Percutaneous Treatment of Mitral Valve Regurgitation

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Disclosures

I and the HYGEIA Hospital «Heart Team» have received research and travel grants from: Medtronic, St Jude, Europe, ABBOTT Vascular, Europe

HYGEIA Hospital Heart Team

Cardiologists: A Halapas, M Chrissoheris, K Spargias
CT Surgeons: N Boumboulis, S Skardoutsos, A Tsolakis, S Pattakos
Anesthesiologist: I Nikolaou
Vascular Surgeons: I Bellos, S Kaliafas
Radiologists: C Mourmouris, F Laspas
Mitral valve Regurgitation
Epidemiology

Over 4 million Europeans suffer from significant MR
>250,000 new patients are diagnosed with significant MR annually
Many do not undergo surgery, leading to worsening conditions and heart failure

97% MR  3% MS
47% AR , 53% AS

MR Severity is Associated with Cardiac Events Even in Asymptomatic DMR Patients

Kaplan-Meier estimates of mean rates of cardiac events among patients with asymptomatic MR under medical management (values in parentheses are survival rates at 5 years)

Higher Effective Regurgitant Orifice (ERO) is predictive of greater mortality after diagnosis.

Severity of MR in Heart Failure Patients is Independently Predictive of Survival Probability

Survival of Heart Failure Patients with MR by Degree of MR adjusted for demographics and clinical variables at baseline

Percutaneous MV devices that have gone by the wayside

Current percutaneous technologies for MV repair have been developed on the basis of some of the same principles as the standard open approaches.

**Leaflet repair/ Chordal implantation**
- Mitraclip → FMR and DMR
- Neochord → DMR

**LV remodeling**
- iCoapsys technology → FMR

**Annuloplasty /Annulus Repair**
- Indirect
  - Carillon Contour System → FMR
- Direct → QuantumCor device

**MV Replacement**
- Sapien XT
  - Valve in valve
  - Valve in ring
The only transacatheter treatment of MR repair in clinical use today: MitraClip

More than 10,000 patients treated
The early concept development of TAVR paralleled that of percutaneous MV approaches.

Despite a similar timeline for the early work for both aortic and mitral technologies, the rapid pace of development of TAVR has clearly overtaken the development of percutaneous MVR.

The relative complexity of both the MV apparatus and the spectrum of pathology producing MR is responsible for this more complicated and slower development.

Primary, Degenerative (DMR) or Organic MR

Usually refers to an anatomic defect of one or more structures comprising the mitral valve apparatus, the annulus, the leaflets, the chordae tendineae, and the papillary muscles.

Spectrum of degenerative mitral disease

Secondary or Functional MR (FMR)

In FMR valve leaflets and chordae are structurally normal.
MR is secondary due to LV enlargement and remodelling.

IHD

DCM
The Surgical Data
Degenerative/Organic MR vs Functional MR

Degenerative/Organic MR
- Valve surgery in patients with DMR well defined offering low operative mortality (1.4-3.8%) and good long-term outcomes

Functional MR
- Very little data exists on the success and long-term durability in the surgical treatment (mainly restrictive annuloplasty) of this patient type
- Surgery is often avoided due to high operative risk and data suggesting no mortality benefit
- In addition, operative mortality is notable increased (6-10%)
The Surgical Data
Degenerative/Organic MR vs. Functional MR

Degenerative/Organic MR
- Valve surgery in patients with DMR well defined offering low operative mortality (1.4-3.8%) and good long-term outcomes

Functional MR
- High hospital mortality up to 18% in 30 days
- Long hospital stay (median >10 days)
- High recurrence rate (up to 30%)
- Unproven survival benefit

Surgery vs mitraclip volume (patients/month)
San Raffaele hospital (2000-2011)
Mitral Regurgitation
A Largely Untreated Patient Population

Medical therapies to alter the natural history of VHD are extremely limited.
Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary or most importantly secondary MR despite optimal medical therapy who fulfill the echo criteria of eligibility are judged INOPERABLE or at HIGH SURGICAL RISK by a ‘heart team’ have a life expectancy greater than 1 year

recommendation class IIb, level of evidence C
Indication for MitraClip
ESC HF Guidelines 2012

