Worldwide Results and Review of MitraClip®: What Is the Future?
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Disclosure Information

The following relationships exist:

Consultant: Medtronic, Abbott Vascular

Off label use of products and investigational devices will be discussed in this presentation
Introduction

- The MV apparatus is anatomically complex

**Primary/Degenerative MV regurgitation (DMR)**
Structural changes to the mitral valve apparatus
(i.e., MV prolapse, chordal rupture, or myxomatous MV disease)

**Secondary / Functional MV regurgitation (FMR)**
Functional changes
(i.e., dilation of the left atrium, MV annulus, or left ventricle)

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Terminology

- **Transcatheter Mitral Valve Repair (TMVR)**
  - MitraClip®
  - Transcatheter repair technologies
    - valve-in-valve therapy for failing MV bioprostheses,
    - failing mitral valve rings
    - valve-in-MAC

- **Specific abbreviation:**
  - TMVR: transcatheter mitral valve repair
  - TMVr: transcatheter mitral valve replacement
  - TMVI: transcatheter mitral valve implantation

MitraClip® Device

- The clip is a polyester-covered cobalt chromium device
- 2 arms that are opened and closed by control mechanisms
- Has an arm span of approximately 2 cm when opened
- The width of the clip is 4 mm

History of MitraClip® and Future

Suture-Based Designs

- Percutaneous Edge-to-Edge prototype
- First MitraClip Implantation (2003)
- Minor Changes for Safety (2011)
- MitraClip XT (2017)

Clip-Based Designs

- Evalve Company (1999)
- MitraClip CE Mark Approval (2008)
- MitraClip NT (2016)
Rationale for use MitraClip®

- Coaptation of Leaflets
  - Reduces MR

- Creates tissue bridge
  - Limits dilatation of annulus
  - Septal-lateral (A-P) dimension
  - Supports durability of repair

- Restrains LV wall
  - Limits LV dilatation
Global MitraClip Experience

Over 42,000 Patients Treated Globally¹

1. Includes clinical and commercial procedures as of 30/11/2016. Source: Data on file at Abbott Vascular
Treatment of MR with MitraClip® showed superior safety compared with surgery, but less effective reduction in MR at 1 year

OBJECTIVES: To evaluate the final 5-year clinical outcomes and durability of percutaneous MV repair with the MitraClip® device compared with conventional MV surgery

METHODS: Patients with grade 3 or 4 MR were randomly assigned to MitraClip® or conventional MV surgery in a 2:1 ratio (178:80). Patients prospectively consented to 5 years of follow-up
### TABLE 1 Baseline Characteristics: All-Treated Cohort

<table>
<thead>
<tr>
<th></th>
<th>Percutaneous Repair</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>67.0 ± 12.7 (178)</td>
<td>64.7 ± 12.6 (80)</td>
</tr>
<tr>
<td>Female</td>
<td>36.5 (65/178)</td>
<td>33.8 (27/80)</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>59.9 ± 10.1 (176)</td>
<td>61.3 ± 10.7 (80)</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>9.6 (17/178)</td>
<td>17.5 (14/80)</td>
</tr>
<tr>
<td>II</td>
<td>40.4 (72/178)</td>
<td>32.5 (26/80)</td>
</tr>
<tr>
<td>III</td>
<td>43.8 (78/178)</td>
<td>45.0 (36/80)</td>
</tr>
<tr>
<td>IV</td>
<td>6.2 (11/178)</td>
<td>5.0 (4/80)</td>
</tr>
<tr>
<td>MR etiology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functional</td>
<td>27.0 (48/178)</td>
<td>22.5 (18/80)</td>
</tr>
<tr>
<td>Degenerative</td>
<td>73.0 (130/178)</td>
<td>77.5 (62/80)</td>
</tr>
<tr>
<td>Degenerative with anterior/bileaflet flail/prolapse</td>
<td>32.6 (58/178)</td>
<td>27.5 (22/80)</td>
</tr>
<tr>
<td>Degenerative with posterior flail/prolapse</td>
<td>37.6 (67/178)</td>
<td>47.5 (38/80)</td>
</tr>
<tr>
<td>Degenerative with neither flail nor prolapse</td>
<td>2.8 (5/178)</td>
<td>2.5 (2/80)</td>
</tr>
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All-Treated Cohort: Efficacy Endpoint and Components at 5 years

