Transcatheter Aortic Valve Replacement

Jesse Jorgensen, MD
Medical Director, Cardiac Catheterization Laboratory
Greenville Health System
Greenville, South Carolina, USA
January 30, 2016
Aortic Stenosis is Life Threatening and Progresses Rapidly

Valvular Aortic Stenosis in Adults (Average Course)

- Survival after onset of symptoms 50% at 2 yrs, 20% at 5 yrs
- Surgical intervention should be performed promptly once even minor symptoms occur²


Aortic Valve Replacement Improves Survival

Patient Survival

Surgical AVR:
Not Available To All Patients

31.8% did not undergo intervention, most frequently because of comorbidities.
Aortic Stenosis Undertreatment is Profound

![Graph showing percentage of patients with and without Aortic Valve Replacement (AVR) over different years.](image-url)
Mortality With Standard Therapy Is Worse Than With Certain Metastatic Cancers

![Bar chart showing 5-year survival rates for different cancers.](chart.png)

- Breast Cancer*: 23%
- Lung Cancer*: 4%
- Colorectal Cancer*: 12%
- Prostate Cancer*: 30%
- Ovarian Cancer*: 28%
- Severe Inoperable AS†: 3%

Percutaneous Aortic Valve Development

- Professor Alain Cribier (Rouen, France) First described percutaneous aortic valve interventions in 1985

- Proved that a stent could be deployed without removing the diseased native valve

- Implanted first percutaneous aortic valve on a patient on April 16, 2002
Edwards SAPIEN Transcatheter Valve

- Bovine pericardial tissue
- Stainless steel frame
- PET skirt

The Carpentier-Edwards ThermaFix process* is intended to minimize the risk of calcification, helping preserve valve performance.
Edwards SAPIEN

Edwards SAPIEN THV
23 and 26 mm valves

RetroFlex
22 and 24 F sheaths
Self Expanding Technology: CoreValve (Medtronic)

2007 CE Mark
2014 FDA Approval
Evolut R System

Transcatheter Valve (26, 29 mm)
Supra-annular design, optimized sealing

Catheter Delivery System
14Fr-equivalent profile

Loading System

Meredith EuroPCR 2015
TAVR Access

1. Transfemoral
2. Direct Aortic
3. Subclavian
4. Transapical
TAVR Patient Evaluation

STS Score

<4 Low Risk
4-8 Intermediate Risk
>8 High Risk

* Inoperable: >50% death or serious irreversible condition

Agarwal S et al. Heart 2015;101:169-177
Patient-Focused Multidisciplinary Heart Team Approach

- Multidisciplinary in all aspects:
  - Patient selection
  - Procedure Planning
  - Patient Treatment
  - Post Operative care
Valve Sizing: TEE
Valve Sizing: CT
CTA: Critical for determining Access
Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela S. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*
TAVR Results:
Mean Gradient & Valve Area
PARTNER Cohort B
Primary Endpoint

HR [95% CI] = 0.56 [0.43, 0.73]
P (log rank) < .0001

Δ at 1 yr = 20.0%
NNT = 5.0 pts

Δ at 2 yrs = 24.7%
NNT = 4.0 pts

Numbers at Risk

<table>
<thead>
<tr>
<th>Treatment</th>
<th>1yr</th>
<th>2yr</th>
<th>3yr</th>
<th>4yr</th>
<th>5yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edwards SAPIEN THV</td>
<td>138</td>
<td>124</td>
<td>110</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>Standard Therapy</td>
<td>121</td>
<td>85</td>
<td>62</td>
<td>42</td>
<td></td>
</tr>
</tbody>
</table>

Greenville Health System
All Cause Mortality (ITT): 5 year Follow up

Median Survival

- Standard Rx (n = 179)
- TAVR (n = 179)

HR [95% CI] = 0.50 [0.39, 0.65]

*p (log rank) < 0.0001

*In an age and gender matched US population without comorbidities, the mortality at 5 years is 40.5%.