**Table 13** Indications for mitral valve surgery in chronic secondary mitral regurgitation

<table>
<thead>
<tr>
<th>Indication</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery is indicated in patients with severe MR undergoing CABG, and LVEF &gt;30%.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Surgery should be considered in patients with moderate MR undergoing CABG.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Surgery should be considered in symptomatic patients with severe MR, LVEF &lt;30%, option for revascularization, and evidence of viability.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Surgery may be considered in patients with severe MR, LVEF &gt;30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have low comorbidity, when revascularization is not indicated.</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

Surgery and MitraClip share the same recommendation class and level of evidence.

The percutaneous mitral clip procedure may be considered in patients with symptomatic severe secondary MR despite optimal medical therapy (including CRT if indicated), who fulfil the echo criteria of eligibility, are judged inoperable or at high surgical risk by a team of cardiologists and cardiac surgeons, and who have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).
Mitral-valve (MV) repair with the use of a surgical approach to create a double-orifice valve was first performed by Alfieri in 1991.

Durable results in surgically-treated patients without annuloplasty have been described in selected patients for as long as 12 years after surgical repair.

Mitra-Clip System
Mitra-Clip device

- 8mm length, 4mm wide made of cobalt chromium with 2 arms
- On the inner portion of the clip are 2 “grippers” adjacent to each arm to secure the leaflets as they are “captured
- Clip arms and grippers are covered with polyester to promote healing
- MRI Safe to 3 Tesla
- Real-time positioning during procedure
- Surgically removable when required
## Worldwide Experience

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>N*</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVEREST I (Feasibility)</td>
<td>Feasibility patients</td>
<td>55</td>
</tr>
<tr>
<td>EVEREST II (Pivotal)</td>
<td>Pre-randomized patients</td>
<td>60</td>
</tr>
<tr>
<td>EVEREST II (Pivotal)</td>
<td>Non-randomized patients (High Risk Study)</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>Randomized patients (2:1 Clip to Surgery)</td>
<td>279 (184 Clip, 95 Surgery)</td>
</tr>
<tr>
<td>REALISM (Continued Access)</td>
<td>Non-randomized patients</td>
<td>859</td>
</tr>
<tr>
<td>Compassionate/Emergency Use</td>
<td>Non-randomized patients</td>
<td>66</td>
</tr>
<tr>
<td>ACCESS Europe Phase I</td>
<td>Non-randomized patients</td>
<td>567</td>
</tr>
<tr>
<td>ACCESS Europe Phase II</td>
<td>Non-randomized patients</td>
<td>286</td>
</tr>
<tr>
<td>Commercial Use</td>
<td>Commercial patients</td>
<td>7,864</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>10,019</strong></td>
</tr>
</tbody>
</table>
MitralClip Therapy - Current Global Adoption

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treating Centers</td>
<td>278</td>
</tr>
<tr>
<td>Patients (clinical and commercial)</td>
<td>10,019</td>
</tr>
<tr>
<td>Patients (commercial)</td>
<td>8,717</td>
</tr>
<tr>
<td>Implant Rate (^2)</td>
<td>96%</td>
</tr>
<tr>
<td>Acute MR reduction</td>
<td>99%</td>
</tr>
</tbody>
</table>

- Treating Centers: 278
- Patients (clinical and commercial): 10,019
- Patients (commercial): 8,717
- Implant Rate \(^2\): 96%
- Acute MR reduction: 99%

- Mixed: 11%
- DMR: 22%
- FMR: 67%

1. First-time procedures only. Includes commercial patients, ACCESS I and ACCESS II patients.
2. Successful implants only.
Acute Hemodynamic effect of MitraClip

Mitraclip vs. Medical Rx in high risk patients

**EVEREST HRS. Freedom from death**

![Graph showing freedom from death comparison between Mitraclip and Medical Rx in high risk patients.](image)

- **High Risk Study**: 75.4%
- **Concurrent Comparator Group**: 55.3%

Statistical significance:
- **p = 0.047**

**Figure 3** Kaplan-Meier Curve for Survival: All Patients

CGG = concurrent comparator group; HRS = High Risk Study.

