Mitral Valve: Next Generation Devices

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I, Eberhard Grube have the following financial interest/arrangement that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation:

**Speaker Bureau/ SAB:** Medtronic, Boston Scientific, HighLife, Jena Valve, Protembis

**Equity Interest:** Cardiovalve, Claret, Shockwave, Valve medical, CardioMech, Millipede, Imperative Care, Pi-Cardia, Ancora, Laminar, ReNiva Medical
Painfully, we learned that the Mitral Valve is very different from the Aortic Valve.
Expanding portfolio of transcatheter mitral repair and replacement

- **Chordal Replacement**
  - NeoChord
  - Harpoon

- **Leaflet Repair**
  - MitraClip
  - PASCAL

- **Annuloplasty**
  - Cardioband (Carillon)

- **Combo procedures**

- **Replacement**
  - Tendyne, Intrepid, Tiara, Cardiovalve, HighLife, etc.

- **MitraClip XTR/W & NTR/W**
- PASCAL

- **Tendyne**
- **Intrepid**
The TMV repair landscape is rapidly changing. Data showed good safety performance but need improvement in efficacy and user friendliness.

A real milestone has only been achieved by the Edge-to-Edge Technique of the MitraClip.
MITRAL VALVE REPAIR – TMVr

New Devices?
Transcatheter *transseptal* chordal replacement are the next phase for this technology but remain at an early stage, with most devices either in preclinical development or limited human experience.

**Transseptal Systems**

- **NeoChord NeXus**
  - Leaflet capture → Anchor → Tensioning
  - **Milestones:**
    - Early experience in 3 cases

- **ChordArt**
  - Leaflet → Anchor
  - **Milestones:**
    - Experience: 5 cases in feasibility study

- **Pipeline**
  - Anchor → Pledget → Adjust & Lock
  - **Milestones:**
    - Experience: FIH completed

3 Patients Successfully Treated

- Discharged at day 4

Significant MR Reduction Achieved

- MR reduction from severe (4+) to maximum trace in both patients

Durable & Stable Anchoring

- Stable leaflet connection and papillary muscle anchor, patients are doing well at 30 days (N=1) and 60 days (N=1)
Pre and Post Implant Mitral Valve – 2D
Pre and Post Implant Mitral Valve – Color

Pre-implant

Post-implant
The Saturn TMVR is a single device characterized by:

An Annular Structure mechanically connected to a Central Valve.
SATURN ADAPTIVE TECHNOLOGY (InnovHeart)

A SOLUTION TO ADDRESS THE CHALLENGES AND WIDE VARIABILITY OF NATIVE ANNULUS SIZES

- Size reduction of the Mitral Annulus
- Stabilization of the Mitral Annulus
TRANSCATHETER MITRAL VALVE REPLACEMENT
Design and Procedure Goals

- Ease of implantation
- Agnostic to etiology of MR
- Reliable elimination of MR
- Less recurrence of MR
LIMITED APPLICABILITY OF CURRENT TMVR DESIGNS TO “REAL WORLD ANATOMY” (HIGH SCREENING FAILURE RATES)

TMVR designs have limited ability to cover all architectural variations seen in MR patients.

Unlike TAVR, the development of a universal device tool (“one-design fits all”) may be challenging.
## CURRENT TMVR INVESTIGATION LANDSCAPE

<table>
<thead>
<tr>
<th>Access</th>
<th>TMVR device</th>
<th>Cases known</th>
<th>Nb of sizes</th>
<th>Level of maturity</th>
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<tbody>
<tr>
<td>TA</td>
<td>Tendyne</td>
<td>800+</td>
<td>13</td>
<td>CE-marked &amp; US Pivotal ongoing</td>
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<tr>
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<tr>
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<tr>
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<td>34 TS</td>
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<td>Feasibility well underway Indication extensions coming</td>
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<td>4</td>
<td>Feasibility</td>
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<tr>
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<td>Evoque/EOS</td>
<td>14+ TS</td>
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<td>Feasibility restarted with EOS</td>
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<tr>
<td>TA-TS</td>
<td>4C</td>
<td>8+ TS</td>
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<tr>
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<td>Cephea</td>
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<tr>
<td>TS</td>
<td>Cardiovalve</td>
<td>5+ TS</td>
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Information gathered from available sources as of May 2021
0% patients had MR ≥ 1+ @ 1 year with current transapical TMVR Technologies
INTREPID (MEDTRONIC) TMVR TRANS-SEPTAL SYSTEM

