Current and Future Trials on Transcatheter Mitral Valve Repair/Replacement

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Disclosure Statement of Financial Interest

**Saibal Kar, MD, FACC**

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

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<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td>• Grant/Research Support</td>
<td>• Abbott Vascular, Boston Scientific, Gore, Edwards Lifesciences</td>
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<tr>
<td>• Consulting Fees/Honoraria</td>
<td>• Abbott Vascular, Boston Scientific, Gore</td>
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<td>• Other Financial Benefit</td>
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Treatment of Mitral Regurgitation

- Treatment of MR will require a tool box
  - There is role for both replacement and repair
- Repair where possible is preferable
- Replacement is required
  - Non repairable valve
  - Combined MR/MS
  - Functional MR ??
Percutaneous therapy for mitral regurgitation

- Percutaneous MV repair is considered as standard therapy for selected patients with severe MR
  - Excellent safety
  - Compatible efficacy
  - Durability up to 4 years

- There are several percutaneous MV replacement devices, but they are still in FIM or preclinical studies
Commercial TMVR/r Devices Landscape

• MitraClip:
  – PMR or DMR (10/24/2013): prohibitive surgical risk
  – SMR or FMR (03/14/2019): all surgical risk

• SAPIEN 3:
  – Mitral valve-in-valve (06/05/2017): high or greater surgical risk
Investigational TMVR/r Devices Landscape

• Pivotal:
  – Intrepid; Tendyne; Carillon; Cardioband; Neochord; MitraClip; PASCAL

• Early feasibility study
  – Neovasc; EVOQUE; CardioValve; Highlife; AltaValve; Transcatheter Mitral Cerclage Annuloplasty (TMCA); M3; MVRx; Caisson; Accucinch
Finally

WIDER CLIP ARMS, 4 CLIP SIZES
Provide increased coaptation area with wider Clip options

CONTROLLED GRASPING ACTUATION
Ability to simultaneously as well as optimize individual leaflet grasping

CONTINUOUS LAP MONITORING
Integrated left atrial pressure monitoring capability in the SGC

DELIVERY SYSTEM DESIGNED FOR THE MITRAL VALVE
Precise and predictable steering specifically for the mitral valve

MitraClip G4 commercial available in US, CE Mark approval pending
Baseline TEE : X plane

Bicommissural view

Left ventricular outflow tract view
Baseline TEE : LVOT view with color
Disappearance of MR
Creation of bridge with no significant gradient
The PASCAL Implant Contains Three Differentiated Features for Efficacy and Safety

- Central spacer
- Broad, contoured paddles
- Independent leaflet capture

CAUTION: Investigational device. Limited by Federal (or United States) law to investigational use.
Clinical summary: PASCAL

- The CLASP I study is completed
  - Safe
  - Effective uptill one year
- CE Mark approved in Feb 2019
- Investigational in US
- Randomized study vs MitraClip is ongoing in the US
The Edwards PASCAL trAnScatheter Mitral Valve RePair System Pivotal Clinical Trial (CLASP IID/IIF Trial)

- Prospective, multicenter, randomized, controlled pivotal trial
- Purpose: Evaluate the safety and effectiveness of the PASCAL Repair System compared to the MitraClip System in patients with degenerative and functional mitral regurgitation
- IID Principal Investigators
  - Scott Lim, MD
  - Robert Smith, MD
  - Linda Gillam, MD
- IIF Principal Investigators
  - Jeff Popma, MD
  - Vinod Thourani, MD
  - Paul Grayburn, MD

Patients with Clinically Significant Mitral Regurgitation

Heart Team Assessment

- MR 3+ to 4+ as assessed by echo core lab
- Eligible for transcatheter mitral valve repair
- Patient suitable for both devices

DMR FMR

CLASP IID
(prohibitive risk)

- PASCAL Repair System
- MitraClip System

CLASP IIF

- PASCAL Repair System + GDMT
- MitraClip System + GDMT

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

Primary Endpoints, Non-Inferiority
- MR severity reduction at 6 months
- Major adverse events (MAEs) at 30 days

Primary Endpoints, Non-Inferiority
- All-cause mortality and HF rehospitalization at 2 years
- Major adverse events (MAEs) at 30 days

Currently Enrolling (NCT03706833)
Type A: Isolated P2 prolapse/flail

Type B: Multisegment prolapse/flail (P1-P2, P2-P3 or P1-P2-P3)

Type C: Anterior Prolapse/flail, Paracommissural, Annular and Leaflet Calcifications

