Structural Options for the “No-Option” patient

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Abbott Northwestern – Minneapolis Heart Institute
Disclosure

• No disclosure

Case 1

• 81-yr male with shortness of breath and dyspnea on exertion
  • Prior TF-TAVR with 26mm S3 (6 years ago) – well functioning valve
  • Persistent AF s/p AVN ablation and SC-PPM placement
  • Mild non-obstructive coronary artery disease
  • Hypertension
  • Diabetes
• NYHA III
• GDMT – Metoprolol, Lisinopril and Empagliflozin
Cardiac CTA

Severe Mitral Annular Calcification
MAC Score 7
Mitral regurgitation - Epidemiology

- Mitral regurgitation is the second most common heart valve disease in Europe and US
- Its prevalence increases with age, with a prevalence rate of up to 9% in individuals >75 years old
- Surgery has been shown to improve survival in patients with symptomatic primary mitral regurgitation

Mitral regurgitation - Outcomes

Recommendations for intervention
2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease

Catherine M. Otto Circulation. Volume: 143, Issue: 5, Pages: e72-e227
Mitral TEER – Anatomical Complexity


Up to 50% of patients with MR and an indication for intervention may not receive treatment

What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery?

Marianne Mirabel1, Bernard Jung2, Gabrielle Baro3, David Mestico-Zekouri4, Delphine Déjardin1, Jean-Louis Vanoverschelde1, Eric G. Butzchart5, Philippe Ravous6, and Alec Vahanian7

Isolated MR
(n = 877)

Severe MR
(n = 546)

No severe MR
(n = 331)

Symptoms missing
n = 6

No symptoms
n = 144

Symptoms
n = 396

No intervention
n = 193 (49%)

Intervention
n = 203 (51%)

Aortic stenosis

Intervention
Class I % [95% CI]

1009 1271 79.4 [77.1-81.6]

Aortic regurgitation

114 147 77.6 [69.9-84.0]

Mitral stenosis

115 168 66.5 [60.8-75.4]

Primary mitral regurgitation

204 414 71.0 [66.4-75.3]

Lung B. Circulation, Volume: 140, Issue: 14, October 2019 Pages: 1156-1169
Characteristics of patients denied surgery

Mitral Annular Calcification (MAC)

- Prevalence varies between 5 - 42%
- Most commonly occurs in the posterior aspect of the annulus
- Only 1% of patients with MAC exhibit circumferential calcification of the annulus
- Severe MAC can lead to mitral stenosis and/or regurgitation
- Technical difficulties for surgery:
  - Decalcification (Resect)
  - Intra-atrial device position
  - Extracardiac valved conduit (Respect)
  - Higher risk of complications
Respect vs Resect

<table>
<thead>
<tr>
<th>Working around the calcified annulus (respect)</th>
<th>Decalcification and annular reconstruction (resect)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
<td><strong>Disadvantages</strong></td>
</tr>
<tr>
<td>• Simpler and shorter surgeries</td>
<td>• Replacement as opposed to repair (except for untraditional and supersized annuloplasty, on the basis of configuration of calcium)</td>
</tr>
<tr>
<td>• Lower risk of AV groove disruption</td>
<td>• Higher PVLs that are less likely to heal</td>
</tr>
<tr>
<td>• TMVR: possible percutaneous approach, promising</td>
<td>• Suture around calcium: risk of injury to circumflex artery, and less commonly conduction system or coronary sinus</td>
</tr>
<tr>
<td></td>
<td>• Intra-annular: smaller sized valve and high PVLs</td>
</tr>
<tr>
<td></td>
<td>• Supra-annular: PVLs with atrial rupture due to subjection to ventricular pressures</td>
</tr>
<tr>
<td></td>
<td>• Combined intra and supra-annular (with or without collar): significant valve downsizing</td>
</tr>
<tr>
<td></td>
<td>• Extra-anatomic bypass: only with stenosis, unphysiologic, last resort</td>
</tr>
<tr>
<td></td>
<td>• TMVR: experimental, requires dense near-circumferential MAC, unknown long-term durability</td>
</tr>
</tbody>
</table>

