Latest Innovation in Mitral Valve Repair

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☑ I have the following potential conflicts of interest to declare:

Receipt of honoraria or consultation fees: Edwards Lifesciences
Edwards PASCAL Transcatheter Valve Repair System

**Implant**

Central spacer intended to fill the regurgitant orifice area

Spacer and broad, contoured paddle design reduce stress on leaflets

Clasps allow for independent leaflet capture and the ability to fine-tune leaflet position

For professional use. See instructions for use for full prescribing information. CE Marked medical device.
Delivery system

22 French guide sheath

Design allows for catheter manoeuvring in three independent planes

Independent catheters allow predictable implant positioning
Reduction of MR

Pre-procedural TEE
Moderate-Severe MR

Post-procedural TEE
Mild MR
PASCAL Repair System - Key advantages

**Optimised leaflet capture**
- Empowering delivery system with direct manoeuvring in three planes
- Independent leaflet capture

**Designed for effective MR reduction**
- Broad paddles maximise leaflet coaptation
- Central spacer fills the regurgitant orifice area

**Excellent safety profile**
- Spacer and contoured paddles design reduce stress on leaflets
- Implant elongation helps promote safe subvalvular manoeuvring
Single arm, multicenter, prospective study to evaluate the safety, performance, and clinical outcomes of the PASCAL Transcatheter Valve Repair System for patients with clinically significant mitral regurgitation.
### Key study criteria

#### Inclusion Criteria

- Age ≥18 years
- New York Heart Association (NYHA) functional Class ≥ II despite optimal therapy
- Candidacy for transcatheter mitral valve repair determined by Heart Team
- Clinically significant mitral regurgitation (moderate-to-severe or severe mitral regurgitation) confirmed by transesophageal echocardiography (TEE) and transthoracic echocardiography (TTE)
- The primary regurgitant jet is non-commissural. If a secondary jet exists, it must be considered clinically insignificant

#### Exclusion Criteria

- Mitral valve area (MVA) <4.0 cm² as measured by planimetry
- Left ventricular ejection fraction (LVEF) <20%
- Echocardiographic evidence of intracardiac mass, thrombus, or vegetation
- Physical evidence of right-sided congestive heart failure and echocardiographic evidence of severe right ventricular dysfunction
- Concurrent medical condition with a life expectancy of less than 12 months in the judgment of the investigator
## Study endpoints

<table>
<thead>
<tr>
<th>Primary Endpoints</th>
<th>Secondary Endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Safety</strong></td>
<td>30 days, 6 months and 1 year</td>
</tr>
<tr>
<td>• Composite of Major Adverse Events (MAEs) at 30 days: Cardiovascular mortality, stroke, myocardial infarction, new need for renal replacement therapy, severe bleeding and re-intervention for study device-related complications</td>
<td>• All-cause mortality</td>
</tr>
<tr>
<td>• Device success</td>
<td>• Composite of MAEs</td>
</tr>
<tr>
<td>• Procedural success</td>
<td>• Mitral regurgitation reduction</td>
</tr>
<tr>
<td>• Clinical success</td>
<td>• Change in NYHA and 6MWT</td>
</tr>
<tr>
<td></td>
<td>• Change in quality of life (KCCQ and EQ5D)</td>
</tr>
</tbody>
</table>

NYHA – New York Heart Association; 6MWT – Six Minute Walk Test; KCCQ – Kansas City Cardiomyopathy Questionnaire; EQ5D – EuroQoL Health Questionnaire
Participating sites

- Hygeia, GR
- Royal Prince Alfred, AU
- Prince Charles, AU
- San Raffaele, IT
- Atlantic Health System, NJ
- Carolinas Healthcare System, NC
- Sunnybrook, ONT
- Cedars-Sinai, CA
- University of Virginia, VA
- Northshore, IL
- St. Michael’s, ONT
- Sunnybrook, ONT
- St. Paul’s, BC
- Henry Ford, MI
- The Heart Hospital, TX
- St. Paul’s, BC
**Patient flow**

- **Intent to treat**
  - $N=62$
  - Death $n=1$
  - Withdrew from study $n=1$

- **30 day follow up**
  - $N=60$
  - Death $n=1$

- **6 month follow up**
  - $N=57$
  - Exited study $n=2$

CEC adjudicated; ¹procedure-related, not device-related; ²not procedure-related or device-related
## Study demographics