**Kapadia TCT Sept 2014**
Repeat Hospitalization: TAVR vs. Standard Treatment

**Graph:**
- **Standard Rx (n = 179)**
- **TAVR (n = 179)**

- **Rehospitalization (%)**
  - 0% at 0 months
  - 27.0% at 12 months
  - 34.9% at 24 months
  - 43.1% at 36 months
  - 46.3% at 48 months
  - 47.6% at 60 months

- **HR [95% CI] = 0.40 [0.29, 0.55]**
- **p (log rank) < 0.0001**

Kapadia TCT Sept 2014
PARTNER B Mean Gradient and Valve Area at 5 years

Kapadia TCT Sept 2014
Stroke following TAVR: Inoperable cohort

**STROKE AT 30 DAYS, 1 YEAR, AND 2 YEARS**

- **Edwards SAPIEN THV (n = 179)**
- **Standard Therapy (n = 179)**

<table>
<thead>
<tr>
<th>Time</th>
<th>Edwards SAPIEN THV</th>
<th>Standard Therapy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Days</td>
<td>7.3</td>
<td>1.7</td>
<td>.01</td>
</tr>
<tr>
<td>1 Year</td>
<td>11.2</td>
<td>5.5</td>
<td>.06</td>
</tr>
<tr>
<td>2 Years</td>
<td>13.8</td>
<td>5.5</td>
<td>.01</td>
</tr>
</tbody>
</table>
Vascular Complications: TAVR vs. Standard Treatment
Transcatheter Aortic Valve Replacement Using a Self-Expanding Bioprosthesis in Patients With Severe Aortic Stenosis at Extreme Risk for Surgery

Jeffrey J. Popma, MD,* David H. Adams, MD,† Michael J. Reardon, MD,‡ Steven J. Yakubov, MD,§ Neal S. Kleiman, MD,‡ David Heimansohn, MD,¶ James Hermiller, Jr, MD,‖ G. Chad Hughes, MD,¶ J. Kevin Harrison, MD,¶ Joseph Coselli, MD,# Jose Diez, MD,¶ Ali Kafi, MD,** Theodore Schreiber, MD,*** Thomas G. Gleason, MD,↑↑ John Conte, MD,↑↑ Maurice Buchbinder, MD,↑↑ G. Michael Deeb, MD,↑↑↑ Blasé Carabello, MD,↑↑↑ Patrick W. Serruys, MD, PriD,¶¶ Sharla Chenoweth, MS,↑↑↑ Jae K. Oh, MD,↑↑↑ for the CoreValve United States Clinical Investigators

Boston, Massachusetts; New York, New York; Houston, Texas; Columbus, Ohio; Indianapolis, Indiana; Durham, North Carolina; Detroit and Ann Arbor, Michigan; Pittsburgh, Pennsylvania; Baltimore, Maryland; Palo Alto, California; Rotterdam, the Netherlands; and Minneapolis and Rochester, Minnesota
CoreValve Extreme Risk Clinical Outcomes at 1 and 12 Months

<table>
<thead>
<tr>
<th>Outcome</th>
<th>30 Days (N = 489)</th>
<th>12 Months (N = 489)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from any cause or major stroke</td>
<td>48 (9.8)</td>
<td>127 (26.0)</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>From any cause</td>
<td>41 (8.4)</td>
<td>119 (24.3)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>44 (8.3)</td>
<td>88 (18.3)</td>
</tr>
<tr>
<td>Stroke</td>
<td>19 (4.0)</td>
<td>31 (7.0)</td>
</tr>
<tr>
<td>Major</td>
<td>21 (4.3)</td>
<td>19 (4.3)</td>
</tr>
<tr>
<td>Minor</td>
<td>9 (1.9)</td>
<td>14 (3.2)</td>
</tr>
<tr>
<td>TIA</td>
<td>3 (0.6)</td>
<td>5 (1.1)</td>
</tr>
<tr>
<td>MACCE</td>
<td>60 (12.3)</td>
<td>143 (29.2)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>6 (1.2)</td>
<td>9 (2.0)</td>
</tr>
<tr>
<td>Periprocedural</td>
<td>6 (1.2)</td>
<td>6 (1.2)</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>0 (0)</td>
<td>3 (0.7)</td>
</tr>
<tr>
<td>Reintervention</td>
<td>5 (1.1)</td>
<td>8 (1.8)</td>
</tr>
<tr>
<td>Major or life-threatening bleeding</td>
<td>179 (36.7)</td>
<td>206 (42.8)</td>
</tr>
<tr>
<td>Life-threatening or disabling</td>
<td>62 (12.7)</td>
<td>83 (17.6)</td>
</tr>
<tr>
<td>Major</td>
<td>121 (24.9)</td>
<td>136 (28.5)</td>
</tr>
<tr>
<td>Major vascular complications</td>
<td>40 (8.2)</td>
<td>41 (8.4)</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>97 (11.8)</td>
<td>57 (11.8)</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>13 (2.7)</td>
<td>13 (2.7)</td>
</tr>
<tr>
<td>Cardiac perforation</td>
<td>9 (1.8)</td>
<td>9 (1.8)</td>
</tr>
<tr>
<td>Device migration</td>
<td>0 (0)</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Device embolization</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