Whitlow et al. JACC 2012;59:130–9
Percutaneous mitral valve interventions in the real world: Early and 1-year results from ACCESS-EU

European post approval study of MitraClip (Abbott Vascular, Santa Clara, CA) in high-risk, elderly population with mostly functional MR (n = 567)

<table>
<thead>
<tr>
<th></th>
<th>30 Days</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>3.4%</td>
<td>17.3%</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.7%</td>
<td>1.1%</td>
</tr>
<tr>
<td>MI</td>
<td>0.7%</td>
<td>1.4%</td>
</tr>
</tbody>
</table>

Procedure improved MR severity vs. baseline, such that nearly 80% of patients were ≤ grade 2+ at 12 months (P < 0.0001).

MitraClip is effective and safe in patients at high surgical risk, elderly, and mainly affected by FMR

ACCESS EU - Real-World Clinical Experience

79% MR < 2+
at 1 year

71% NYHA class I or II
at 1 year

Maisano F, et al. Percutaneous Mitral Valve Interventions in the Real World: Early and One Year Results From the ACCESS-EU, a Prospective, Multicenter, Non-Randomized Post-Approval Study of the MitraClip® Therapy in Europe. J Am Coll Cardiol. 2013 Jun;
The EVEREST II High Surgical Risk cohort included 351 high risk patients pooled from the EVEREST II High Risk Study and the EVEREST II REALISM Continued Access Study.

Purpose is to describe the clinical benefits, including improvements in LV function and clinical symptoms, observed following treatment with the MitraClip in high surgical risk patients with DMR.

71% reduction in rate of CHF re-hospitalizations.
The EVEREST II Randomized Clinical Trial: Three Year Outcomes
The EVEREST II Randomized Clinical Trial: Three Year Outcomes

Mitral Regurgitation Severity

MitraClip (N=178)
84% MR ≤ 2+ at 3 Years

Surgery (N=80)
96% MR ≤ 2+ at 3 Years

Matched N =
BL 149
1Y 126
2Y 119
3Y

0+
1+
2+
3+
4+

p < 0.05 for all changes from Baseline within groups
The EVEREST II Randomized Clinical Trial:
Three Year Outcomes

**Left Ventricular End Diastolic Volume**

- **Mean LVEDV (mL)**
  - MitraClip (N=178)
  - ΔLVEDV = -30 mL at 3 Years
- **Mean LVEDV (mL)**
  - Surgery (N=80)
  - ΔLVEDV = -44 mL at 3 Years

**Left Ventricular End Systolic Volume**

- **Mean LVESV (mL)**
  - MitraClip (N=178)
  - ΔLVESV = -6 mL at 3 Years
- **Mean LVESV (mL)**
  - Surgery (N=80)
  - ΔLVESV = -11 mL at 3 Years

\[ p < 0.05 \text{ for all changes from Baseline within groups} \]
The EVEREST II Randomized Clinical Trial:
Three Year Outcomes

NYHA Functional Class

MitraClip (N=178)
97% NYHA I/II at 3 Years

Surgery (N=80)
98% NYHA I/II at 3 Years
## Four-Year Results of a RCT of Percutaneous vs. Surgery Repair

EVEREST II randomized 279 pts with grade 3 or 4+ MR to MitraClip (n = 184) or surgical repair/replacement (n = 95)

<table>
<thead>
<tr>
<th>4-Year Follow-up</th>
<th>MitraClip (n = 161)</th>
<th>Surgery (n = 73)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Efficacy Endpoint</td>
<td>39.8%</td>
<td>53.4%</td>
<td>0.070</td>
</tr>
<tr>
<td>Mitral Valve Surgery or Reoperation</td>
<td>24.8%</td>
<td>5.5%</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Primary efficacy endpoint = freedom from death, surgery for mitral valve dysfunction, and grade 3+ or 4+ MR.