<table>
<thead>
<tr>
<th></th>
<th>N=62</th>
<th>% (n) or Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>76.5 ± 8.8</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>37.1% (23)</td>
<td></td>
</tr>
<tr>
<td>NYHA Functional Class III or IV</td>
<td>51.6% (32)</td>
<td></td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functional</td>
<td>55.7% (34)</td>
<td></td>
</tr>
<tr>
<td>Degenerative</td>
<td>36.1% (22)</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>8.2% (5)</td>
<td></td>
</tr>
<tr>
<td>MR Severity ≥3+</td>
<td>100.0% (62)</td>
<td></td>
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</tbody>
</table>
Procedural characteristics

<table>
<thead>
<tr>
<th></th>
<th>N=62</th>
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</thead>
<tbody>
<tr>
<td><strong>Successful Implant Rate</strong>*</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td>(59)</td>
</tr>
<tr>
<td>Mean # of Devices Implanted</td>
<td>1.5</td>
</tr>
<tr>
<td>Procedure Time (Skin to Skin), mins</td>
<td>140.9 ± 66.2</td>
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</table>

*Device is deployed as intended and the delivery system is successfully retrieved as intended at the time of the patient's exit from the cardiac catheterization laboratory*
### Favorable safety profile at 30 days

<table>
<thead>
<tr>
<th>CEC Adjudicated Events</th>
<th>N=62</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiovascular Mortality</strong></td>
<td>1.6% (1)</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td>0.0% (0)</td>
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<tr>
<td><strong>Myocardial Infarction</strong></td>
<td>0.0% (0)</td>
</tr>
<tr>
<td><strong>New Need for Renal Replacement Therapy</strong></td>
<td>0.0% (0)</td>
</tr>
<tr>
<td><strong>Severe Bleeding</strong>*</td>
<td>6.5% (4)</td>
</tr>
<tr>
<td><strong>Re-Intervention for Study Device-Related Complications</strong></td>
<td>1.6% (1)</td>
</tr>
<tr>
<td><strong>Composite MAE Rate</strong></td>
<td>6.5% (4)</td>
</tr>
</tbody>
</table>

Four patients experienced six events:
- (n=1) Procedure-related severe bleeding and cardiovascular mortality
- (n=1) Re-intervention for study device-related complications and severe bleeding
- (n=2) Procedure-related severe bleeding, at GI level

*Severe bleeding is major, extensive, life-threatening or fatal bleeding, as defined by MVARC*
MR reduction at 30 days and sustained at 6 months (core lab\textsuperscript{1})

98% of patients with MR ≤2+ and 81% of patients with MR ≤1+ at 6 months

Paired analysis

\textsuperscript{a}Wilcoxon Signed-Rank Test

\textsuperscript{1}Core Lab - Dr. Linda D. Gillam – Cardiovascular Core Lab at Morristown Medical Center, Morristown, NJ, USA
Clinically significant improvements in functional status and exercise capacity at 30 days and sustained at 6 months

Paired analysis

NYHA Functional Class

<table>
<thead>
<tr>
<th></th>
<th>30 Days</th>
<th>6 Months</th>
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<tbody>
<tr>
<td>IV</td>
<td>P&lt;0.0001&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td></td>
<td>P&lt;0.0001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td></td>
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6MWT

<table>
<thead>
<tr>
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<th>30 Days</th>
<th>6 Months</th>
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<tbody>
<tr>
<td>Δ&lt;36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Δ&lt;21</td>
<td></td>
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</table>

NYHA – New York Heart Association; 6MWT – 6 Minute Walk Test

<sup>a</sup>Wilcoxon Signed-Rank Test; <sup>b</sup>T-test
Clinically and statistically significant improvements in QoL at 30 days and sustained at 6 months

Paired analysis

**KCCQ**

<table>
<thead>
<tr>
<th></th>
<th>30 Days</th>
<th>6 Months</th>
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</thead>
<tbody>
<tr>
<td><strong>Δ</strong></td>
<td>17</td>
<td>17</td>
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</tbody>
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**P**<0.0001<sup>a</sup>

**EQ5D**

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<thead>
<tr>
<th></th>
<th>30 Days</th>
<th>6 Months</th>
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<tbody>
<tr>
<td><strong>Δ</strong></td>
<td>10</td>
<td>11</td>
</tr>
</tbody>
</table>

**P**<0.0001<sup>a</sup>

<sup>a</sup>T-test

KCCQ – Kansas City Cardiomyopathy Questionnaire; EQ5D – EuroQoL Health Questionnaire
Study conclusions

• PASCAL Transcatheter Valve Repair System was safe and performed as intended for patients with severe mitral regurgitation

• At 6 months, the reduction of MR was significant and sustained with 98% of patients with MR ≤2+ and 81% of patients with MR ≤1+

• Significant improvements in functional status, exercise capacity, and quality of life sustained at 6 months

• Continued follow-up and additional studies are warranted to validate these initial promising results
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