P < 0.0001
Performance Goal = 43%
26.0% [22.1, 29.9]
CoreValve Hemodynamics and Functional Improvement

![Graph showing hemodynamics and functional improvement over time.](image-url)
CoreValve Extreme Risk 2 year Outcomes

- **All-Cause Mortality:**
  - 0 months: 7%
  - 1 year: 24.3%
  - 2 years: 36.5%

- **Cardiovascular Mortality:**
  - 0 months: 7%
  - 1 year: 18.3%
  - 2 years: 26.5%

- **Major Stroke:**
  - 0 months: 4.3%
  - 1 year: 4.3%
  - 2 years: 5.1%

- **Events**, %:
  - Any stroke: 7.0 8.7
  - Major: 4.3 5.1
  - Minor: 3.2 4.1
  - Myocardial infarction: 2.0 2.8
  - Reintervention: 1.8 1.8
  - VARC bleeding: 42.8 45.3
    - Life threatening or disabling: 18.0 20.8
    - Major: 28.3 29.1
  - Major vascular complications: 8.4 8.4
  - Permanent pacemaker implant: 26.4 28.9
  - Per ACC guidelines: 19.5 22.0

* Percentages obtained from Kaplan Meier estimates
TAVR is AT LEAST as good as Surgical AVR in High Risk patients
Echo Aortic Valve Gradients: Sapien TAVR vs. SAVR
PARTNER A Primary Endpoint: 1 Year All-Cause Mortality TAVR vs SAVR

HR [95% CI] = 0.93 [0.71, 1.22]
P (log rank) = 0.62

<table>
<thead>
<tr>
<th></th>
<th>No. at Risk</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAVR</td>
<td>348</td>
<td>298</td>
</tr>
<tr>
<td>AVR</td>
<td>351</td>
<td>252</td>
</tr>
</tbody>
</table>
Cohort A Quality of Life: TAVR vs. SAVR
High Risk: TAVR vs SAVR

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Transcatheter Replacement (N = 348)</th>
<th>Surgical Replacement (N = 351)</th>
<th>P Value</th>
<th>Transcatheter Replacement (N = 348)</th>
<th>Surgical Replacement (N = 351)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients (%)</td>
<td>no. of patients (%)</td>
<td></td>
<td>no. of patients (%)</td>
<td>no. of patients (%)</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>From any cause</td>
<td>12 (3.4)</td>
<td>22 (6.5)</td>
<td>0.07</td>
<td>84 (24.2)</td>
<td>89 (26.8)</td>
<td>0.44</td>
</tr>
<tr>
<td>From cardiac causes</td>
<td>11 (3.2)</td>
<td>10 (3.0)</td>
<td>0.90</td>
<td>47 (14.3)</td>
<td>40 (13.0)</td>
<td>0.63</td>
</tr>
<tr>
<td>Repeat hospitalization</td>
<td>15 (4.4)</td>
<td>12 (3.7)</td>
<td>0.64</td>
<td>58 (18.2)</td>
<td>45 (15.5)</td>
<td>0.38</td>
</tr>
<tr>
<td>Death or repeat hospitalization</td>
<td>25 (7.2)</td>
<td>33 (9.7)</td>
<td>0.24</td>
<td>120 (34.6)</td>
<td>119 (35.9)</td>
<td>0.73</td>
</tr>
<tr>
<td>Stroke or transient ischemic attack</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Either</td>
<td>19 (5.5)</td>
<td>8 (2.4)</td>
<td>0.04</td>
<td>27 (8.3)</td>
<td>13 (4.3)</td>
<td>0.04</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>3 (0.9)</td>
<td>1 (0.3)</td>
<td>0.33</td>
<td>7 (2.3)</td>
<td>4 (1.5)</td>
<td>0.47</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>3 (0.9)</td>
<td>1 (0.3)</td>
<td>0.34</td>
<td>3 (0.9)</td>
<td>2 (0.7)</td>
<td>0.84</td>
</tr>
<tr>
<td>Major</td>
<td>13 (3.8)</td>
<td>7 (2.1)</td>
<td>0.20</td>
<td>12 (3.5)</td>
<td>8 (2.4)</td>
<td>0.07</td>
</tr>
<tr>
<td>Death from any cause or major stroke</td>
<td>24 (6.9)</td>
<td>28 (8.2)</td>
<td>0.52</td>
<td>92 (26.5)</td>
<td>93 (28.0)</td>
<td>0.68</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0</td>
<td>2 (0.6)</td>
<td>0.16</td>
<td>1 (0.4)</td>
<td>2 (0.6)</td>
<td>0.69</td>
</tr>
<tr>
<td>Vascular complication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>59 (17.0)</td>
<td>13 (3.8)</td>
<td>&lt;0.001</td>
<td>62 (18.0)</td>
<td>16 (4.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Major</td>
<td>38 (11.0)</td>
<td>11 (3.2)</td>
<td>&lt;0.001</td>
<td>39 (11.3)</td>
<td>12 (3.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine &gt;3 mg/dl (265 μmol/liter)</td>
<td>4 (1.2)</td>
<td>4 (1.2)</td>
<td>0.95</td>
<td>12 (3.9)</td>
<td>8 (2.7)</td>
<td>0.41</td>
</tr>
<tr>
<td>Renal-replacement therapy</td>
<td>10 (2.9)</td>
<td>10 (3.0)</td>
<td>0.95</td>
<td>18 (5.4)</td>
<td>20 (6.5)</td>
<td>0.56</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>32 (9.3)</td>
<td>67 (19.5)</td>
<td>&lt;0.001</td>
<td>49 (14.7)</td>
<td>85 (25.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>0</td>
<td>1 (0.3)</td>
<td>0.32</td>
<td>2 (0.6)</td>
<td>3 (1.0)</td>
<td>0.63</td>
</tr>
<tr>
<td>New-onset atrial fibrillation†</td>
<td>30 (8.6)</td>
<td>56 (16.0)</td>
<td>0.006</td>
<td>42 (12.1)</td>
<td>60 (17.1)</td>
<td>0.07</td>
</tr>
<tr>
<td>New pacemaker</td>
<td>13 (3.8)</td>
<td>12 (3.6)</td>
<td>0.89</td>
<td>19 (5.7)</td>
<td>16 (5.0)</td>
<td>0.68</td>
</tr>
</tbody>
</table>