About 20% of MitraClip patients underwent mitral surgery within the first six months after treatment, but then MitraClip-treated patients had similar event rates over the next few years.

About half the failures in the first six months were due to loss of the insertion of one leaflet into the clip, “partial leaflet attachment.”
Single Leaflet Device Attachment

EVEREST Trials

Loss of insertion of a single ongoing insertion of the opposing leaflet

N=710
July 2003 - Nov 2010
**MitraClip Clip Delivery System**
Approved by FDA on October 24, 2013

**Indication for Use:**
“The MitraClip Clip Delivery System is indicated for the percutaneous reduction of significant symptomatic mitral regurgitation (MR ≥ 3+) due to primary abnormality of the mitral apparatus [degenerative MR] in patients who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the mitral regurgitation.”

Data as of 10/24/2013. Source: Abbott Vascular
Response to Mitra-Clip

Hemodynamic response → durable MR reduction

Clinical response → Significant improvements in NYHA Class & HF hospitalization rate

Prognostic response → reverse remodelling & improved survival
Mitral Clip: Greek Experience

Heart Team
Hygeia Hospital
### Mitral Clip: Greek Experience

#### BASELINE DEMOGRAPHICS – CLINICAL CHARACTERISTICS

<table>
<thead>
<tr>
<th></th>
<th>HYGEIA N=20</th>
<th>ACCESS N=567</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AGE (±SD), Years</strong></td>
<td>71±12</td>
<td>74±10</td>
</tr>
<tr>
<td><strong>MALE (%)</strong></td>
<td>75</td>
<td>64</td>
</tr>
<tr>
<td><strong>HISTORY OF CHF (%)</strong></td>
<td>100</td>
<td></td>
</tr>
<tr>
<td><strong>CORONARY ARTERY DISEASE (%)</strong></td>
<td>70</td>
<td>63</td>
</tr>
<tr>
<td><strong>PREVIOUS CABG/MI (%)</strong></td>
<td>60/60</td>
<td>37</td>
</tr>
<tr>
<td><strong>ATRIAL FIBRILLATION (%)</strong></td>
<td>64</td>
<td>68</td>
</tr>
<tr>
<td><strong>COPD (%)</strong></td>
<td>36</td>
<td></td>
</tr>
<tr>
<td><strong>CHRONIC RENAL FAILURE (%)</strong></td>
<td>64</td>
<td>42</td>
</tr>
<tr>
<td><strong>DIABETES (%)</strong></td>
<td>55</td>
<td></td>
</tr>
<tr>
<td><strong>EUROSCORE (%) mean</strong></td>
<td>25.8</td>
<td>23</td>
</tr>
<tr>
<td><strong>STS MORTALITY AND MORBIDITY (%) mean</strong></td>
<td>28.6</td>
<td></td>
</tr>
</tbody>
</table>
## Mitral Clip: Greek Experience

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>Hygeia N=20</th>
<th>Access N=567</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degenerative MR (%)</td>
<td>40</td>
<td>23</td>
</tr>
<tr>
<td>Functional MR (%)</td>
<td>55</td>
<td>77</td>
</tr>
<tr>
<td>Ischemic, (%)</td>
<td>(83)</td>
<td>(42)</td>
</tr>
<tr>
<td>Non-Ischemic, (%)</td>
<td>(17)</td>
<td>(58)</td>
</tr>
<tr>
<td>NYHA Class III/IV (%)</td>
<td>95</td>
<td>85</td>
</tr>
<tr>
<td>MR Grade</td>
<td>3.8±0.4</td>
<td>≥3+ in 98%</td>
</tr>
<tr>
<td>ERO (mm²)</td>
<td>36.7±10.6</td>
<td>NA</td>
</tr>
<tr>
<td>Ejection Fraction (Mean, %)</td>
<td>44.2±17</td>
<td>NA</td>
</tr>
<tr>
<td>Ejection Fraction &lt;40 (%)</td>
<td>45</td>
<td>53</td>
</tr>
</tbody>
</table>
# Mitral Clip: Greek Experience

