Clinical Outcomes at 3 Years Following Self-Expanding Transcatheter Aortic Valve Replacement in the CoreValve US Extreme Risk Pivotal Trial

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For the CoreValve US Clinical Investigators
Dr. Hermiller serves on the Steering Committee for the reported trial and as a Medtronic Faculty Educator.

Medtronic personnel performed all statistical analyses and assisted in the graphical display of the data.
Patients initially treated with TAVR were considered inoperable or at extreme-risk with predicted mortality or severe morbidity (≥ 50%) with SAVR.

Although surgical candidates (high risk) are now often treated with TAVR, the extreme risk population continues to constitute a significant proportion of all patients undergoing TAVR.

The long-term outcomes, therefore, in these patients can provide important insights for decision makers.
Pivotal Trial Design

CoreValve US Pivotal Trial

Extreme Risk
- Iliofemoral Access > 18 Fr Sheath
  - CoreValve Iliofemoral N=489
  - CoreValve Non-Iliofemoral N=150

High Risk
- Randomization 1:1
  - CoreValve
  - SAVR
Methods

• Primary analysis cohort comprised all enrolled subjects with an attempted iliofemoral implant procedure

• Event rates reported as Kaplan-Meier estimates

• Serial echocardiographic measurements based on site-reported data at all time points
Subjects Enrolled
N=719
Roll-in subjects = 63

Eligible Subjects
N=656
Attempted implant via NIF = 150
Exited prior to procedure = 17

Attempted Iliofemoral Implant
N=489

Patients at 1 Year
N=367
Died = 121
Study Exit = 1

Patients at 2 Years
N=307
Died = 58
Study Exit = 2

Patients at 3 Years
N=240
Died = 58
Study Exit = 8
Visit pending = 1
Study Compliance

Clinical Assessments

Baseline
N=489
100% Follow-up
(n=489/489)

1 Month
N=449
98.2% Follow-up
(n=441/449)

1 Year
N=367
99.2% Follow-up
(n=364/367)

2 Years
N=307
94.1% Follow-up
(n=289/307)

3 Years
N=240
91.3% Follow-up
(n=219/240)
## Baseline Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=489</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>83.2 ± 8.7</td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>47.9</td>
<td></td>
</tr>
<tr>
<td>STS Predicted Risk of Mortality</td>
<td>10.3 ± 5.5</td>
<td></td>
</tr>
<tr>
<td>New York Heart Association class III/IV</td>
<td>91.8</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>41.5</td>
<td></td>
</tr>
<tr>
<td>Insulin requiring diabetes</td>
<td>18.4</td>
<td></td>
</tr>
<tr>
<td>Prior stroke</td>
<td>13.7</td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>81.8</td>
<td></td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>30.9</td>
<td></td>
</tr>
<tr>
<td>Prior coronary artery bypass grafting</td>
<td>39.5</td>
<td></td>
</tr>
<tr>
<td>Prior percutaneous coronary intervention</td>
<td>37.0</td>
<td></td>
</tr>
<tr>
<td>Prior balloon aortic valvuloplasty</td>
<td>20.4</td>
<td></td>
</tr>
</tbody>
</table>
## Comorbidities, Frailty, Disabilities

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prohibitive Anatomy</strong></td>
<td></td>
</tr>
<tr>
<td>Severe aortic calcification*</td>
<td>17.2</td>
</tr>
<tr>
<td>Hostile mediastinum</td>
<td>11.9</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td></td>
</tr>
<tr>
<td>Severe chronic lung disease</td>
<td>23.5</td>
</tr>
<tr>
<td>Home oxygen</td>
<td>29.9</td>
</tr>
<tr>
<td><strong>Frailty</strong></td>
<td></td>
</tr>
<tr>
<td>Anemia with prior transfusion</td>
<td>22.8</td>
</tr>
<tr>
<td>Albumin $&lt; 3.3$ g/dL</td>
<td>18.2</td>
</tr>
<tr>
<td>5-Meter gait speed $&gt; 6$ secs</td>
<td>84.2</td>
</tr>
<tr>
<td><strong>Disabilities</strong></td>
<td></td>
</tr>
<tr>
<td>Assisted living</td>
<td>27.6</td>
</tr>
<tr>
<td>$\geq 2$ Katz ADL deficits</td>
<td>20.9</td>
</tr>
<tr>
<td>Wheelchair bound</td>
<td>16.6</td>
</tr>
</tbody>
</table>

*N=489

* Aorta calcification measured on screening CTA
CoreValve US Pivotal Trial Extreme Risk Iliofemoral 3-Year Results
All-Cause Mortality or Major Stroke

P < 0.0001

Performance Goal = 43%

26.0
[22.1, 29.9]

37.9
52.0
3-Year Mortality

- All-Cause
- Cardiovascular

Mortality

0% 10% 20% 30% 40% 50% 60% 70% 80%

0 12 24 36

Months

489 369 305 164

TCT 2015
3-Year Major Stroke

Graph showing the percentage of major strokes over time. The Y-axis represents the percentage of major strokes ranging from 0% to 80%, and the X-axis represents the number of months ranging from 0 to 36. The data points are labeled at various months: 0 (489), 12 (361), 24 (298), and 36 (157), with corresponding percentages of 4.3%, 5.1%, and 9.0%.
## Secondary Endpoints