Atrial Flange Deployment  
Ventricular Deployment  
Final Result

Firas Zahr, MD, TCT2021
Echocardiographic Outcomes: MR Severity (N=14)

Core lab adjudicated. Data reported on implanted cohort.
• 15 patients reported @30days as part of an EFS
  • 2/3 DMR, 1/3 FMR
  • No mortality, stroke, reintervention or new pacemaker implantation
  • Favorable hemodynamics with almost complete elimination of MR 30d
  • Improved NYHA class
  • Technical success acute: 14/15 (93%) -> 1 conversion to surgery
  • ASD closure: 11/15 (73%)
  • 30D bleeding: 7/17 (47%)

• FDA approval to add TS delivery to the Apollo pivotal US trial
EVOQUE & EVOQUE EOS

- **Evoque**
  - 15 cases in mitral reported in May 2020 (EFS + Compassionate use)
    - 93% technical success (1 conversion to surgery)
    - 186 min average procedure time
    - 14% PVL closure
    - 7% 30D mortality: 1/15
  - Then, went on to tricuspid experience

- **Evoque EOS**
  - Redesign of Evoque, fully retrievable and recapturable
  - Evaluated within EFS, just started
Edwards EVOQUE Eos Mitral Valve Replacement System: Investigation of Safety and Performance After Mitral Valve Replacement With Transcatheter Device

Prospective, multicenter, single arm and non-randomized study

Purpose:
Evaluate the safety and function of the Edwards EVOQUE Eos mitral valve replacement system

Principal Investigators:
• Rajendra Makkar, MD

Patients with Symptomatic ≥ Moderate Mitral Regurgitation

Heart Team Assessment

EVOQUE Eos mitral valve replacement system

Primary Outcome:
• Composite of major adverse events. Proportion of patients with major adverse events at 30 days

Follow-up: 30 days, 3 months, 6 months, 1 year and annually through 5 years

NCT02718001
TMVR
THE FUTURE

Repositionability and Transseptal Delivery

Minimal Anatomic Exclusions:
.

Improved Imaging

CT and 3D Printing
New Innovative Solutions
Posterior leaflet enhancement and replacement is a new focus area for TMV repair and these devices are early in their experience.

**Polares**
Posterior neoleaflet to restore leaflet coaptation

**Milestones:**
Experience: CU cases

**SUTRA**
Trileaflet valve design with annular anchoring

**Milestones:**
Experience: Pre-clinical

**Half Moon**
Intended to restore valve coaptation

**Milestones:**
Experience: FIH completed
POLARES PLAR SYSTEM

The implant, its delivery and anchoring system

- Posterior view
- Anterior view

Primary anchor
Secondary anchors
Implant Deployment and Acute Result
POLARES PRE AND POST RESULT

Pre-implant

Post-implant
3 LEAFLET-HALF VALVE DESIGN WITH ATRIAL ANCHORING

Native Mitral Valve

Anterior leaflet

Posterior leaflet

P1

P2

P3

Optimal Coaptation

Tri-leaflet Posterior Leaflet Design

Anterior leaflet
PRE-CLINICAL RESULTS 4D CT FROM ONE ANIMAL (SUTRA)

Neo-Leaflet coapting well with AML

Confidential Information
**HALF MOON - COAPTATION AUGMENTATION DEVICE**

- **Design details**
  - Contoured ePTFE **baffle** fills regurgitant orifice from the posterior side and provides a new coaptation surface for the native leaflets
  - Posterior **clip** orients device and provides sub-annular fixation
  - Flexible atrial **brim** provides additional fixation and supra-annular stabilization
  - Transfemoral delivery via **29 Fr** system enables repositionability and recovery

Designed to eliminate regurgitation by restoring physiologic coaptation in a diseased mitral valve.

*CAUTION: INVESTIGATIONAL DEVICE. LIMITED BY FEDERAL LAW (USA) TO INVESTIGATIONAL USE.*
HALF MOON - COAPTATION AUGMENTATION DEVICE*

- Baffle designed to swing anteriorly during systole
- Clip and Brim work in tandem to provide fixation
HALF MOON - COAPTATION AUGMENTATION DEVICE*

Post-Implant Results

Pre-implant

Post-implant

Firas Zahr, MD, TCT2021
IS TMVR READY FOR PRIME TIME?