<table>
<thead>
<tr>
<th>PROCEDURAL CHARACTERISTICS</th>
<th>HYGEIA (N=20)</th>
<th>ACCESS (N=567)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SUCCESSFULL IMPANTATION (%)</strong></td>
<td>95</td>
<td>99.6</td>
</tr>
<tr>
<td><strong>NUMBER OF CLIPS DEPLOYED: 0 / 1/ &gt;1 (%)</strong></td>
<td>5 / 65 / 30</td>
<td>0.4 / 60 / 39.6</td>
</tr>
<tr>
<td><strong>FLUOROSCOPY TIME (Min, mean)</strong></td>
<td>0:43:30</td>
<td>NA</td>
</tr>
<tr>
<td><strong>ICU / TOTAL HOSPITAL STAY (Days, mean)</strong></td>
<td>1.0 / 4.4</td>
<td>2.5 / 7.7</td>
</tr>
<tr>
<td><strong>DISCHARGE HOME, (%)</strong></td>
<td>100</td>
<td>79.6</td>
</tr>
</tbody>
</table>
MitraClip Implant Rate and Number of Clips Implanted

95% Implant Rate
N=20

- 4 MitraClips (N=0)
- 3 MitraClips (N=1)
- 2 MitraClips (N=5)
- 1 MitraClip (N=13)
- 0 MitraClips (N=1)
<table>
<thead>
<tr>
<th>Peri-procedural &amp; 30-days Events</th>
<th>HYGEIA N=20</th>
<th>ACCESS EU (N=567)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (%)</td>
<td>0</td>
<td>3.4</td>
</tr>
<tr>
<td>Stroke (%)</td>
<td>0</td>
<td>0.7</td>
</tr>
<tr>
<td>Myocardial Infarction (%)</td>
<td>0</td>
<td>0.7</td>
</tr>
<tr>
<td>Renal Failure (%)</td>
<td>5</td>
<td>4.8</td>
</tr>
<tr>
<td>Respiratory Failure (%)</td>
<td>0</td>
<td>0.7</td>
</tr>
<tr>
<td>Need for Resuscitation (%)</td>
<td>0</td>
<td>1.8</td>
</tr>
<tr>
<td>Cardiac Tamponade (%)</td>
<td>0</td>
<td>1.1</td>
</tr>
<tr>
<td>RBC Transfusion (%)</td>
<td>10</td>
<td>3NA.9</td>
</tr>
<tr>
<td>Major Vascular Complications</td>
<td>0</td>
<td>NA</td>
</tr>
</tbody>
</table>
## MitraClip 30-Days

<table>
<thead>
<tr>
<th>Metric</th>
<th>HYGEIA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=20</td>
</tr>
<tr>
<td>NYHA ≤2 (%)</td>
<td>81%</td>
</tr>
<tr>
<td>Mean MV Gradient, (mmHg)</td>
<td>3.3±1.4</td>
</tr>
<tr>
<td>MV area, (cm²)</td>
<td>2.7±1.2</td>
</tr>
<tr>
<td>MR grade (+)</td>
<td>1.2±0.4</td>
</tr>
</tbody>
</table>
Mitral Regurgitation Grade

6-months

p<0.01
NYHA Functional Class 30-Days

- Baseline:
  - Class II: 20% of patients
  - Class III: 30% of patients
  - Class IV: 50% of patients

- 30-Days:
  - Class I: 40% of patients
  - Class II: 30% of patients
  - Class IV: 30% of patients

- 81% NYHA Class I or II at 30-Days

N = 20 Matched Cases
### MITRACLIP

#### Clinical Outcomes at 6-months

<table>
<thead>
<tr>
<th></th>
<th>HYGEIA Cohort (N=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
<td>10%</td>
</tr>
<tr>
<td><strong>NYHA ≤2 (%)</strong></td>
<td>82%</td>
</tr>
</tbody>
</table>
Degenerative / Organic MR

- 83 year-old female
- NYHA-III dyspnea, despite optimal HF therapy
- EF 65%
- MR 4+ due to P2 prolapse
  fibroelastic deficiency, ruptured chord
- Pulmonary HTN (sPAP 80 mmHg)
- Chronic Atrial Fibrillation
- Euroscore 18.5%
X-plane mode

