Treating mitral regurgitation with transcatheter repair

Patient’s follow-up and future therapeutics

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Disclosure Statement of Financial Interest

I currently have, or have had over the last two years, an affiliation or financial interests or interests of any order with a company or I receive compensation or fees or research grants with a commercial company:

Consulting Fees/Honoraria:
Abbott vascular, Edwards Life Sciences, Valtech
- General comments
- What is the future?
  - Technique
  - Evidence
- Challenges
- What else?
Percutaneous Repair Techniques with Approval in Europe
Current adoption of MITRACLIP therapy

Treating Centres: 777
Patients (clinical and commercial): Over 40,000
Implant Rate\(^1\): 97%
Functional MR\(^2\): 64%
Degenerative MR\(^2,3\): 22%
Mixed: 14%
MITRACLIP Clinical trial experience and regulation


First Case

EVEREST I Feasibility (N=55)

EVEREST II Roll-In & RCT (N=339)

EVEREST II HRR (N=78)

REALISM (N=965)

ACCESS-EUROPE (N=853)

MITRACLIP ANZ (N=78)

PAS-1 (N=1,998)

PAS-2 (N=554)

COAPT (N=482 Randomized)*

MITRACLIP JAPAN (N=30)

Abbott-Sponsored Studies
- Study closed
- Enrollment complete; follow-up ongoing
- Study enrolling

Proposed enrollment completion

* As of October 26, 2016
• General comments
• What is the future?
  * Technique
  * Evidence
  * Challenges
• What else?
MitraClip is not a palliative therapy... when performed properly,

**MITRAL HEART TEAM**

- Correct patient selection
- Procedural performance
- Periprocedural imaging
- Assessment of intraprocedural outcomes

(Courtesy of F Maisano)
Line of coaptation
Learning curve

Single Leaflet Attachment

MitraClip Implant Rate
## Registries on MitraClip

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>DMR</th>
<th>MR ≤2</th>
<th>In-hospital death</th>
</tr>
</thead>
<tbody>
<tr>
<td>STS/ACC TVT (US)</td>
<td>86%</td>
<td>93%</td>
<td>2.3%</td>
</tr>
<tr>
<td>SENTINEL (EU)</td>
<td>28%</td>
<td>95%</td>
<td>2.9%</td>
</tr>
<tr>
<td>ACCESS (EU)</td>
<td>23%</td>
<td>91%</td>
<td></td>
</tr>
<tr>
<td>TRAMI (DE)</td>
<td>29%</td>
<td>95%</td>
<td>2.9%</td>
</tr>
<tr>
<td>MitraSwiss (CH)</td>
<td>38%</td>
<td>85%</td>
<td>4.0%</td>
</tr>
<tr>
<td>France (FR)</td>
<td>23%</td>
<td>88%</td>
<td>3.3%</td>
</tr>
<tr>
<td>GRASP (IT)</td>
<td>24%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Netherlands (NL)</td>
<td>18%</td>
<td>93%</td>
<td></td>
</tr>
<tr>
<td>MARS (Asia)</td>
<td>46%</td>
<td>94%</td>
<td>4.2%</td>
</tr>
<tr>
<td>EVEREST I</td>
<td>79%</td>
<td>74%</td>
<td>0.9%</td>
</tr>
<tr>
<td>EVEREST II RCT</td>
<td>51%</td>
<td>77%</td>
<td>1.1%</td>
</tr>
<tr>
<td>EVEREST II HRS</td>
<td>30%</td>
<td>86%</td>
<td>2.6%</td>
</tr>
</tbody>
</table>
Advanced techniques for Degenerative MR

- Implantation of 2 or more clips
- Grasping during asystole (Adenosine infusion)
- Grasping during rapid pacing
- Volume control (ventilation manoeuvres)
- Use of two delivery systems
Zipping technique

(Courtesy H. Ince)
Better technology

New MitraClip® NT (Nitinol)

