Edwards Cardioband
Mitral Valve Reconstruction System

Introduction and overview
Types of mitral regurgitation

Functional Mitral Regurgitation (FMR)

- LV dysfunction
dilated annulus
  - Non-ischemic or ischemic
dilated cardiomyopathy

- LA dysfunction
dilated annulus
  - Chronic atrial fibrillation,
hypertension.

Loss of leaflet coaptation due to:
- Annular enlargement
- Papillary muscle displacement
  causing leaflet tethering / tenting

Degenerative Mitral Regurgitation (DMR)

- Advanced Barlow’s Disease
- Fibroelastic deficiency

Leaflet prolapse due to:
- Leaflet deformities or lesions
- Ruptured / elongated chordae
- Papillary muscle rupture

Most patients with isolated FMR are conservatively managed today\(^1\)

\[
\begin{array}{cccccc}
\text{LVEF} & \text{Conservative management} & \text{Isolated MV surgery} \\
0\%-20\% & 88.6 & 11.4 \\
20\%-30\% & 94.1 & 5.9 \\
30\%-40\% & 91.6 & 8.4 \\
40\%-50\% & 88.2 & 11.8 \\
50\%-60\% & 81.6 & 18.4 \\
\end{array}
\]

\(N=1538\)  \(N=440\)  \(N=298\)  \(N=313\)  \(N=479\)

\(^1\) Duke Databank: 1,538 pts with echocardiographic 3+ to 4+ FMR and LVEF ≥20% between 2000 and 2010 not undergoing CABG

Courtesy of M. Mack MD, FACC, Baylor Scott & White Health
Medically managed patients with severe MR have poor outcomes†

- **20%**
  - One year mortality rate

- **50%**
  - Five year mortality rate

- **Very high**
  - Rate of heart failure hospitalization

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**Graph:**
- **20%**
  - Year 1
- **41%**
  - Year 2
- **50%**
  - Year 3
- **58%**
  - Year 4
- **68%**
  - Year 5

- **Very high**
  - Proportion of surviving patients hospitalized for heart failure

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† Sachin S. Goel, JACC Volume 63, Issue 2, January 2014
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Cardioband mitral delivery system

Stand

Cardioband mitral system implant
Cardioband Mitral System procedure

1. Access via transseptal puncture & system insertion
2. Implant deployment
3. Implant size adjustment
Edwards Cardioband
Mitral Valve Reconstruction System

European CE mark trial
Cardioband Mitral System CE mark trial

- Single arm, multicenter, prospective study with intra-subject comparisons to evaluate the performance and safety of the Cardioband mitral system for repair of functional mitral regurgitation

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Study admission criteria

**Inclusion**
- Age >18 years
- Symptomatic patients (NYHA Class II-IV) despite optimal medical therapy, including CRT if indicated
- LVEF ≥25%, LVEDD ≤70mm
- Moderate to severe functional MR
- Subject is high risk to undergo MV surgery (as assessed by a cardiac surgeon and a cardiologist, at the site and according to ESC/EACTS guidelines on the management of valvular heart disease)

**Exclusion**
- Untreated clinically significant CAD requiring revascularization
- Pulmonary hypertension >70mmHg at rest
- Renal insufficiency requiring dialysis
- Right-sided congestive heart failure with echocardiographic evidence of severe right ventricular dysfunction and severe tricuspid regurgitation
- Heavily calcified annulus or leaflets
- Any recent cardiovascular intervention
- CVA or TIA within 6 months or severe carotid stenosis (>70% by ultrasound)
- Mitral valve anatomy which may preclude proper device treatment

### Endpoints

#### Safety
- **Overall rate of Major Serious Adverse Events (SAEs) and Serious Adverse Device Effects (SADE)** up to 24 months
- **Major SAEs:** Death, myocardial infarction, cardiac tamponade, device related cardiac surgery, stroke

#### Performance
- **Technical success** rate of the implantation of the Edwards Cardioband system
- **Technical feasibility** of Edwards Cardioband system adjustment
- **Edwards Cardioband system ability to reduce mitral valve regurgitation (MR)** intra-procedure, at hospital discharge and at 30 days

#### Primary Endpoints
- **MR severity at 6, 12 and 24 months**
- **Change in 6MWT** in 6, 12 and 24 months
- **Change in quality of life (MLHFO)** at 6, 12 and 24 months

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1 Events defined according to VARC-2 guidelines
2 MLHFO – Minnesota Living with Heart Failure Questionnaire

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Participating sites

- St. Antonius Ziekenhuis, NL (n=1)
- Bichat Hospital (n=13)
- Zurich University Hospital (n=4)
- Presidio Ospedaliero Ferrarotto (n=1)
- San Raffaele Hospital (n=10)
- Asklepios, St. Georg (n=10)
- Medizinische Klinik Universitätsklinikum Bonn (n=16)
- Heart Center University of Köln (n=4)
- LMU Klinikum der Universität München, Campus Großhadern (n=1)
- Universitätsmedizin der Johannes Gutenberg Universität Mainz (n=1)
- Rambam Health Care Campus (n=1)

