Self-expanding TAVR in Patients with a Failed Surgical Bioprosthesis: 1 Year Results from the CoreValve US Expanded Use Study

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On behalf of the CoreValve US Investigators
Author Disclosures

- Medtronic: Surgical Advisory Board, Proctor and Research Investigator FDA Trials *
- Edwards: Consultant and Research Investigator FDA Trials *
- Boston Scientific: Research Investigator FDA Trials *
- Terumo: Consultant and Proctor *
- Gore: Research Investigator FDA Trials*

* No Personal Reimbursement
CoreValve US Expanded Use Study

- Prospective, non-randomized multicenter trial
- Evaluate safety & efficacy of the self-expanding Medtronic CoreValve
- Failure mode of bioprosthetic SAV: stenosis, insufficiency or combined disease
- Patients considered unsuitable for open surgery
- Patients vetted through screening committee
Study Device and Access Routes

4 valve sizes (23, 26, 29, 31mm) (17-29 mm annular range)

18Fr delivery system

Transfemoral
Subclavian
Direct Aortic
Study Disposition

Valve in Valve Patients Enrolled
N=113

Attempted Implant
N=109

Implanted
N=107

Exited Prior to Procedure (n=4)
  3 Died
  1 Physician withdrew subject

1 Died
1 Exited
Study Compliance

- Screening: 100% (113/113)
- Baseline: 100% (111/111)
- Procedure: 100% (109/109)
- Discharge: 100% (107/107)
- 1 Month Follow-Up: 99.1% (105/106)
- 6 Month Follow-Up: 94.9% (94/99)
- 12 Month Follow-Up: 96.7% (88/91)
## Failure Mode of Previously Implanted Bioprosthetic Valve

<table>
<thead>
<tr>
<th>Modality</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stenosis</td>
<td>67 (61.5%)</td>
</tr>
<tr>
<td>Insufficiency</td>
<td>16 (14.7%)</td>
</tr>
<tr>
<td>Combined</td>
<td>26 (23.9%)</td>
</tr>
<tr>
<td><strong>All</strong></td>
<td><strong>109</strong></td>
</tr>
</tbody>
</table>
### Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic, % or mean ± SD</th>
<th>All N=109</th>
<th>Insufficiency N=16</th>
<th>Stenosis N=67</th>
<th>Combined N=26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>77.1 ± 10.5</td>
<td>78.5 ± 13.0</td>
<td>75.9 ± 9.7</td>
<td>79.4 ± 11.0</td>
</tr>
<tr>
<td>Male*</td>
<td>68.8</td>
<td>100.0</td>
<td>59.7</td>
<td>73.1</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>2.0 ± 0.2</td>
<td>2.0 ± 0.2</td>
<td>2.0 ± 0.2</td>
<td>1.9 ± 0.3</td>
</tr>
<tr>
<td>STS score (Mortality), %</td>
<td>9.5 ± 5.6</td>
<td>8.0 ± 4.5</td>
<td>9.5 ± 5.7</td>
<td>10.4 ± 6.0</td>
</tr>
<tr>
<td>STS score (Morbidity or Mortality), %</td>
<td>35.5 ± 10.9</td>
<td>33.3 ± 10.8</td>
<td>35.3 ± 10.9</td>
<td>37.5 ± 11.1</td>
</tr>
<tr>
<td>Logistic EuroSCORE</td>
<td>26.1 ± 17.2</td>
<td>27.1 ± 22.6</td>
<td>26.0 ± 16.4</td>
<td>25.8 ± 16.2</td>
</tr>
<tr>
<td>NYHA Class III/IV</td>
<td>89.0</td>
<td>87.5</td>
<td>89.6</td>
<td>88.5</td>
</tr>
<tr>
<td>Diabetes mellitus*</td>
<td>45.0</td>
<td>6.3</td>
<td>56.7</td>
<td>38.5</td>
</tr>
<tr>
<td>Insulin requiring diabetes</td>
<td>11.9</td>
<td>0.0</td>
<td>17.9</td>
<td>3.8</td>
</tr>
<tr>
<td>Prior Stroke</td>
<td>13.8</td>
<td>6.3</td>
<td>17.9</td>
<td>7.7</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>55.0</td>
<td>50.0</td>
<td>58.2</td>
<td>50.0</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>33.9</td>
<td>37.5</td>
<td>31.3</td>
<td>38.5</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>79.8</td>
<td>75.0</td>
<td>80.6</td>
<td>80.8</td>
</tr>
<tr>
<td>Chronic lung disease/COPD</td>
<td>68.8</td>
<td>68.8</td>
<td>68.7</td>
<td>69.2</td>
</tr>
</tbody>
</table>

