Percutaneous Mitral Valve Therapies

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Within the past 12 months, I have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Physician Name</th>
<th>Company/Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeffrey J. Popma, MD</td>
<td>Research Grants: Cordis, Boston Scientific, Medtronic, Abbott-Guidant, eV3, LabCoat</td>
</tr>
<tr>
<td></td>
<td>Medical Advisory Board: Cordis, Boston Scientific, Abbot Vascular</td>
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</tbody>
</table>
Transcatheter Mitral Valve

Mitral Valve Pathology

Mitral Valve Therapies

   Edge-edge repair

   Chordal Shortening

   Coronary Sinus Annuloplasty

   Direct Annuloplasty

   MV Replacement
Device Landscape 2011
Percutaneous MV Repair

Edge-to-edge
- Evalve MitraClip*

Chordal Shortening
- Cardiosolutions
- Mitra-Spacer*
- NeoChord
- Valtech VChordal

Coronary sinus Annuloplasty
- Cardiac Dimensions Carillon*
- Edwards Monarch*
- Viacor PTMA*
- Cerclage annuloplasty

MV replacement
- EndoValve
- CardiAQ
- Valtech Cardiovalve
- ValveXchange

Direct Annuloplasty
- Mitralign Bident*
- GDS Accucincher*
- ReCor (US)*
- Quantum Cor (RF)
- Valtech Cardioband
- Micardia enCor

*In patients
First Question: Degenerative or Functional?

Degenerative mitral valve regurgitation: best practice revolution

- FED
- FED+
- Forme Fruste
- Barlow’s

Leaflet Tissue
Second Question: What is the Surgical Risk (STS PROM)?

FED

FED+

Forme Fruste

Barlow’s

Increasing Repair Difficulty

Percutaneous Methods for Mitral Valve Repair → Functional MR

- **Leaflet Coaptation**
  - Edge-to-Edge Repair
  - Alfieri Stitch

- **Annular Reshaping**
  - Cinching
  - Annuloplasty
Percutaneous Mitral Valve Repair

MitraClip® System
The MitraClip: Global Experience
(through 4/20/2011)

~3,135 patients
at ~80 hospitals in EU
and 40 clinical trial sites in
the U.S. have been treated
with the MitraClip device

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
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<tbody>
<tr>
<td>EVEREST I</td>
<td>55</td>
</tr>
<tr>
<td>EVEREST II Roll-in</td>
<td>60</td>
</tr>
<tr>
<td>EVEREST II HRR</td>
<td>78</td>
</tr>
<tr>
<td>EVEREST II Randomized</td>
<td>184</td>
</tr>
<tr>
<td>REALISM (Continued Access)</td>
<td>571</td>
</tr>
<tr>
<td>Commercial use (EU)</td>
<td>2187</td>
</tr>
</tbody>
</table>

Source: Abbott Vascular
EVEREST II Randomized Clinical Trial

279 Patients enrolled at 37 sites
Significant MR (3+-4+)
73% DMR, 27% FMR
Specific anatomical criteria
Randomized 2:1

Device Group
MitraClip System
N=184

Control Group
Surgical Repair or Replacement
N=95

Echocardiography Core Lab and Clinical Follow-Up
Baseline, 30 days, 6 months, 1 year, 18 months, and annually through 5 years

Feldman T et al. NEJM 2011;364:1395-406
EVEREST II RCT: Patient Flow

Randomized Cohort
n=279

Device Group
n=184
- Treated
n=178

Acute Procedural Success
Achieved
n=137 (77.0%)

Acute Procedural Success
Not Achieved
n=41 (23.0%)*
*20 of 41 no implant

28 had MV surgery
9 had MV surgery
37/178 total (20.8%)

30 days
n=136
99% Clinical Follow-up

12 months
n=134
98.5% Clinical Follow-up
98% Echo Follow-up

Surgical Group
n=95
- Treated
n=80
(86% MV repair)

Per Protocol

Feldman T et al. NEJM 2011;364:1395-406
### EVEREST II RCT: Primary Safety Endpoint

**Per Protocol Cohort**

<table>
<thead>
<tr>
<th>30 Day MAE, non-hierarchical</th>
<th># Patients experiencing event</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Device Group (n=136)</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
</tr>
<tr>
<td>Major Stroke</td>
<td>0</td>
</tr>
<tr>
<td>Re-operation of Mitral Valve</td>
<td>0</td>
</tr>
<tr>
<td>Urgent / Emergent CV Surgery</td>
<td>0</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>0</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>0</td>
</tr>
<tr>
<td>Deep Wound Infection</td>
<td>0</td>
</tr>
<tr>
<td>Ventilation &gt;48 hrs</td>
<td>0</td>
</tr>
<tr>
<td>New Onset Permanent Atrial Fib</td>
<td>0</td>
</tr>
<tr>
<td>Septicemia</td>
<td>0</td>
</tr>
<tr>
<td>GI Complication Requiring Surgery</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>All Transfusions ≥2 units*</td>
<td>12 (8.8%)</td>
</tr>
<tr>
<td><strong>TOTAL % of Patients with MAE</strong></td>
<td><strong>9.6%</strong></td>
</tr>
</tbody>
</table>

*p<0.0001*

*p<0.0001 if include Major Bleeding only* (95% CI 34.4%, 60.4%)

Feldman T et al. NEJM 2011;364:1395-406
EVEREST II: Mitral Regurgitation Grade
Baseline, 1 and 2 Years (matched)
Intention to Treat