*All percentages are Kaplan–Meier estimates at the specific time point and thus do not equal the number of patients divided by the total number in the study group.

† The presence of new-onset atrial fibrillation was determined in an electrocardiography core laboratory.
Paravalvular Aortic Regurgitation: Sapient TAVR vs. SAVR
CV Mortality Stratified by PV Leak (ITT)

Delta at 1 yr = 14.4%
NNT = 6.9 pts

Delta at 2 yr = 9.7%
NNT = 10.3 pts

p (log rank) = 0.381

Numbers at Risk

<table>
<thead>
<tr>
<th></th>
<th>None to Mild</th>
<th>Moderate or Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 yr</td>
<td>147</td>
<td>17</td>
</tr>
<tr>
<td>6 mo</td>
<td>118</td>
<td>12</td>
</tr>
<tr>
<td>12 mo</td>
<td>107</td>
<td>11</td>
</tr>
<tr>
<td>18 mo</td>
<td>95</td>
<td>10</td>
</tr>
<tr>
<td>24 mo</td>
<td>72</td>
<td>8</td>
</tr>
</tbody>
</table>
Corevalve High Risk

Patients Screened
N=995

Randomized
N=795

Intention to Treat TAVR
N=394

Exited (n=4)
2 Deaths
2 Withdrawals

As Treated TAVR
N=390

Iliofemoral
N=323
Non-iliofemoral
N=67

Intention to Treat SAVR
N=401

Exited (n=44)
5 Deaths
36 Withdrawals
3 Others

As Treated SAVR
N=357

Adams ACC 2014
Primary Endpoint: 1 Year All-cause Mortality

- Surgical: 19.1%
- Transcatheter: 14.2%

P = 0.04 for superiority

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>357</th>
<th>341</th>
<th>297</th>
<th>353</th>
<th>274</th>
<th>329</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transcatheter</td>
<td>390</td>
<td>377</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adams ACC 2014
All Stroke

- Surgical
- Transcatheter

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical</td>
<td>357</td>
<td>322</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>274</td>
</tr>
<tr>
<td>Transcatheter</td>
<td>390</td>
<td>363</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>334</td>
</tr>
</tbody>
</table>