*P < 0.05 across failure modes. All other characteristics were not statistically significant.
## SAV Characteristics

<table>
<thead>
<tr>
<th>Characteristic, % or mean ± SD</th>
<th>All N=109</th>
<th>Insufficiency N=16</th>
<th>Stenosis N=67</th>
<th>Combined N=26</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SAV Age (yrs)</strong>*</td>
<td>10.0 ± 4.6</td>
<td>9.4 ± 3.8</td>
<td>8.8 ± 3.9</td>
<td>13.5 ± 5.1</td>
</tr>
<tr>
<td><strong>Type of bioprosthetic surgical valve</strong>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homograft</td>
<td>8.3</td>
<td>25.0</td>
<td>3.0</td>
<td>11.5</td>
</tr>
<tr>
<td>Stented</td>
<td>85.3</td>
<td>62.5</td>
<td>91.0</td>
<td>84.6</td>
</tr>
<tr>
<td>Stentless</td>
<td>6.4</td>
<td>12.5</td>
<td>6.0</td>
<td>3.8</td>
</tr>
<tr>
<td><strong>SAV Tissue Type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bovine Pericardial</td>
<td>53.8</td>
<td>30.0</td>
<td>58.7</td>
<td>50.0</td>
</tr>
<tr>
<td>Porcine</td>
<td>46.2</td>
<td>70.0</td>
<td>41.3</td>
<td>50.0</td>
</tr>
<tr>
<td><strong>SAV Labeled Size Group</strong>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small (19-21mm)</td>
<td>36.3</td>
<td>14.3</td>
<td>42.4</td>
<td>31.8</td>
</tr>
<tr>
<td>Medium (23-25mm)</td>
<td>52.9</td>
<td>42.9</td>
<td>51.5</td>
<td>63.6</td>
</tr>
<tr>
<td>Large (27-29mm)</td>
<td>10.8</td>
<td>42.9</td>
<td>6.1</td>
<td>4.5</td>
</tr>
</tbody>
</table>

*P<0.05 across failure modes. All other characteristics were not statistically significant.
TAV/SAV Sizing

- Internal stent diameter (ID) of SAV using valve in valve application developed by Dr. Vinayak Bapat & UBQO Technology

- Nominal valve size from the labeled valve size
### TAV Sizes Implanted

<table>
<thead>
<tr>
<th>TAV Size, %*</th>
<th>All N=109</th>
<th>Insufficiency N=16</th>
<th>Stenosis N=67</th>
<th>Combined N=26</th>
</tr>
</thead>
<tbody>
<tr>
<td>23mm</td>
<td>56.1</td>
<td>25.0</td>
<td>67.7</td>
<td>46.2</td>
</tr>
<tr>
<td>26mm</td>
<td>28.0</td>
<td>31.3</td>
<td>24.6</td>
<td>34.6</td>
</tr>
<tr>
<td>29mm</td>
<td>12.1</td>
<td>37.5</td>
<td>7.7</td>
<td>7.7</td>
</tr>
<tr>
<td>31mm</td>
<td>3.7</td>
<td>6.3</td>
<td>0.0</td>
<td>11.5</td>
</tr>
</tbody>
</table>

*P<0.05 across failure modes.*
## Device and Procedural Success

<table>
<thead>
<tr>
<th>Device Success (92.5%)</th>
<th>Procedural Success (90.7%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Correct Position of Device in the Proper Anatomic Location: No Impedance to Device function 1 (0.9%) malposition</td>
<td>2. Absence of In-hospital MACCE</td>
</tr>
<tr>
<td>3. One Valve in the Proper Anatomic Location</td>
<td>3. No Acute Coronary Artery Occlusion</td>
</tr>
</tbody>
</table>
All-Cause Mortality or Major Stroke

Number at risk:
- 0 months: 109
- 1 month: 105
- 2 months: 97
- 3 months: 97
- 4 months: 97
- 5 months: 97
- 6 months: 97
- 7 months: 97
- 8 months: 97
- 9 months: 97
- 10 months: 97
- 11 months: 87
- 12 months: 87