* Within group difference (p<0.05); † Between group difference at 1 year (p<0.05); ‡ Between group difference at 2 year (p<0.05)

Ted Feldman, ACC 2011 Late Breaking Trial
**EVEREST II: LV Volumes**

Baseline, 1 and 2 Years (matched)

**Intention to Treat**

* * Within group difference (p<0.05)
† † Between group difference at 1 year (p<0.05)
‡ ‡ Between group difference at 2 year (p<0.05)

**LV End Diastolic Volume**

<table>
<thead>
<tr>
<th></th>
<th>BL</th>
<th>1 Yr</th>
<th>2 Yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percutaneous</td>
<td>157</td>
<td>133</td>
<td>124</td>
</tr>
<tr>
<td>Surgery</td>
<td>158</td>
<td>119</td>
<td>110</td>
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</table>

**LV End Systolic Volume**

<table>
<thead>
<tr>
<th></th>
<th>BL</th>
<th>1 Yr</th>
<th>2 Yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percutaneous</td>
<td>62</td>
<td>57</td>
<td>55</td>
</tr>
<tr>
<td>Surgery</td>
<td>60</td>
<td>55</td>
<td>50</td>
</tr>
</tbody>
</table>

Ted Feldman, ACC 2011 Late Breaking Trial
EVEREST II: Kaplan-Meier Freedom from Death Intentation to Treat

Surgery = 95.0%
Percutaneous = 94.9%
p=0.78

Surgery = 91.1%
Percutaneous = 89.8%
p=0.95

At Risk: 0 Days 6m 1yr 1.5yr 2yr 3yr
Percutaneous 184 166 163 153 133 52
Surgery 95 78 74 71 63 25

Ted Feldman, ACC 2011 Late Breaking Trial
EVEREST II: Landmark Analysis of Kaplan-Meier Freedom from MV Surgery (Percutaneous)/Re-operation (Surgery) Intention to Treat

![Graph showing Kaplan-Meier analysis of freedom from surgery or reoperation comparing surgery and percutaneous procedures.](image)

- **Surgery**: 98.7% Freedom from Surgery (Device) or Reoperation (Surgery) vs. 95.6% for Percutaneous, with a p-value of 0.52.
- **Percutaneous**: 96.3% Freedom from Surgery (Device) or Reoperation (Surgery) vs. 97.3% for Surgery, with a p-value of 0.32.

### At Risk

<table>
<thead>
<tr>
<th>Time</th>
<th>Percutaneous</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Days</td>
<td>184</td>
<td>95</td>
</tr>
<tr>
<td>6m</td>
<td>138</td>
<td>77</td>
</tr>
<tr>
<td>1yr</td>
<td>131</td>
<td>72</td>
</tr>
<tr>
<td>1.5yr</td>
<td>124</td>
<td>69</td>
</tr>
<tr>
<td>2yr</td>
<td>109</td>
<td>61</td>
</tr>
<tr>
<td>3yr</td>
<td>44</td>
<td>24</td>
</tr>
</tbody>
</table>

Ted Feldman, ACC 2011 Late Breaking Trial
EVEREST II: NYHA Functional Class
At Baseline, 1 and 2 Years (matched)
Intention to Treat

* Within group difference (p<0.05)
† Between group difference at 1 year (p<0.05)
‡ Between group difference at 2 year (p<0.05)
EVEREST II RCT MitraClip Arm
MR Reduction by Etiology

DMR Cohort
- Baseline: 3+/4+ 34.5%
- 12 Months: 1+ 11.5%
- 2+ 36.8%
- 3+/4+ 17.2%

FMR Cohort
- Baseline: 3+/4+ 40.6%
- 12 Months: 1+ 12.5%
- 2+ 25.0%
- 3+/4+ 21.9%

n=135 (DMR Cohort)
=87 (12 Months DMR Cohort)
n=49 (FMR Cohort)
=32 (12 Months FMR Cohort)

Ted Feldman, TCT 2010
EVEREST II RCT MitraClip Arm
Left Ventricular Function by Etiology
LV End Diastolic and End Systolic Volumes

DMR Cohort
n=88, matched data

FMR Cohort
n=30, matched data

LVEDV
LVESV

p<0.0001
p=0.002
p=0.0002
p=0.04

Baseline
12 Months

Ted Feldman, TCT 2010
EVEREST II RCT MitraClip Arm
NYHA Functional Class by Etiology

DMR Cohort
n=93, matched data

FMR Cohort
n=31, matched data

<table>
<thead>
<tr>
<th>NYHA Functional Class</th>
<th>Baseline</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>I/II</td>
<td>97.8%</td>
<td>96.7%</td>
</tr>
<tr>
<td>III</td>
<td>22.2%</td>
<td>33.3%</td>
</tr>
<tr>
<td>IV</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
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</table>

Differences are significant at p<0.0001
EVEREST II High Surgical Risk Cohort

Enrollment

EVEREST II High Surgical Risk Cohort
N = 372

EVEREST II High Surgical Risk Trial*
N = 78 Enrolled

REALISM High Surgical Risk Trial^*
N = 294 Enrolled

1 Year
N = 78

1 Year
N = 133

EVEREST II High Surgical Risk Cohort
With 1 Year Follow-Up
N = 211

* EVEREST HR defined by predicted surgical mortality ≥12% using STS risk calculator or surgeon estimate from co-morbidities

^ ACCESS EU high risk defined by EuroSCORE ≥20%

Ted Feldman. EuroPCR 2011
EVEREST II High Surgical Risk Cohort

Mitral Regurgitation Grade