primary Endpoint (AT)
All-Cause Mortality or Disabling Stroke

HR [95% CI] = 0.87 [0.71, 1.07]
p (log rank) = 0.180

All-Cause Mortality or Disabling Stroke (%)

Months from Procedure

Number at risk:
Surgery 944 826 807 779 766 743 731 715 694
TAVR 994 917 906 878 842 825 811 791 774
TF Primary Endpoint (AT)
All-Cause Mortality or Disabling Stroke

HR: 0.78 [95% CI: 0.61, 0.99]
p (log rank) = 0.04

TF Surgery
TF TAVR

Months from Procedure

0 3 6 9 12 15 18 21 24

Number at risk:
TF Surgery 722 636 624 600 591 573 565 555 537
TF TAVR 762 717 706 685 663 652 644 634 612
Echocardiography Findings (VI)
Aortic Valve Area

Valve Area (cm²)

No. of Echos
Surgery 861 727 590 488
TAVR 899 829 695 567

p < 0.001
p = NS

Error bars represent ± Standard Deviation
Paravalvular Regurgitation (VI)  
3-Class Grading Scheme

- **P < 0.001**
- **≥ Moderate** 8.0%  
- **Mild** 26.8%  
- **P < 0.001**  
- **≥ Moderate 0.6%**  
- **Mild 3.5%**

### No. of echos

<table>
<thead>
<tr>
<th></th>
<th>30 Days</th>
<th>2 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAVR</td>
<td>872</td>
<td>600</td>
</tr>
<tr>
<td>Surgery</td>
<td>757</td>
<td>514</td>
</tr>
</tbody>
</table>
Severity of PVR at 30 Days and All-cause Mortality at 2 Years (VI)

- **Moderate/Severe**
- **Mild**
- **None/Trace**

**Overall Log-Rank p = 0.001**

**Mod/Sev (reference = None/Trace)**

- p (Log-Rank) < 0.001

**Mild (reference = None/Trace)**

- p (Log-Rank) = 0.82

<table>
<thead>
<tr>
<th>Months from Procedure</th>
<th>None/Trace</th>
<th>Mild</th>
<th>Moderate/Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>701</td>
<td>210</td>
<td>36</td>
</tr>
<tr>
<td>3</td>
<td>678</td>
<td>204</td>
<td>32</td>
</tr>
<tr>
<td>6</td>
<td>664</td>
<td>199</td>
<td>32</td>
</tr>
<tr>
<td>9</td>
<td>647</td>
<td>194</td>
<td>26</td>
</tr>
<tr>
<td>12</td>
<td>628</td>
<td>198</td>
<td>26</td>
</tr>
<tr>
<td>15</td>
<td>621</td>
<td>188</td>
<td>24</td>
</tr>
<tr>
<td>18</td>
<td>612</td>
<td>182</td>
<td>22</td>
</tr>
<tr>
<td>21</td>
<td>605</td>
<td>180</td>
<td>22</td>
</tr>
<tr>
<td>24</td>
<td>595</td>
<td>175</td>
<td>21</td>
</tr>
</tbody>
</table>

Number at risk:
- None/Trace: 701
- Mild: 210
- Moderate/Severe: 36

All-Cause Mortality (%):
- **None/Trace**: 0%
- **Mild**: 14.1%
- **Moderate/Severe**: 34.0%
Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D.,
Raj R. Makkar, M.D., Lars G. Svensson, M.D., Ph.D., Susheel K. Kodali, M.D.,
Vinod H. Thourani, M.D., E. Murat Tuzcu, M.D., D. Craig Miller, M.D.,
Howard C. Herrmann, M.D., Darshan Doshi, M.D., David J. Cohen, M.D.,
Augusto D. Pichard, M.D., Samir Kapadia, M.D., Todd Dewey, M.D.,
Vasilis Babaliaris, M.D., Wilson Y. Szeto, M.D., Mathew R. Williams, M.D.,
Dean Kereiakes, M.D., Alan Zajarias, M.D., Kevin L. Greason, M.D.,
Brian K. Whisenant, M.D., Robert W. Hodson, M.D., Jeffrey W. Moses, M.D.,
Alfredo Trento, M.D., David L. Brown, M.D., William F. Fearon, M.D.,
Philippe Pibarot, D.V.M., Ph.D., Rebecca T. Hahn, M.D., Wael A. Jaber, M.D.,
William N. Anderson, Ph.D., Maria C. Alu, M.M., and John G. Webb, M.D.,
for the PARTNER 2 Investigators*
The PARTNER S3i Trial
Study Design

Intermediate Risk Symptomatic Severe Aortic Stenosis

P2 S3i
n = 1078

ASSESSMENT: Optimal Valve Delivery Access

Transfemoral (TF)

TF TAVR

Transapical / Transaortic (TA/TAo)

TA/TAo TAVR

P2A
n = 2032

ASSESSMENT: Transfemoral Access

Yes

Transfemoral (TF)

1:1 Randomization

TF TAVR

VS

Surgical AVR

No

Transapical / TransAortic (TA/TAo)

1:1 Randomization

TA/Tao TAVR

VS

Surgical AVR

Primary Endpoint: All-Cause Mortality, All Stroke, or Mod/Sev AR at One Year
## PARTNER Trials
### Device Evolution