Mortality or Major Stroke (%)
- 0% to 20%
- 20% to 40%
- 40% to 60%
- 60% to 70%
- 70%

Months Post-Procedure
- 0
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12

- 2.8% at 1 month
- 8.4% at 6 months
- 15.2% at 12 months

CoreValve US Clinical Trials
All-Cause Mortality or Major Stroke

Months Post-Procedure

Number at risk:

0: 109, 105, 97, 87
1: 109, 106, 99, 89
2: 109, 106, 99, 89

0% 10% 20% 30% 40% 50% 60% 70%

Mortality or Major Stroke (%)
All-Cause Mortality by SAV Failure Mode

- **Stenosis**
- **Insufficiency**
- **Combined**

P-value (log-rank) = 0.34

Mortality (%)

- 0% months: 3.8%
- 1% months: 1.5%
- 2% months: 0.0%
- 3% months: 7.7%
- 4% months: 7.7%
- 5% months: 0.0%
- 6% months: 7.7%
- 7% months: 0.0%
- 8% months: 17.4%
- 9% months: 7.7%
- 10% months: 6.7%

Number at risk:

- 67 65 59 51
- 16 16 16 14
- 26 25 24 24
## Secondary Endpoints

<table>
<thead>
<tr>
<th>Outcome, %*</th>
<th>30 Days</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Stroke</td>
<td>0.9</td>
<td>4.1</td>
</tr>
<tr>
<td>Major Stroke</td>
<td>0.9</td>
<td>3.1</td>
</tr>
<tr>
<td>Ischemic</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>TIA</td>
<td>0.0</td>
<td>1.1</td>
</tr>
<tr>
<td>Reintervention</td>
<td>0.9</td>
<td>4.0</td>
</tr>
<tr>
<td>Surgical</td>
<td>0.9</td>
<td>2.9</td>
</tr>
<tr>
<td>Bleed</td>
<td>23.0</td>
<td>27.1</td>
</tr>
<tr>
<td>Life Threatening or Disabling</td>
<td>6.5</td>
<td>11.6</td>
</tr>
<tr>
<td>Major Bleed</td>
<td>16.6</td>
<td>16.6</td>
</tr>
<tr>
<td>Major Vascular Complication</td>
<td>11.0</td>
<td>11.0</td>
</tr>
<tr>
<td>Acute Kidney Injury</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>MI</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>New Permanent Pacemaker Implant</td>
<td>6.6</td>
<td>11.7</td>
</tr>
</tbody>
</table>

*Percentages obtained from Kaplan Meier estimates*
Hemodynamic Outcomes

- Effective Orifice Area (cm²)
- Mean Gradient (mmHg)

Baseline data site reported (dashed line)
Follow-up data core lab reported (solid line)
What is the impact of a higher mean valve gradient?

Baseline data site reported (dashed line)
Follow-up data core lab reported (solid line)
All-Cause Mortality by Discharge Gradient

- Mortality (%)
  - <20mmHg
  - ≥20mmHg

P-value (log-rank) = 0.06

Number at risk:
<table>
<thead>
<tr>
<th>Months Post-Procedure</th>
<th>&lt;20mmHg</th>
<th>≥20mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>1</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>2</td>
<td>63</td>
<td>31</td>
</tr>
<tr>
<td>3</td>
<td></td>
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<tr>
<td>4</td>
<td></td>
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<tr>
<td>5</td>
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<td>6</td>
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<td>9</td>
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<tr>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>58</td>
<td>26</td>
</tr>
</tbody>
</table>

CoreValve US Clinical Trials
All-Cause Mortality by Discharge Gradient

What is driving a higher gradient at discharge?

P-value (log-rank) = 0.06

Mortality (%)
- <20mmHg
- ≥20mmHg

Number at risk:
- 65 36
- 65 36
- 63 31
- 58 26
- 21
Factors That May Impact Mean Gradient

- Modality of Failure
- Surgical Valve Size
- Predicted Patient Prosthesis Mismatch: (PPM)
Mean Gradient by Predicted PPM

- Severe PPM (N=11)
- Moderate PPM (N=37)
- No PPM (N=43)

Baseline data site reported (dashed line)
Follow-up data core lab reported (solid line)
Mean Gradient by SAV Size

- Small (N=36)
- Medium (N=54)
- Large (N=10)

Baseline data site reported (dashed line)
Follow-up data core lab reported (solid line)
Mean Gradient by Failure Mode