Freedom from MR >2+/4+ according to MV anatomical type

Courtesy of R. Colli, Padova
Clinical Summary: Neochord

- CE Mark approved
- >1000 cases
- Ideal for simple prolapse of P2, with non dilated annulus
- Has been tried with transcatheter annuloplasty techniques
- Ongoing clinical trial in US: Neochord vs open surgical repair
- Transseptal approach is being developed
Carillon and Cardioband devices

• Carillon indirect annuloplasty Device
  – Randomized sham controlled study
  – Carillon vs GDMT
  – Grade 2 to 4 MR functional MR

• Cardioband device
  – Following COAPT change of design of study
Transcatheter Mitral Valve Replacement studies
Tendyne and Intrepid valves have most largest clinical experience

Pivotal Phase

Tendyne TMV
Medtronic Intrepid™ TMVI
## Comparison of SUMMIT and APOLLO

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<thead>
<tr>
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<th>SUMMIT</th>
<th>APOLLO</th>
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<tbody>
<tr>
<td>Investigational Device</td>
<td>Tendyne™ TMVI</td>
<td>Intrepid™ TMVI</td>
</tr>
<tr>
<td>Valve Securement</td>
<td>Tether and apical pad</td>
<td>Cleats</td>
</tr>
<tr>
<td>Retrievability</td>
<td>Fully-retrievable after deployment until final tether cut</td>
<td>Retrievable until deployed</td>
</tr>
<tr>
<td>No. Valve Sizes</td>
<td>23 total (15 SP, 8 LP)</td>
<td>3</td>
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<tr>
<td>Delivery Catheter</td>
<td>36 Fr</td>
<td>35 Fr</td>
</tr>
<tr>
<td>Control Treatment</td>
<td>MitraClip</td>
<td>Mitral Valve Surgery</td>
</tr>
<tr>
<td>No. Randomized Subjects</td>
<td>382</td>
<td>450-650</td>
</tr>
<tr>
<td>No. Non-randomized Subjects</td>
<td>313</td>
<td>250-550</td>
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<tr>
<td>No. MAC Subjects</td>
<td>103</td>
<td>N/A</td>
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<tr>
<td>Anatomic Screen Pass Rate</td>
<td>48% (57/118)</td>
<td>42% (154/364)</td>
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Transseptal TMVR
Early Feasibility Trial phase

- EVOQUE
- M3 Edwards TMV
- Cardiovalve
- Highlife
Edwards SAPIEN M3 System

Dock Delivery
- SAPIEN M3 Dock

Valve Delivery
- SAPIEN M3 Valve

Final Implant
- Commander Delivery System
EVOQUE Mitral Valve Replacement System

- Unique anchoring mechanism utilizes annulus, leaflets, and chords, respecting the native mitral anatomy
- Intra-annular sealing skirt and frame to minimize PV leak
- Low atrial and ventricular profile to reduce procedural complications
- Integrates Edwards bovine pericardial leaflet design and tissue treatment
- Both valve sizes (44 and 48 mm) compatible with one size delivery system

CAUTION: Investigational device. Limited by Federal (or United States) law to investigational use.
EVOQUE Delivery System

- Low profile 28Fr transseptal steerable delivery system (for both valve sizes) increases maneuverability and may reduce the need for septal closure
- Stabilizer system allows for increased ease of control during procedure
- Multiple planes of flexion enable coaxiality
- Independent depth control allows for precise positioning

Courtesy of Howard C. Herrmann, MD; Perelman School of Medicine; University of Pennsylvania; Philadelphia, PA, USA

CAUTION: Investigational device. Limited by Federal (or United States) law to investigational use.
Potential Trials for DMR

Chang Fu  FDA
Potential Trials for FMR

- 2° or FMR
  - Clipable Anatomy?
    - Y: EF ≥ 20% and ≤ 50% AND LVEDD ≤ 70mm
      - MitraClip plus GDMT
      - TEST therapy vs. Control: MitraClip plus GDMT
    - N: Prohibitive surgical risk?
      - Y: TEST therapy vs. Control: GDMT
      - N: TEST therapy vs. Control: MVr preferred/MVR bailout only.

Chang Fu  FDA
Tiara TMVI

- Early transapical experience
- Most cases were compassionate cases done in Canada and Europe
- Early feasibility study in US is not enrolling patients
Repair vs. Replacement

• Percutaneous MV replacement seems technically more complex than percutaneous MV repair

• In most patient cohorts, surgical MV repair results in superior outcomes to replacement

• Percutaneous MV replacement may need to be applied in patients who would also get a surgical replacement in operating room
Conclusions

- Transcatheter Mitral Valve implantation is much more challenging than TAVR
- Unique challenges,
- Several devices are in very early phases of clinical trial
- In the light of Mitraclip, there will be challenges in case selection of transcatheter TMVI