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<tr>
<td>Valve Technology</td>
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<tr>
<td><img src="valve1.png" alt="Image" /></td>
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<td>Available Valve Sizes</td>
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<td>Available Valve Sizes</td>
</tr>
<tr>
<td>23 mm, 26 mm</td>
<td>23 mm, 26 mm, 29 mm</td>
<td>20 mm, 23 mm, 26 mm, 29 mm</td>
</tr>
<tr>
<td>Characteristic</td>
<td>TAVR (n = 1077)</td>
<td>Surgery (n = 944)</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Age - yrs</td>
<td>81.9 ± 6.6</td>
<td>81.6 ± 6.8</td>
</tr>
<tr>
<td>Male - %</td>
<td>61.7</td>
<td>55.0</td>
</tr>
<tr>
<td>BMI - kg/m²</td>
<td>28.7 ± 6.1</td>
<td>28.4 ± 6.2</td>
</tr>
<tr>
<td>Median STS Score - %</td>
<td>5.2 [4.3, 6.3]</td>
<td>5.4 [4.4, 6.7]</td>
</tr>
<tr>
<td>NYHA Class III or IV - %</td>
<td>72.5</td>
<td>76.1</td>
</tr>
</tbody>
</table>

mean ± SD, median [IQR]
## Unadjusted Clinical Events

### At 30 Days and 1 Year (AT)

<table>
<thead>
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<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAVR</td>
<td>Surgery</td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause</td>
<td>1.1</td>
<td>4.0</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>0.9</td>
<td>3.1</td>
</tr>
<tr>
<td><strong>Neurological Events</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disabling Stroke</td>
<td>1.0</td>
<td>4.4</td>
</tr>
<tr>
<td>All Stroke</td>
<td>2.7</td>
<td>6.1</td>
</tr>
<tr>
<td><strong>All-cause Death and</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Disabling Stroke</strong></td>
<td>2.0</td>
<td>8.0</td>
</tr>
</tbody>
</table>
Paravalvular Regurgitation

- **Severe**
- **Moderate**
- **Mild**
- **None/Trace**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>30 Days</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>P2A Surgery</td>
<td>755</td>
<td>610</td>
</tr>
<tr>
<td>S3i TAVR</td>
<td>992</td>
<td>875</td>
</tr>
</tbody>
</table>

- **P < 0.001**
The PARTNER S3i Trial
Lancet

Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis

Recent IMC THV Cases
Cardiogenic Shock

58 YO Man transferred on .08 Epi with EF ~10%, Lactate 10, SBP ~85, critical aortic stenosis

Venous Cannula for cardiopulmonary bypass
Failed Bioprosthetic Mitral Valve

77 YO woman with porcine MVR now with severe MR and acute HF

Transseptal Delivery and Balloon Inflation of S3 Valve

S3 THV within Mosaic valve
Institutional Outcomes Report
2016Q3
Intermountain Medical Center
407533

Aggregation Date: Jan 17, 2017 11:59:59 PM
### Intermountain TVT TAVR Report

<table>
<thead>
<tr>
<th>Q4 2015 – Q3 2016 Population &amp; In Hospital Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population (N=220)</strong></td>
</tr>
<tr>
<td>Median Age</td>
</tr>
<tr>
<td>High or Extreme Risk</td>
</tr>
<tr>
<td>Intermediate or Low Risk</td>
</tr>
<tr>
<td>81%</td>
</tr>
<tr>
<td>78%</td>
</tr>
<tr>
<td>22%</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
</tr>
<tr>
<td>1.4%</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
</tr>
<tr>
<td>0.9%</td>
</tr>
<tr>
<td><strong>Vascular Access Complication</strong></td>
</tr>
<tr>
<td>1.8%</td>
</tr>
<tr>
<td><strong>Length of Stay</strong></td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td>2.0 Days</td>
</tr>
<tr>
<td>2.8 Days</td>
</tr>
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</table>

S3i like results in a mixed risk population

“The risk of major complication is about 3%. So if you turn that around...”
Partner 3: Low Risk

1228 Patients
Primary Endpoint: 1 Year death, Stroke, Rehospitalization

Key Inclusion Criteria:
• ≥ 65 years of age
• TF Access (~5.5 mm)
• Predicted operative risk < 3%

Key Exclusion Criteria:
• Frailty
• CAD or Mitral Regurgitation warranting surgery
• Bicuspid valve
Friday: randomized to PCI/TAVR in P3 Trial
75 YO man SOB carrying luggage up stairs at Heathrow
I do not have a crystal ball and no one of knows what is around the corner. However, I can tell you this:
- Your valve is not going to get any better.
- And you are only going to worry about it until it is taken care of.

Early TAVR

- Severe aortic stenosis.
- Good exercise capacity without symptoms.
- Randomized to TAVR now vs. w/ symptoms.
Final Thoughts

Patients Win

- Each patient who stands to live with a quality of life independent of aortic stenosis has an option to receive aortic valve replacement with an acceptable procedural risk.

- The heart team strives to reach a consensus on the preferred therapy for each individual patient.

- The heart team contributes our unique training, experience, perspectives, and energies to the best option for each individual patient.
Thank You

Intermountain Medical Center

Structural Heart Disease Program
801-507-4795

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