What remains to be done in MR

- Longterm results of transcatheter interventions
- Indications for transcatheter interventions in patients with severe primary MR at lower surgical risk
- Potential impact of MV interventions (surgery and transcatheter)
  on survival in patients with severe secondary MR
- Selection of criteria to identify responders to TEER for secondary MR (severity criteria, concept of „disproportional MR“)
- The role of newer transcatheter treatment options (annuloplasty, combined repair techniques, valve replacement)

My answer is No!
Mitral – Where We Are After 15 Years?
# THE FUSION AND ACQUISITION FRENZY: (MARKET EXPECTATIONS)

<table>
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<th>Produkt</th>
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<td>Tendyne</td>
<td>Abbott</td>
<td>2015</td>
<td>~130</td>
<td>$250 + Milestones</td>
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</table>

**THE FUSION AND AQUISITION FRENZY:**

Around $50 Mio USD per Patient for Transcatheter Mitral Valve Therapy.
THE TMVR\textsuperscript{2} WARS

REPAIR VS. REPLACEMENT

Competitive or Complementary?
The MV repair issues

- The TMV repair landscape is rapidly changing. Devices are relatively safe but efficacy and user friendliness have to be improved
  - complex, time consuming and require training
  - efficacy???
  - not ideal for early symptomatic patients
- The results so far have been disappointing.
- Real milestone has only been achieved by the Edge-to-Edge Techniques which however has its own limitations.
- In the near future the number of TEER will increase but other innovative solutions will emerge
Why is TMVR still an unsolved issue?

• In 2015, 3 TMVR technologies for trans-apical delivery acquired for $1+Bn
• In 2016, the cardiology community concluded “future of TMVR is trans-septal”
• In 2021, limitations remain important
  • Current devices still have one or several of the following shortcomings:
    • Pure trans-apical applicability
    • When trans-septal, large French size
      • -> need for ASD closure and surgical cut-down/repair to the femoral vein
    • Persistent peri-valvular leaks
    • Valve/Leaflet thrombosis
    • Difficulty in achieving an adequate position consistently
    • Cannot accommodate for large anatomies
    • Cannot treat LVOTO risk patients
  • Current clinical studies still have to identify the ideal patient population
So why did we still migrate to valve replacement?

For multiple reasons:

• Repair is a longer and more complex procedure with technology that was developed slowly
• We enjoyed being in a “comfort zone” of doing TAVR in 45 minutes - so why not to replicate it in Mitral?
• The Industry also resented to move from the “comfort zone” of making TAVR devices
• We are holding until MR becomes severe to treat these patients
• No alternative drug therapy exist to date so the gold standard remain surgery

The Result:

After 15 years we still don’t have a TMVR device that is ready for prime time...
TREATMENT OF SEVERE MR IN 2021:
Making a case for the development of catheter-based therapies

• Surgery is the standard of care for patients with severe symptomatic MR
• TEER has demonstrated beneficial outcomes in prohibitive/high risk Primary MR and selected (COAPT eligible) Secondary MR patients
  • Other important (and more frequent) MR patient categories have not been studied and optimal MR reduction with TEER remains challenging in patients with complex anatomies
• The High Risk MR population therefore represents a big opportunity for catheter based innovations.
• Severe MR+HF in the elderly is:
  • Highly prevalent
  • Frequently rejected from surgery
  • Not represented in surgical trials and
  • Frequently re.hospitalized
CATHETER-BASED TECHNOLOGIES MAY IMPROVE PROCEDURAL OUTCOMES IN THESE HIGH-RISK PATIENTS

Less Invasive mitral valve intervention may be performed with fewer peri-operative complications

Progression towards minimally invasive interventions impact clinical outcomes, QoL and health care cost
A CALL FROM THE BATTLEFIELD:

To further understand all aspects of the mitral disease and its needs, we have to get OUT OF THE BOX and out of the ZONE OF COMFORT, to become creative in identifying and implementing new approaches and better solutions to this unmet clinical challenge for low risk patients.
THERE ARE NO LIMITS TO WHAT YOU CAN ACCOMPLISH, EXCEPT THE LIMITS YOU PLACE ON YOUR OWN THINKING.

- BRIAN TRACY
Thank you for your kind attention!