Log-rank P = 0.10

Adams ACC 2014
## Other Endpoints

<table>
<thead>
<tr>
<th>Events*</th>
<th>1 Month</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAVR</td>
<td>SAVR</td>
</tr>
<tr>
<td>Vascular complications (major), %</td>
<td>5.9</td>
<td>1.7</td>
</tr>
<tr>
<td>Pacemaker implant, %</td>
<td>19.8</td>
<td>7.1</td>
</tr>
<tr>
<td>Bleeding (life threatening or disabling), %</td>
<td>13.6</td>
<td>35.0</td>
</tr>
<tr>
<td>New onset or worsening atrial fibrillation, %</td>
<td>11.7</td>
<td>30.5</td>
</tr>
<tr>
<td>Acute kidney injury, %</td>
<td>6.0</td>
<td>15.1</td>
</tr>
</tbody>
</table>

* Percentages reported are Kaplan-Meier estimates and log-rank P values

Adams ACC 2014
Post implant, there were significant differences (P < 0.001) between TAVR and SAVR at each time point for both EOA and mean gradient.
Paravalvular Regurgitation

There was significantly lower PVL with SAVR over TAVR at each time point (P<0.001)
Vascular Safety: Get Smaller

Terumo Solopath: 15f insertion, balloon expandable to 19f. Corevalve compatible
Edwards evolution of valve design

SAPIEN                      SAPIEN XT                  SAPIEN 3
Evolution of the Edwards Balloon-Expandable Transcatheter Valves

- SAPIEN (2006)
- SAPIEN XT (2009)
- SAPIEN 3 (2013)

* Sheath compatibility for a 23 mm valve
PARTNER II Study Design

Symptomatic Severe Aortic Stenosis

Operable
(STS ≥4)

ASSESSMENT by Heart Valve Team

Transcatheter Aortic Valve Replacement (TAVR)

TF TAVR SAPIEN XT

1:1 Randomization

NR1 (Small Vessel) 100
NR2 (Transapical) 100
NR3 (MVA) 100
NR4 (TAo) 100
NR5 (29 mm TF) 50
NR6 (29 mm TA) 50

Primary Endpoint: All-Cause Mortality + Disabling Stroke at Two Years (Non-inferiority)

Transapical (TA) / TransAortic (TAo)

TF TAVR SAPIEN XT

1:1 Randomization

1:1 Randomization

No

ASSESSMENT: Transapical Access

Inoperable

n = 560 Randomized Patients

Yes

ASSESSMENT: Transcatheter Access

Two Parallel Randomized Trials +6 Nested Registries

n = 2000 Randomized Patients

Operable

Transcatheter (TF)

1:1 Randomization

TF TAVR SAPIEN XT

Surgical AVR

Primary Endpoint: All-Cause Mortality + Disabling Stroke + Repeat Hospitalization at One Year (Non-inferiority)
PARTNER II Inoperable Cohort

Symptomatic Severe Aortic Stenosis

ASSESSMENT by Heart Valve Team

Inoperable

ASSESSMENT: Transfemoral Access

1:1 Randomization

n = 560 Randomized Patients

TF TAVR SAPIEN XT vs TF TAVR SAPIEN

Primary Endpoint: All-Cause Mortality + Disabling Stroke + Repeat Hospitalization at One Year (Non-inferiority)

Leon ACC 2013
PARTNER II Mortality and Stroke

HR [95% CI] = 0.93 [0.66, 1.33]
p (log rank) = 0.706

HR [95% CI] = 0.98 [0.43, 2.14]
p (log rank) = 0.926
PARTNER II: Comparison of Valve Function
### PARTNER II: Comparison Vascular Complications

<table>
<thead>
<tr>
<th>Events</th>
<th>SAPIEN (n=271)</th>
<th>SAPIEN XT (n=282)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td><strong>Vascular:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major</td>
<td>42</td>
<td>15.5</td>
<td>27</td>
</tr>
<tr>
<td>Minor</td>
<td>20</td>
<td>7.4</td>
<td>14</td>
</tr>
<tr>
<td><strong>Bleeding:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disabling</td>
<td>34</td>
<td>12.6</td>
<td>22</td>
</tr>
<tr>
<td>Major</td>
<td>44</td>
<td>16.4</td>
<td>44</td>
</tr>
<tr>
<td>Patients with transfusions</td>
<td>80</td>
<td>29.5</td>
<td>73</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Events</th>
<th>SAPIEN (n=271)</th>
<th>SAPIEN XT (n=282)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Perforation</td>
<td>13</td>
<td>4.8</td>
<td>2</td>
</tr>
<tr>
<td>Dissection</td>
<td>25</td>
<td>9.2</td>
<td>12</td>
</tr>
<tr>
<td>Hematoma</td>
<td>16</td>
<td>5.9</td>
<td>10</td>
</tr>
</tbody>
</table>
Partner II S3 Trial