Simultaneously project 2 orthogonal views

2C
LVOT

2c
LVOT
Live 3-D Zoom: Mitral Valve Surgeon’s View
MVQ analysis

P2 prolapse with area of mal-coaptation in the A2-P2 segment
X-Plane with Color Flow Doppler
Transeptal Puncture

Critical Height 3.5-4.0cm above the annulus
Steerable Guide Catheter in Left Atrium
Clip Delivery System in Left Atrium

2011/10/27 02:13:26PM
YGEIA HOSPITAL

VR 5H° 40 180
7cm
Live 3D
3D 47%
3D 40dB

89 bpm
Mitra Clip Alignment Above Valve at Center of MR jet
MitraClip with open arms, above mitral valve:

Alignment over A2-P2
LV view of the Mitra Clip with open arms:

Assessment for perpendicularity to coaptation line
LVOT view during grasping of the mitral valve leaflets
Assessment of stability of leaflet grasping
Post Mitra Clip: Assessment for MS

Planimetry of two orifices combined: 2.4 cm$^2$

Mean Transmitral Gradient: 1 mmHg
Commisural view post Mitra Clip
LVOT view post Mitra Clip: Trace MR
Double Orifice MV post MitraClip Deployment
30-Days Follow up

Functional Class NYHA I

MR trace
15-Months

no heart failure re-admissions
Functional - Ischemic MR

- 66 year-old male
- CABG in 1996
- Ischemic Cardiomyopathy
- EF 25%
- NYHA IV
- Multiple heart failure admissions
- EuroScore 30%
- STS 3.1%
Assessment post 1st Clip
Decision for 2\textsuperscript{nd} Clip
Assessment for Mitral Stenosis
Release of 2\textsuperscript{nd} Clip
30-Day Follow up

Patient reports feeling significantly better
improved exercise tolerance
Conclusion

Results achieved with the MitraClip are durable through 4 years.

The MitraClip therapy provides an additional therapeutic option for select patients with severe MR who are deemed too high risk for open MV surgery.
Conclusion

Results achieved with the MitraClip are durable through 4 years.

The MitraClip therapy provides an additional therapeutic option for select patients with severe MR who are deemed too high risk for open MV surgery.
Mitral Clip and Reimbursement

Germany – full reimbursement with DRG

Switzerland – full reimbursement with DRG

Netherlands – full reimbursement with DRG as of Jan 2014

Turkey – full reimbursement

UK – expecting NHS reimbursement within few days

USA – expecting FDA approval within few weeks.
**How are Patients with Isolated FMR Treated?**

**COAPT: Trial design**
- ~420 patients enrolled at up to 75 US sites
- Significant FMR (≥3+ by core lab)
- Not appropriate for mitral valve surgery (local heart team)
- Specific anatomical criteria
- Randomize 1:1
  - MitraClip
    - N=210
  - Control group
    - Standard of care
    - N=210
- Clinical and TTE follow-up:
  - 1, 6, 12, 18, 24, 36, 48, 60 months

**RESHAPE-HF: Trial design**
- ~800 patients enrolled at up to 50 EU sites
- Significant FMR (≥3+ by core lab)
- Chronic heart failure despite optimal medical therapy
- Specific anatomical criteria
- Randomize 1:1
  - MitraClip
    - N=400
  - Control group
    - Standard of care
    - N=400
- Clinical and TTE follow-up:
  - 1, 6, 12, 18, 24 months

**Primary efficacy endpoint (superiority)**
- Recurrent HF hospitalization (ITT)

**Primary safety endpoint (noninf)**
- SLDA, device embolizations, endocarditis, MS device-related complications requiring non-elective CV surgery

**Death or recurrent HF hospitalization (ITT)**
5ο Συνέδριο Ομάδας Εργασίας
Αιμοδυναμικής & Επεμβατικής Καρδιολογίας της ΕΚΕ – ICE
Ιωάννινα 5-6/12/2013