Baseline data site reported (dashed line)
Follow-up data core lab reported (solid line)
Mean Gradient at 1 Month – SAV Size

- Stenosis: 9.7 mmHg
- Combined: 14.9 mmHg
- Insufficiency: 14.7 mmHg

- Large: 18.6 mmHg, 20.6 mmHg, 15.2 mmHg
- Medium: 17.4 mmHg, 12.5 mmHg, 11.6 mmHg
- Small: 15.2 mmHg, 12.5 mmHg
Mean Gradient at 1 Month - PPM

- Stenosis: No PPM = 14.7, Moderate PPM = 21.4, Severe PPM = 25.2
- Combined: No PPM = 17.6, Moderate PPM = 15.8, Severe PPM = 17.3
- Insufficiency: No PPM = 13.1
Mean Gradient at 1 Month – PPM & SAV

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Number of Patients: 28

Mean Gradient (mmHg)

- No PPM
- Moderate PPM
- Severe PPM

- Small: 15.5
- Medium: 16.1
- Large: 12.6

- Small: 21.1
- Medium: 21.9
- Large: 30.8

No PPM
Moderate PPM
Severe PPM
Total Aortic Regurgitation

Percentage of Patients

- Baseline (N=105)
  - None/Trace: 19.0%
  - Mild: 41.0%
  - Moderate: 21.0%
  - Severe: 19.0%
- 1 Month (N=98)
  - None/Trace: 26.5%
  - Mild: 70.4%
  - Moderate: 21.0%
  - Severe: 19.0%
- 6 Months (N=89)
  - None/Trace: 29.2%
  - Mild: 68.5%
  - Moderate: 21.0%
  - Severe: 19.0%
- 12 Months (N=78)
  - None/Trace: 6.4%
  - Mild: 25.6%
  - Moderate: 67.9%
  - Severe: 19.0%

The baseline data were reported by site echocardiography and all post-procedure follow-up data were provided by a Core Lab.
NYHA Classification

- **Baseline (N=109):**
  - NYHA I: 6.4%
  - NYHA II: 72.5%
  - NYHA III: 21.1%

- **1 Month (N=104):**
  - NYHA I: 31.7%
  - NYHA II: 58.7%
  - NYHA III: 9.6%

- **6 Months (N=90):**
  - NYHA I: 28.9%
  - NYHA II: 66.7%
  - NYHA III: 3.3%
  - NYHA IV: 1.1%

- **12 Months (N=82):**
  - NYHA I: 19.5%
  - NYHA II: 73.2%
  - NYHA III: 7.3%
KCCQ Overall Summary Score Improvement from Baseline

Δ = 30.26  
P < 0.001

Δ = 31.83  
P < 0.001

Δ = 31.78  
P < 0.001

CoreValve

Baseline
Conclusions

- TAV/SAV is safe and effective therapy for patients with failing surgical bioprosthetic valves (SAV) who are not candidates for open heart surgery.

- High Device Success: 92.5%, 1/107 Malposition of valve (0.9%); High Procedural Success: (90.7%), No acute coronary artery occlusion.

- The mortality or stroke rate at 1 year is lower than the published data for this patient population treated with medical or open surgical therapy.

- TAV/SAV significantly improves the quality of life as reflected by the improvement of the NYHA classification and the KCCQ score.
Conclusions II

- Residual mean valve gradient (MVG) ≥ 20 mm/HG at discharge appears to be associated with higher mortality within the 1st year.

- Factors which are associated with a high residual MVG are small SAV size and patient prosthesis mismatch (PPM).

- Combination of stenosis, small SAV size and PPM has largest impact on MVG at 30 days and mortality within the 1st year.

- The limiting factor for TAV/SAV procedure is the SAV implanted at the initial procedure: It is imperative that the most appropriately matched SAV size to patient size is implanted to avoid PPM.
Thank You
On Behalf of the US CoreValve Investigators
Predicted SAVR PPM Category

Specific make, model and size of SAVR: Clinically determine EOA from surgical valve IFU data.

Patient’s BSA at time of TAV in SAV procedure:

\[ \text{EOAi} = \frac{\text{EOA}}{\text{BSAm}^2} \]

PPM category from predicted EOAi:
- No PPM: > 0.85 cm²/m²
- Moderate PPM: > 0.65 but < 0.85 cm²/m²
- Severe PPM: < 0.65 cm²/m²