Symptomatic Severe Aortic Stenosis

**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

**SAPIEN 3**
- 2 Single Arm Non-Randomized Historical-Controlled Studies
  - PII A SAVR
  - PIA SAPIEN

**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

**n = 1076 Patients**
**n = 583 Patients**

Kodali ACC 2015
Mortality and Stroke: S3HR
At 30 Days (As Treated Patients)

**Mortality**
- All-Cause
- Cardiovascular

**Stroke**
- All Stroke
- Disabling

O:E = 0.26
(STS 8.6%)

S3HR:
- Mortality: 2.2 All-Cause, 1.4 Cardiovascular
- Stroke: 1.5 All Stroke, 0.9 Disabling
All-Cause Mortality at 30 Days
Edwards SAPIEN Valves (As Treated Patients)

PARTNER I and II Trials
Overall and TF Patients

- P1B (TF): 6.3% (175 patients)
- P1A (All): 5.2% (344 patients)
- P1A (TF): 3.7% (240 patients)
- P2B (TF): 4.5% (271 patients)
- P2B XT (TF): 3.5% (282 patients)
- S3HR (All): 2.2% (583 patients)
- S3HR (TF): 1.6% (491 patients)
- S3I (All): 1.1% (1072 patients)
- S3I (TF): 1.1% (947 patients)

Kodali ACC 2015
All Strokes at 30 Days
Edwards SAPIEN Valves

PARTNER I and II Trials

Neurologist evaluations (pre- and post)

<table>
<thead>
<tr>
<th>Group</th>
<th>SAPIEN</th>
<th>SAPIEN XT</th>
<th>SAPIEN 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1B (TF)</td>
<td>179</td>
<td>276</td>
<td>284</td>
</tr>
<tr>
<td>P1A (Overall)</td>
<td>344</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P2B (TF)</td>
<td>4.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P2B XT (TF)</td>
<td>4.3%</td>
<td>1.5%</td>
<td></td>
</tr>
<tr>
<td>S3HR (Overall)</td>
<td></td>
<td>1076</td>
<td></td>
</tr>
<tr>
<td>S3i (Overall)</td>
<td></td>
<td>583</td>
<td></td>
</tr>
</tbody>
</table>
Paravalvular Leak: S3HR & S3i
(Valve Implant Patients)

- None/Trace
- Mild
- Moderate
- Severe

Percent of evaluable echos

- 0% 0.1% 3.7%
- 20% 41.3%
- 40% 55.0%
- 60%
- 80%
- 100%

No. of Echos

30 Days

1504

Kodali ACC 2015
Moderate/Severe PVL at 30 Days
Edwards SAPIEN Valves

PARTNER I and II Trials

<table>
<thead>
<tr>
<th>SAPIEN</th>
<th>P1B (TF)</th>
<th>P1A (Overall)</th>
<th>P2B (TF)</th>
<th>P2B XT (TF)</th>
<th>S3HR (Overall)</th>
<th>S3i (Overall)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>179</td>
<td>344</td>
<td>276</td>
<td>284</td>
<td>583</td>
<td>1076</td>
</tr>
<tr>
<td>SAPIEN XT</td>
<td>0%</td>
<td>11.5%</td>
<td>16.9%</td>
<td>24.2%</td>
<td>2.9%</td>
<td>4.2%</td>
</tr>
<tr>
<td>SAPIEN 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TAVR Growth in U.S.

Sites Enrolled in the TVT Registry

Complications in patients undergoing TAVR

Neurological Complications

- TIA: 0.3% (2012-13) vs. 0.2% (2014)
- Stroke (any): 2.1% (2012-13) vs. 2.2% (2014)

Bleeding and Vascular Complications

- Major Bleeding: 5.5% (2012-13) vs. 4.2% (2014)
- Life Threatening or Disabling Bleeding: 6.4% (2012-13) vs. 4.3% (2014)
- Vascular complication (any): 5.6% (2012-13) vs. 4.2% (2014)
So, What’s New?
Valves Under Development

(A) Lotus (Boston Scientific Inc., Natick, Massachusetts), (B) Direct Flow (Direct Flow Medical Inc., Santa Rosa, California), (C) HLT (Braico Inc., Princeton, New Jersey), (D) Portico (St. Jude Medical Inc., St. Paul, Minnesota), (E) Engager (Medtronic Inc., Minneapolis Minnesota), (F) JenaClip (JenaValve Inc., Munich, Germany), (G) Acurate valve (Syneris Inc., Ecublens, Switzerland), and (H) Isovare (Braile Biomédica Inc., São José do Rio Preto, Brazil) valves.
Cerebral Emboli During TAVR and SAVR Using Transcranial Doppler