- Ready update, June 2016
  - Nitinol Grippers with 160° opening
  - Better steerability of CDS
  - Less sleeve shortening
  - Less need of M Knob rotation resulting in less CDS tension
  - Facilitated CDS removal in case of clip not implanted

- Further update
  - Redesign of CDS and Handle for an easy to use one-operator device

(Courtesy of S Van Bardeleben)
• General comments
• What is the future?
  Technique
  Evidence
  Challenges
  What else?
RCT’s In Secondary MR

- COAPT ~501 patients
- RESHAPE- HF2 ~166 patients
- MATTERHORN ~35 patients
- MITRA CRT ~30 patients
Multicentre Study of Percutaneous Mitral Valve Repair MitraClip Device in Patients With Severe Secondary MR (MITRA-FR)

- MitraClip vs optimal therapy alone
- Estimated Enrollment: 288 at 22 sites - 214 enrolled as of Aug 16th
- Primary Outcome Measure: All-cause mortality and cardiovascular death/heart failure hospitalization
- Inclusion Criteria:
  - Core Laboratory Characterized by a Regurgitation Volume > 30 mL/beat or a regurgitant orifice area > 20 mm²
  - New York heart Association Class ≥ II
  - Left ventricular ejection fraction between 15% and 40%
  - Minimum of 1 hospitalization for heart failure within 12 months preceding randomization
  - Assessed by the investigator to be on optimal standard of care therapy for heart failure
  - Assessed by the heart team to be not eligible to a mitral surgery intervention

5 patients left !!!!! B BRAVO
« Multicenter and randomized study of MITRACLIP® transcatheter mitral valve repair in patients with severe primary mitral regurgitation eligible to high risk surgery »
MITRA HR

<table>
<thead>
<tr>
<th>Sponsor</th>
<th>CHU DE NANTES</th>
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</thead>
<tbody>
<tr>
<td>Coordinator</td>
<td>Pr Guérin Patrice</td>
</tr>
<tr>
<td>Study center(s)</td>
<td>29 330 patients</td>
</tr>
<tr>
<td>Type</td>
<td>Medical Device</td>
</tr>
<tr>
<td>Study duration</td>
<td>Overall duration of the study: 62 month</td>
</tr>
<tr>
<td></td>
<td>Enrollment period: 36 month</td>
</tr>
<tr>
<td></td>
<td>Patient follow-up period: 26 month</td>
</tr>
<tr>
<td>Design</td>
<td>multi-center</td>
</tr>
<tr>
<td></td>
<td>Medical Device</td>
</tr>
<tr>
<td></td>
<td>Randomized Stratified</td>
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<tr>
<td></td>
<td>Open label</td>
</tr>
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<td></td>
<td>Prospective</td>
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</table>
Main inclusion criteria

- Mitral valve anatomy appropriate to Mitraclip therapy and mitral valve surgery (repair or replacement)
- Patients (over 18 years old) are judged eligible for mitral valve surgery by the local heart team but are at high surgical risk, defined as:
  - age \( \geq 75 \) years and STS score \( \geq 6\% \) or one frailty index or one major organ system compromise or one possible procedure-specific impediment (using MVARC definitions)
  - or age \( < 75 \) years and STS score \( > 8\% \) or at least one other high risk criteria following the MVARC definitions
Main objective:
Show non-inferiority for clinical efficacy of an endovascular treatment strategy with the MitraClip® as compared to a surgical treatment strategy at 12 months.

Principal secondary objective:
Show superiority for safety over 30 days of an endovascular treatment strategy in the MitraClip® arm in comparison with surgery.
“Valvular Heart Disease II Survey”

- **Primary objectives:**
  - to analyse existing practices in the management of patients with severe native heart valve disease or any previous valvular intervention
  - to compare these practices with existing ESC guidelines

- **Secondary objectives:**
  - In-hospital and 6-month mortality & morbidity after enrolment in the study according to the chosen management strategy

- **Other Objectives:**
  - Use of diagnostic procedures
  - Use and results of valve interventions
  - Management of patients after a valve intervention
  - Assessment of specific subgroups of patients of interest because of their increasing incidence (Elderly; Interventions in asymptomatic; Heart Failure patients; ...)