<table>
<thead>
<tr>
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<th>5 Years</th>
<th>5 Years if Event-Free at 1 Year</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Percutaneous Repair (n = 154)</td>
<td>Surgery (n = 56)</td>
</tr>
<tr>
<td>Freedom from death, MV surgery, or reoperation, and 3+ or 4+ MR</td>
<td>44.2 (68)</td>
<td>64.3 (36)</td>
</tr>
<tr>
<td>Death</td>
<td>20.8 (32)</td>
<td>26.8 (15)</td>
</tr>
<tr>
<td>MV surgery or reoperation</td>
<td>27.9 (43)</td>
<td>8.9 (5)</td>
</tr>
<tr>
<td>3+ or 4+ MR</td>
<td>12.3 (19)</td>
<td>1.8 (1)</td>
</tr>
</tbody>
</table>

Values are % (n). *Includes patients that completed the 5-year visit and had MR grade available or died or had MV surgery before withdrawal from the study. MR = mitral regurgitation; MV = mitral valve.

Prospective registries of patients who received the MitraClip®
Patients with MR in the United States

OBJECTIVES:
To report 12-month outcomes in high-risk patients

METHODS:
Grades 3 to 4 MR
Surgical mortality risk of >12% - STS Risk
Mitral Regurgitation Grade

SMVR remains the gold standard for severe DMR.
Results with TMVR in prohibitive-risk DMR patients have not been previously reported.

OBJECTIVES:
To evaluate treatment of MR in patients with severe DMR at prohibitive surgical risk undergoing TMVR.
# Surgical & Interventional - Therapy for MR

<table>
<thead>
<tr>
<th></th>
<th>Degenerative</th>
<th>Functional</th>
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</thead>
<tbody>
<tr>
<td><strong>Low Surgical Risk</strong></td>
<td>Surgical Mitral Repair</td>
<td></td>
</tr>
<tr>
<td><strong>High Surgical Risk</strong></td>
<td>Commercial MitraClip</td>
<td>International Practice-3 CE Devices</td>
</tr>
</tbody>
</table>
To report short and mid-term outcomes
ACCESS-EU study, a European prospective, multicenter, nonrandomized post-approval study of MitraClip® therapy.
A total of 567 patients
14 European sites
The first large database reporting outcomes of the MitraClip® in a high-risk population of patients with prevalence of FMR.
Freedom from Mortality (%) – MitraClip® in FMR

![Graph showing freedom from mortality over days post index procedure. The x-axis represents days post index procedure ranging from 0 to 440 days. The y-axis represents freedom from mortality ranging from 0.0 to 1.0. Data points are shown for baseline, 30 days, 6 months, and 12 months, with the number of patients at risk indicated: 567 at baseline, 534 at 30 days, 475 at 6 months, and 415 at 12 months.]
Severity of MR at Baseline, Discharge, 6 and 12 Months

Change in 6-Min Walk Distance From Baseline, to 6 and 12 Months
EVEREST II High Surgical Risk FMR Patients

Left Ventricular Volumes
N = 96 Matched Cases, Core-Lab Assessed

- LVEDV: Baseline 170 mL, 1 Year 147 mL (P<0.0001)
- LVESV: Baseline 96 mL, 1 Year 85 mL (P<0.0001)

Hospitalizations for CHF
N = 110 Matched Cases

- Annual Rate of CHF Hospitalizations Per Year:
  - 1 Year Prior to MitraClip: 0.65
  - 1 Year Post MitraClip: 0.29 (P<0.001)