**TAVR, N=85**

**SAVR, N=42**

1 patient in each arm suffered a stroke at 30 day follow up

Protection of cerebral events during TAVR

Embrella Embolic Deflector (Edwards Lifesciences)

Triguard (Keystone Heart, Herzliya Pituach, Israel)

Freeman et al. CCI 2014;84(6):885-896
Protection of cerebral events during TAVR

Claret Montage
(Claret Medical, CA)
Valve in Valve Implantation
Valve in Valve Implantation

Original Investigation

Transcatheter Aortic Valve Implantation in Failed Bioprosthetic Surgical Valves

Danny Dvir, MD; John G. Webb, MD; Sabine Bleiziffer, MD; Miralem Pasic, MD, PhD; Ron Waksman, MD; Susheel Kodali, MD; Marco Barbanti, MD; Azeem Latib, MD; Ulrich Schaefer, MD; Josep Rodés-Cabau, MD; Hendrik Treede, MD; Nicolo Piazza, MD, PhD; David Hildick-Smith, MD; Dominique Himbert, MD; Thomas Walther, MD; Christian Hengstenberg, MD; Henrik Nissen, MD, PhD; Raffi Bekerjian, MD; Patrizia Presbitero, MD; Enrico Ferrari, MD; Amit Segev, MD; Arend de Weger, MD; Stephan Windecker, MD; Neil E. Mac, FRCS; Massimo Napodano, MD; Manuel Wilbring, MD; Alfredo G. Cerillo, MD; Stephen Brecker, MD; Didier Tchetche, MD; Thierry Lefebvre, MD; Federico De Marco, MD; Claudia Fiorina, MD; Anna Sonia Petronio, MD; Rui C. Teles, MD; Luca Testa, MD; Jean-Claude Laborde, MD; Martin B. Leon, MD; Ran Kornowski, MD; for the Valve-in-Valve International Data Registry Investigators

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>All (n = 450)</th>
<th>Stenosis (n = 181)</th>
<th>Regurgitation (n = 139)</th>
<th>Combined (n = 139)</th>
<th>P Value</th>
<th>Self-Expandable (n = 213)</th>
<th>Balloon-Expandable (n = 246)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of hospital stay, median (IQR), d</td>
<td>8 (5-12)</td>
<td>7 (5-11)</td>
<td>7 (5-12)</td>
<td>8 (6-13)</td>
<td>.21</td>
<td>7 (5-12)</td>
<td>8 (6-13)</td>
<td>.07</td>
</tr>
<tr>
<td>Thirty-day outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death, No. (%)</td>
<td>35 (7.6)</td>
<td>19 (10.5)</td>
<td>6 (4.3)</td>
<td>10 (7.2)</td>
<td>.04</td>
<td>15 (7)</td>
<td>20 (8.1)</td>
<td>.66</td>
</tr>
</tbody>
</table>

One-year outcomes

<table>
<thead>
<tr>
<th>NYHA functional class, No. (%)</th>
<th>All (n = 450)</th>
<th>Stenosis (n = 181)</th>
<th>Regurgitation (n = 139)</th>
<th>Combined (n = 139)</th>
<th>P Value</th>
<th>Self-Expandable (n = 213)</th>
<th>Balloon-Expandable (n = 246)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I/II</td>
<td>163 (66.2)</td>
<td>62 (84.9)</td>
<td>46 (85.2)</td>
<td>55 (88.7)</td>
<td>.04</td>
<td>88 (81.6)</td>
<td>75 (82.4)</td>
<td>.89</td>
</tr>
<tr>
<td>III/IV</td>
<td>26 (13.8)</td>
<td>11 (15.1)</td>
<td>8 (14.8)</td>
<td>7 (11.3)</td>
<td>.34</td>
<td>10 (18.4)</td>
<td>16 (17.6)</td>
<td>.89</td>
</tr>
<tr>
<td>AV area, mean (SD), cm²</td>
<td>1.38 (0.42)</td>
<td>1.28 (0.20)</td>
<td>1.51 (0.48)</td>
<td>1.36 (0.45)</td>
<td>.01</td>
<td>1.55 (0.41)</td>
<td>1.29 (0.39)</td>
<td>.006</td>
</tr>
<tr>
<td>AV maximal gradient, mean (SD), mm Hg</td>
<td>30 (14.7)</td>
<td>32.3 (14.5)</td>
<td>25.2 (15.4)</td>
<td>22.1 (12.5)</td>
<td>.005</td>
<td>25.3 (11.9)</td>
<td>33.3 (16)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>AV mean gradient, mean (SD), mm Hg</td>
<td>16.9 (8.1)</td>
<td>18.3 (9.5)</td>
<td>13.8 (9.9)</td>
<td>18.4 (8)</td>
<td>.001</td>
<td>13.5 (7)</td>
<td>19.4 (9.6)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