36 countries will participate
Recruitment Q1 2017
Preliminary presentation: ESC 2017

www.escardio.org
"Raising Awareness in Mitral Regurgitation"

- **Objective of the first phase:** evaluate how physicians are able to recognize, diagnose and treat patients with primary and secondary MR appropriately.

- **Contributors:**
  The ESC WG on Valvular Heart Disease; EACVI; EAPCI; ACCA; EHRA; HFA
  The ESC WG on cardiac surgery; The Council for Cardiology Practice

- **7 countries:** Germany, France, Italy, Spain, UK, Poland, Sweden
- **525 physicians:** GP’s; general cardiologists; sub-specialists; surgeons

- **Qualitative and quantitative phases were conducted in 2016**
  Results will be presented in Barcelona 2017

[www.escardio.org](http://www.escardio.org)
Prospective registry including all patients with severe MR and contraindication for surgery who are evaluated for a percutaneous intervention on the mitral valve and who do not participate in MITRA.FR
• General comments
• What is the future?
  Technique
  Evidence
  **Challenges**
• What else?
What is the impact on Survival?

But these are not RCT's

(Gianini. Am J Cardiol 2016)
Velasquez. Am Heart J 2015)
(Swaans. J Am Coll Cardiol Intv 2014)
When is it too late?

Predictors of 1 year mortality after MitraClip

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 75 years</td>
<td>1.29 (0.90–1.87)</td>
<td>0.16</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.13 (0.78–1.64)</td>
<td>0.53</td>
</tr>
<tr>
<td>NYHA IV</td>
<td>1.62 (1.10–2.40)</td>
<td>0.02</td>
</tr>
<tr>
<td>Anaemia</td>
<td>2.44 (1.16–5.12)</td>
<td>0.02</td>
</tr>
<tr>
<td>Previous aortic valve intervention</td>
<td>2.12 (1.32–3.41)</td>
<td>0.002</td>
</tr>
<tr>
<td>Creatinine ≥ 1.5 mg/dL</td>
<td>1.77 (1.24–2.54)</td>
<td>0.002</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>2.12 (1.41–3.20)</td>
<td>0.0003</td>
</tr>
<tr>
<td>LVEF &lt; 30%</td>
<td>1.58 (1.10–2.31)</td>
<td>0.01</td>
</tr>
<tr>
<td>Severe tricuspid regurgitation</td>
<td>1.84 (1.23–2.77)</td>
<td>0.003</td>
</tr>
<tr>
<td>Procedural failure a</td>
<td>4.36 (2.37–8.02)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

(Puls M et al. Eur Heart J 2016;37:703-12)
When is it too late?
MitraClip in Patients with Low EF

(Schafer. ACCESS EU Registry EuroPCR 2015)
# Extended Anatomic Indications for MitraClip?

<table>
<thead>
<tr>
<th>Conditionally suitable valve morphology</th>
<th>Unsuitable valve morphology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathology in Segment 1 oder 3</td>
<td>Perforated mitral valve leaflet or cleft</td>
</tr>
<tr>
<td>Mild calcification outside of the grip-zone of the clip system; ring calcification, post annuloplasty</td>
<td>Severe calcification in the grip-zone</td>
</tr>
<tr>
<td>Mitral valve opening area &gt;3 cm² with good residual mobility</td>
<td>Haemodynamically significant mitral stenosis (valve opening area &lt;3 cm², MPG ≥ 5 mmHg)</td>
</tr>
<tr>
<td>Mobile length of the posterior leaflet 7–&lt;10 mm</td>
<td>Mobile length of the posterior leaflet &lt;7 mm</td>
</tr>
<tr>
<td>Coaption depth ≥11 mm</td>
<td>Rheumatic leaflet thickening and restriction in systol and diastole(Carpentier IIIA)</td>
</tr>
<tr>
<td>Leaflet restriction in systole (Carpentier IIIB)</td>
<td>Barlow’s syndrome with multisegment flail leaflets</td>
</tr>
<tr>
<td>Flail-width &gt;15 mm only with a large ring width and the option for multiple clips</td>
<td></td>
</tr>
</tbody>
</table>
Case papillary muscle