Freedom from Death

Event-free survival:
- 95.3% at 30 Days
- 88.5% at 6 Months
- 77.5% at 12 Months

N at Risk Table
- 0 Day: FMR N = 149
- 30 Days: FMR N = 141
- 6 Months: FMR N = 129
- 1 Year: FMR N = 112

Argenziano M. TCT 2011.
Meta-Analysis of the Usefulness of Miraclip in Patients With Functional Mitral Regurgitation

Fabrizio D’ascenzo, MDa, Claudio Moretti, MDa, Walter Grosso Marra, MDa, Antonio Montefusco, MDa, Pierluigi Omede, MDa, Salma Taha, MDa,b,*, Davide Castagno, MDa, Oliver Gaemperli, MDb, Maurizio Taramasso, MDc, Simone Frea, MDa, Stefano Pidello, MDe, Volker Rudolph, MDF, Olaf Franzen, MDg, Daniel Braun, MDh, Cristina Giannini, MDi, Huseyin Ince, MDj, Leor Perl, MDk, Giuseppe Zoccai, MDl, Sebastiano Marra, MADa, Maurizio D’Amico, MADa, Francesco Maisano, MADm, Mauro Rinaldi, MADa, and Fiorenzo Gaita, MADa

- Meta-regression analysis
- 875 patients were included
- 9 studies
- 1.48 clips (1.3 to 1.7) for patients were implanted
- Median follow-up of 9 months (6 to 12)
Change of Functional and Echo data at FU

- Improvement in 6MWT (meters): +100.00
- Improvement in LV EF (%): -4.00
- Reduction in end diastolic volume (cc): -25.0
- Reduction in end systolic volume (cc): -22.0
- Reduction in sPAP (mmHg): -12.00
- Reduction in left atrial volume (cc): -40.00

Am J Cardiol 2015;116:325e331
COAPT Trial: Design

~610 patients enrolled at up to 100 sites
Symptomatic HF treated with maximally tolerated guideline directed medical therapy
  Significant FMR (≥3+ by echo core lab)
  Not appropriate for MV surgery as determined by site’s local heart team
  Valve anatomy eligible for MitraClip treatment

Randomize 1:1

MitraClip
N~305

Control group
Standard of care
N~305

Clinical and TTE follow-up: Baseline, treatment, 1-week (phone),
  1, 6, 12, 18, 24, 36, 48, 60 months

Primary efficacy endpoint: Hospitalization for heart failure within 2 years
Primary safety endpoint: Device-related complications at 1 year

Principal Investigators: Gregg Stone, Michael Mack
Heart Failure Co-Principal Investigators: William Abraham, JoAnn Lindenfeld

Sponsor: Abbott Vascular
COAPT: Enrollment

Between December 2012 and June 10\textsuperscript{th}, 2017, 600 patients have been randomized at 84 active sites

\textasciitilde 0.15 pts/site/month

COAPT results in 4\textsuperscript{th} quarter 2018
2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease
A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

7.3. Chronic Primary MR

7.3.3. Intervention: Recommendations

**Recommendations for Chronic Primary MR Intervention**

| IIb | B | Transcatheter mitral valve repair may be considered for severely symptomatic patients (NYHA class III to IV) with chronic severe primary MR (stage D) who have favorable anatomy for the repair procedure and a reasonable life expectancy but who have a prohibitive surgical risk because of severe comorbidities and remain severely symptomatic despite optimal GDMT for heart failure (HF).  
124 | 2014 recommendation remains current. |

### 6.1 Primary mitral regurgitation

Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary mitral regurgitation who fulfill the echocardiographic criteria of eligibility and are judged inoperable or at high surgical risk by the Heart Team, avoiding futility.

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### 6.2 Secondary mitral regurgitation

In patients with severe secondary mitral regurgitation and LVEF <30% who remain symptomatic despite optimal medical management (including CRT if indicated) and who have no option for revascularization, the Heart Team may consider a percutaneous edge-to-edge procedure or valve surgery after careful evaluation for a ventricular assist device or heart transplant according to individual patient characteristics.