<table>
<thead>
<tr>
<th>Events*</th>
<th>1 Year</th>
<th>2 Years</th>
<th>3 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any stroke</td>
<td>7.0</td>
<td>8.6</td>
<td>13.7</td>
</tr>
<tr>
<td>Major</td>
<td>4.3</td>
<td>5.1</td>
<td>9.0</td>
</tr>
<tr>
<td>Minor</td>
<td>3.2</td>
<td>4.0</td>
<td>6.3</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2.0</td>
<td>2.8</td>
<td>4.0</td>
</tr>
<tr>
<td>Reintervention</td>
<td>1.8</td>
<td>1.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Valve thrombosis</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>VARC bleeding</td>
<td>42.8</td>
<td>45.5</td>
<td>46.9</td>
</tr>
<tr>
<td>Life threatening or disabling</td>
<td>18.0</td>
<td>21.4</td>
<td>22.4</td>
</tr>
<tr>
<td>Major</td>
<td>28.3</td>
<td>29.1</td>
<td>30.2</td>
</tr>
<tr>
<td>Major vascular complications</td>
<td>8.4</td>
<td>8.4</td>
<td>8.4</td>
</tr>
<tr>
<td>Permanent pacemaker implant</td>
<td>26.9</td>
<td>29.2</td>
<td>32.3</td>
</tr>
<tr>
<td>Per ACC guidelines</td>
<td>19.5</td>
<td>21.9</td>
<td>24.2</td>
</tr>
</tbody>
</table>

* Percentages are Kaplan Meier estimates.
NYHA Class Paired Analysis

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Percentage of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
</tr>
<tr>
<td>1 Month</td>
<td></td>
</tr>
<tr>
<td>1 Year</td>
<td></td>
</tr>
<tr>
<td>2 Years</td>
<td></td>
</tr>
<tr>
<td>3 Years</td>
<td></td>
</tr>
</tbody>
</table>

- **Baseline (N=173)**
  - NYHA I: 10.4%
  - NYHA II: 45.1%
  - NYHA III: 67.6%
  - NYHA IV: 22.0%

- **1 Month (N=173)**
  - NYHA I: 24.9%
  - NYHA II: 41.6%
  - NYHA III: 16.2%
  - NYHA IV: 13.3%

- **1 Year (N=173)**
  - NYHA I: 39.3%
  - NYHA II: 24.9%
  - NYHA III: 35.1%
  - NYHA IV: 0.6%

- **2 Years (N=173)**
  - NYHA I: 56.6%
  - NYHA II: 16.2%
  - NYHA III: 21.1%
  - NYHA IV: 3.5%

- **3 Years (N=173)**
  - NYHA I: 50.9%
  - NYHA II: 13.3%
  - NYHA III: 20.1%
  - NYHA IV: 10.0%
KCCQ Overall Summary Score
Change from Baseline

Differences and p-values based on paired t-test compared with baseline

Baseline
N=454

1 Year
N=265

2 Years
N=212

3 Years
N=146

CoreValve
Baseline

Δ = 27.9
P<0.0001

Δ = 25.2
P<0.0001

Δ = 25.3
P<0.0001

TCT 2015
Echocardiographic Findings

Site-Reported

Effective Orifice Area, cm²

Mean Gradient, mm Hg

- Effective orifice area
- Mean gradient

**Gradient**
- Baseline: 484
- Discharge: 458
- 1 Month: 426
- 1 Year: 336
- 2 Years: 261
- 3 Years: 184

**EOA**
- Baseline: 470
- Discharge: 414
- 1 Month: 397
- 1 Year: 308
- 2 Years: 246
- 3 Years: 172

CoreValve US Clinical Trials

TCT 2015
Paravalvular Regurgitation

Site Reported

CoreValve US Clinical Trials

<table>
<thead>
<tr>
<th>Time</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
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<tbody>
<tr>
<td>Discharge</td>
<td>28.0</td>
<td>65.2</td>
<td>6.9</td>
<td>0.2</td>
</tr>
<tr>
<td>1 Month</td>
<td>26.9</td>
<td>66.7</td>
<td>3.7</td>
<td>0.3</td>
</tr>
<tr>
<td>1 Year</td>
<td>37.0</td>
<td>59.0</td>
<td>4.0</td>
<td>0.4</td>
</tr>
<tr>
<td>2 Years</td>
<td>44.5</td>
<td>50.0</td>
<td>5.1</td>
<td>0.5</td>
</tr>
<tr>
<td>3 Years</td>
<td>47.5</td>
<td>47.0</td>
<td>4.9</td>
<td></td>
</tr>
</tbody>
</table>

N=422, N=417, N=324, N=256, N=183
PVL and All-Cause Mortality

Log-rank $P<0.0001$

PVL severity based on core-lab assessment at discharge.
Pacemaker and All-Cause Mortality

With New PPI
Without New PPI

Log-rank $P=0.62$

<table>
<thead>
<tr>
<th>Months</th>
<th>New PPI</th>
<th>No PPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>104</td>
<td>258</td>
</tr>
<tr>
<td>12</td>
<td>76</td>
<td>196</td>
</tr>
<tr>
<td>24</td>
<td>63</td>
<td>163</td>
</tr>
<tr>
<td>36</td>
<td>37</td>
<td>90</td>
</tr>
</tbody>
</table>

TCT 2015
Conclusions

• At 3 years the CoreValve US Pivotal Extreme Risk Study showed:
  – Durable improvement in hemodynamic valve performance (EOA and mean gradients)
  – Low rates of moderate or severe aortic insufficiency
  – Durable improvements in NYHA functional class
  – The proportion of non-cardiac deaths increase over time
Summary

• The 1-year results from the CoreValve US Pivotal Extreme Risk Trial support the safety and efficacy of this therapy in patients unsuitable for surgical AV replacement.

• The 3-year results confirm favorable clinical outcomes and durable valve performance.
Thank You
On Behalf of the CoreValve US Investigators