MitraClip for SAM in HOCM – AK St. Georg experience
MitraClip after Annuloplasty Failure

(Courtesy of KH Kuck)
• General comments
• What is the future?
  Technique
  Evidence
  Challenges
  *What else?*
Percutaneous Repair Techniques with Approval in Europe
The other mitral valve repair techniques

- Coronary sinus annuloplasty (*Carrillon*) is easy to perform but efficacy is limited (n~300)

- Direct annuloplasty (*CardioBand*) is more difficult to perform but provides a significant and durable reduction in MR (n~150)

- Direct annuloplasty (*Mitralign*) is difficult to perform, has a good safety profile but limited efficacy (n~100)

- Chordal replacement (*NeoChord*) gives promising results in well selected candidates (n~400)
## Planned RCT on Annuloplasty devices

<table>
<thead>
<tr>
<th>Population</th>
<th>Cardioband</th>
<th>Carillon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic HF and FMR</td>
<td>Ischemic or non-ischemic cardiomyopathy; optimized and stable medical HF regimen</td>
<td>Ischemic or non-ischemic cardiomyopathy; optimized and stable medical HF regimen</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>N</th>
<th>~400</th>
<th>~400</th>
</tr>
</thead>
</table>

| Randomized | 2:1 | 2:1 |

| Primary EP | 1 year: Prevalence of MR ≤2+ and hierarchical comparison of all-cause mortality, # of HF hospitalizations, 6 minute walk test and KCCQ | 1-year efficacy: Clinical endpoints and regurgitant volume 1-year safety: Device-related major adverse events |

*(G. Stone TCT 2016)*
Planned RCT on Chordal Replacement

- **US Pivotal trial**
  
  D. Adams / M. Borger  
  NeoChord vs Standard MVr  
  Up to 585 pts, Q4 2016

- **French Trial**

  J.F. Obadia  
  NeoChord vs Standard MVr  
  Up to 194 pts, Q1 2017
Percutaneous Mitral Annuloplasty Things (S. Bolling)
Surgeons combine techniques according to anatomy, etiology and dysfunction
Combining Annuloplasty + MitraClip

(Courtesy of S Van Bardeleben and F Maisano)
Combination of Techniques

_Surgical and upcoming transcatheter experiences will tell us:_

- Which techniques should be combined
- How
- When

= Fully Percutaneous Mitral Repair
Transcatheter Valve Implantation

- **Braile Biomedica**
- **CardiAQ 1st G**
- **CardiAQ Edwards**
- **Cephea**
- **Direct Flow Medical**
- **Twelve Medtronic**
- **M-Valve**
- **Edwards Fortis**
- **HighLife**
- **Navigate**
- **Neovasc Tiara**
- **PermaValve MID**
- **Sinomed**
- **Tendyne Abbott**

**Others:** MitraHeal, Mitrassist, Mitraltech, Mehr Medical, Mitracath, Mitralix MAESTRO, Nakostech, St. George ATLAS, Transcatheter Technologies Tresillo
Multiple Transcatheter Interventions

22 cases of MitraClip in mitral and tricuspid position reported at TCT 2016
Mitral valve interventions in Germany

Percutaneous intervention will allow a larger number of patients with MR to be treated by less invasive surgery or interventional cardiology

(Courtesy of S Van Bardeleben)
« Similar to past innovations in interventional cardiology, trancatheter mitral valve interventions will begin their quest in Waterloo and will make their way towards Eldorado with great enthusiasm, passion and perseverance »

(Piazza N., Windecker S., EuroIntervention 2016)
STOP