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Patient flow

Intent to treat (ITT)
N=62

Patient out of the device indication n=1

Full analysis set (FA)
N=61

No implantation n=1

Per protocol (PP)
N=60

Death n=7
Incomplete follow-up n=8
Secondary intervention n=6

12-month follow up
63% (39/62)\(^2\)

\(^1\) 2/7 patients died due to complications of elective open heart surgery
\(^2\) 39 patients completed echo follow-up at 12 months. 38 patients completed clinical follow-up at 12 months
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Study demographics: full analysis set N=61

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%) or Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>72 ± 7</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>44 (72%)</td>
</tr>
<tr>
<td>Female</td>
<td>17 (28%)</td>
</tr>
<tr>
<td>Euroscore II (%)</td>
<td>7.1</td>
</tr>
<tr>
<td>Baseline NYHA Class of III or IV</td>
<td>52 (85%)</td>
</tr>
<tr>
<td>Ischemic</td>
<td>36 (59%)</td>
</tr>
<tr>
<td>Non ischemic</td>
<td>25 (41%)</td>
</tr>
<tr>
<td>LVEDD (mm) Avg±SD</td>
<td>60 ± 6</td>
</tr>
<tr>
<td>EF (%) Avg±SD</td>
<td>33 ± 11</td>
</tr>
<tr>
<td>Prev CABG</td>
<td>19 (31%)</td>
</tr>
<tr>
<td>COPD</td>
<td>13 (21%)</td>
</tr>
<tr>
<td>Moderate to severe renal failure</td>
<td>46 (75%)</td>
</tr>
<tr>
<td>Severe pulmonary hypertension</td>
<td>15 (25%)</td>
</tr>
<tr>
<td>Afib</td>
<td>46 (75%)</td>
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</tbody>
</table>

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Adjudicated major safety events at 30 days

<table>
<thead>
<tr>
<th>30 Day Events¹</th>
<th>Patients experiencing event, n (%)</th>
<th>Full analysis set N=61</th>
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</thead>
<tbody>
<tr>
<td><strong>Death</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Hemorrhagic stroke</strong></td>
<td>1 (1.6%)</td>
<td></td>
</tr>
<tr>
<td><strong>Need for elective mitral operation</strong></td>
<td>1 (1.6%)</td>
<td></td>
</tr>
<tr>
<td><strong>Myocardial infarction</strong></td>
<td>1 (1.6%)</td>
<td></td>
</tr>
<tr>
<td><strong>Major bleeding complications</strong></td>
<td>2 (3.3%)</td>
<td></td>
</tr>
<tr>
<td><strong>Renal failure</strong></td>
<td>4 (6.6%)</td>
<td></td>
</tr>
<tr>
<td><strong>Respiratory failure</strong></td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Cardiac tamponade</strong></td>
<td>1 (1.6%)</td>
<td></td>
</tr>
</tbody>
</table>

¹ Events defined according to VARC Guidelines (European Heart Journal, 2012, 33:2403-2414).
One additional death case per ITT.

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MR reduction sustained at 12 months in paired analysis by core lab

1 Dr. Paul Grayburn – Baylor University
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28% average reduction in septolateral diameter by core lab\(^1\)

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\(^1\) Dr. Paul Grayburn – Baylor University

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Septolateral reduction maintained at 12 months in paired analysis

Septo Lateral (A-P) Dimension (mm)

Baseline Discharge 30 Days 6 Months 12 Months

p<0.01 N.S.
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Significant functional improvement at 12 months

6MWT

P<0.01  Δ = 58

MLHFQ Score

P<0.01  Δ = -21

NYHA Class

P<0.01

Meters Walked

308

372

200

300

375

400

Baseline  12 Months

n = 29

42

21

0

5

10

15

20

MLHFQ Score

Baseline  12 Months

n = 36

79%

NYHA I/II

% of population

Baseline  12 Months

n = 39

6MWT – Six-minute Walk Test; MLHFQ - Minnesota Living with Heart Failure Questionnaire; NYHA Class - New York Heart Association (NYHA) Functional Classification

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Summary of clinical study conclusions

- Transcatheter mitral repair using Edwards Cardioband mitral valve reconstruction system is safe and feasible
- Provides significant and consistent annular reduction
- Delivers a significant and consistent reduction in mitral regurgitation
- Provides functional improvement in most patients
- Further studies are warranted

For professional use. See instructions for use for full prescribing information, including indications, contraindications, warnings, precautions, and adverse events.

Devices placed on the European market meeting the essential requirements referred to in Article 3 of the Medical Device Directive 93/42/EEC bear the CE marking of conformity. Manufactured by Valtech Cardio Ltd.

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