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Transcatheter mitral valve treatment should be discussed by the **Heart Team** in symptomatic patients who are at high surgical risk or are inoperable.

**More prospective**, randomized controlled trials are needed to determine patients, potential adverse events, device durability, and long-term follow-up.

**MitraClip®** should be used only in **centers** with **high-quality** surgical and **interventional experience**, and training.
MitraClip® - Conclusion

• For Selected patients:
  Reduced MR severity to 2+ or less in 86%
  NYHA functional class
  6-minute walk test improved
  Significant reduction in left ventricular volumes
  Significant reduction is systolic pulmonary pressure
  Atrial fibrillation reduced
  Quality-of-life measures improved
  Decrease in the annual hospitalization rate for HF
  Kaplan–Meier survival: 77.2%
Transcatheter Mitral Valve Repair (TMVR)- Technologies

<table>
<thead>
<tr>
<th>Company</th>
<th>Abbott</th>
<th>NeoChord</th>
<th>Cardiac Dimensions</th>
<th>Valtech Cardio</th>
<th>Mitralign</th>
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<tbody>
<tr>
<td>Name</td>
<td>MitraClip</td>
<td>DS1000</td>
<td>Carillon*</td>
<td>Cardioband</td>
<td>Bident</td>
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<tr>
<td>Description</td>
<td>Edge-to-edge</td>
<td>Implantation</td>
<td>Coronary sinus</td>
<td>Transcatheter</td>
<td>Plication</td>
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<tr>
<td></td>
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<td></td>
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<td>access</td>
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<td>annuloplasty</td>
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<td>Strengths</td>
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<td>and FMR)</td>
<td>background</td>
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<td>other direct</td>
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<td>Weaknesses</td>
<td>Lack of</td>
<td>TA access</td>
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<td>imaging</td>
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<td>MR etiology</td>
<td>DMR and FMR</td>
<td>DMR</td>
<td>FMR</td>
<td>FMR</td>
<td>FMR</td>
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<td>Status</td>
<td>About 40,000</td>
<td>About 300</td>
<td>About 500</td>
<td>About 100</td>
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<tr>
<td></td>
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<th>Medtronic</th>
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<tr>
<td>Name</td>
<td>Tendyne</td>
<td>CardiAQ</td>
<td>Fortis</td>
<td>Twelve</td>
<td>Tiara</td>
</tr>
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<td></td>
<td><img src="image1" alt="Tendyne" /></td>
<td><img src="image2" alt="CardiAQ" /></td>
<td><img src="image3" alt="Fortis" /></td>
<td><img src="image4" alt="Twelve" /></td>
<td><img src="image5" alt="Tiara" /></td>
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<th></th>
<th>Patients treated</th>
<th>First implant</th>
<th>Functional aetiology</th>
<th>Successful deployment</th>
<th>30-day mortality</th>
<th>MR grade 0 at follow-up</th>
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<tbody>
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<td>Tendyne</td>
<td>31</td>
<td>October 2014</td>
<td>86%</td>
<td>21/23 (91%)</td>
<td>1/23 (4%)</td>
<td>19/19 (100%)</td>
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<tr>
<td>CardiAQ</td>
<td>12</td>
<td>June 2012</td>
<td>64%</td>
<td>9/11 (82%)</td>
<td>5/11 (45%)</td>
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<tr>
<td>Fortis</td>
<td>23</td>
<td>February 2014</td>
<td>100%</td>
<td>10/13 (77%)</td>
<td>5/13 (38%)</td>
<td>8/9 (89%)</td>
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<td>Twelve</td>
<td>15</td>
<td>September 2014</td>
<td>73%</td>
<td>14/15 (93%)</td>
<td>2/15 (13%)</td>
<td>13/14 (93%)</td>
</tr>
<tr>
<td>Tiara</td>
<td>15</td>
<td>January 2014</td>
<td>54%</td>
<td>9/11 (82%)</td>
<td>3/11 (27%)</td>
<td>na</td>
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