JAMA 2014; 312(2):162-70
Expanding the Limits

Transapical Transcatheter Aortic Valve for Severe Aortic Regurgitation

Daniel Wendt, MD, PhD* Philipp Kahlert, MD, PhD | Susanne Pasa, MD | Karim El-Chilali, MD | Fadi Al-Rashid, MD | Konstantinos Tsagakis, MD* | Daniel Sebastian Dohle, MD* | Raimund Erbel, MD, PhD* | Heinz Jakob, MD, PhD* | Matthias Thielmann, MD, PhD

---

**Table 4: 3- to 6-Month Echocardiographic Follow-up**

<table>
<thead>
<tr>
<th>Patient</th>
<th>LV Function, %</th>
<th>Proximal vs. 3-6 Months, %</th>
<th>$P_{mean}$ mm Hg</th>
<th>$P_{aortic}$ mm Hg</th>
<th>AFA, cm²</th>
<th>$V_{max}$ m/s</th>
<th>AR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>55</td>
<td>0</td>
<td>16</td>
<td>9</td>
<td>1.9</td>
<td>2.0</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>-10</td>
<td>15</td>
<td>9</td>
<td>1.4</td>
<td>1.9</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>55</td>
<td>+2</td>
<td>18</td>
<td>10</td>
<td>1.5</td>
<td>2.1</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>-10</td>
<td>19</td>
<td>11</td>
<td>1.6</td>
<td>1.6</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>50</td>
<td>+1</td>
<td>28</td>
<td>17</td>
<td>NA</td>
<td>2.1</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>55</td>
<td>+10</td>
<td>14</td>
<td>9</td>
<td>2.2</td>
<td>1.9</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>35</td>
<td>-7</td>
<td>15</td>
<td>9</td>
<td>1.8</td>
<td>1.9</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>35</td>
<td>+10</td>
<td>18</td>
<td>10</td>
<td>NA</td>
<td>1.6</td>
<td>0</td>
</tr>
</tbody>
</table>

**Mortality**

- 30-day all cause: 0 (0)
- 30-day cardiovascular: 0 (0)
- 12-month all cause: 0 (0)
- 12-month cardiovascular: 0 (0)
- Stroke/TIA 30-day: 0 (0)
- Minor bleeding: 0 (0)
- Major bleeding: 0 (0)
- Blood transfusion: 0 (0)
- Acute kidney injury: 1 (0.0)
- Pacemaker implantation: 0 (0)
- Myocardial infarction: 0 (0)
- VARC-2 procedure success: 8 (100)
- Access site complications: 0 (0)
  - Major: 0 (0)
  - Minor: 0 (0)

---

Self-expandable ACURATE TA bioprosthesis (Symetis SA, Ecublens, Switzerland).

Focus shifting from clinical outcomes to procedural efficiency

Babaliaros V et al. JACC Int 2014;7(8):898-904
Bern TAVI Registry:
The European Experience with less than high risk patients

LOW VS. HIGH: RR (95% CI) = 0.27 (0.09–0.77)
INTERMEDIATE VS. HIGH: RR (95% CI) = 0.41 (0.24–0.67)
P < 0.001

<table>
<thead>
<tr>
<th>Number at Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH</td>
</tr>
<tr>
<td>INTERMEDIATE</td>
</tr>
<tr>
<td>LOW</td>
</tr>
</tbody>
</table>

Conclusions

1. TAVR (TAVI) is the current standard of care for inoperable patients with severe AS
2. TAVR is an acceptable option for high risk operable patients
3. TAVR is an acceptable option for patients with prior surgical AVR (And MVR)
4. TAVR may soon be an option for intermediate and low risk patients
Conclusions

• Outcomes will continue to improve with smaller profile delivery systems and methods to reduce paravalvular leak
• Stroke prevention: embolic protection devices
• Dedicated valve designs for pure aortic insufficiency
• TMVR