Dedicated Transcatheter Mitral Valve Devices

- Tendyne
- Intrepid
- Cephea
- Evoque
- AltaValve
- Sapien M3
- HighLife
- Cardiovalve
- Saturn
Tendyne TMVR System Overview

**UNIQUE VALVE-TETHER-PAD DESIGN**
- Repositionable
- Fully retrievable
- No need for CPB or rapid ventricular pacing

**APICAL PAD**
- Placed over ventricular access site

**TETHER DESIGN**
- Enables full retrievability

**VALVE DESIGN**
- Tri-leaflet, bioprosthetic valve
- Outer frame contoured to mitral annulus
- Variety of valve sizes and profiles to accommodate broad range of patient anatomies
- Standard and Low-profile frames options

---

**Study Design**

Symptomatic MR Grade III/IV, or severe mitral annular calcification (MAC)**

Heart Team deems transcatheter treatment more appropriate than surgery and anatomy amenable to Tendyne TMVR?

Randomization (1:1) (N=382)

- YES: Tendyne (Tethered) vs. Tendyne (Tetherless) (Control)
- NO: Exclude Subject

Heart Team deems valve anatomy amenable to transcatheter repair, meets MitraClip indications?

Subject has severe MAC?

- NO: Exclude Subject
- YES: Enroll Subject to MAC Cohort (optional)

Tendyne (MAC CAP Cohort) N=up to 150 (upon FDA approval)

Completed Enrollment

Closed 2023
Roll-in Subjects Up to 2 Per site – 1 year Follow up (n=100)

1-Year Survival

![Graph showing 1-Year Survival](image)

Survival Rate (%)

Time After Index Procedure (Months)

- 74.3%

MR Severity

![Graph showing MR Severity](image)

- Baseline (N=100)
- One Month (N=96)
- Six Month (N=76)
- One Year (N=62)

- None/trivial
- 1+
- 2+
- 3+
- 4+

Rogers J., Thouravi V. TCT 2023

Roll-in Subjects Up to 2 Per site – 1 year Follow up (n=100)

NYHA Classification

![Graph showing NYHA Classification](image)

- Class I
- Class II
- Class III
- Class IV

KCCQ Overall Score

![Graph showing KCCQ Overall Score](image)

- Baseline (N=100)
- One Month (N=96)
- Six Month (N=76)
- One Year (N=62)

Rogers J., Thouravi V. TCT 2023
Severe MAC Cohort 30-Day (n=103)

<table>
<thead>
<tr>
<th>Procedural Events</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural survival</td>
<td>101 (98.1)</td>
</tr>
<tr>
<td>Technical success*</td>
<td>97 (94.2)</td>
</tr>
<tr>
<td>Valve implanted†</td>
<td>103 (100)</td>
</tr>
<tr>
<td>Emergency surgery/intervention</td>
<td>6 (5.8)</td>
</tr>
<tr>
<td>CPB</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Procedural stroke</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>30-Day Events*</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>7 (6.8)</td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>7 (6.8)</td>
</tr>
<tr>
<td>Disabling stroke</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Post-op mitral intervention</td>
<td>2 (2.0)</td>
</tr>
<tr>
<td>Device thrombosis</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>22 (21.4)</td>
</tr>
</tbody>
</table>

*All events adjudicated by independent CEC per MVARC definitions
†One valve retrieved with secondary valve implanted

Severe MAC Cohort 30-Day (n=103)

NYHA Classification

<table>
<thead>
<tr>
<th>Baseline (N=163)</th>
<th>1 Month (N=89)</th>
</tr>
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<tbody>
<tr>
<td>Class I</td>
<td>72.8%</td>
</tr>
<tr>
<td>Class II</td>
<td>26.2%</td>
</tr>
<tr>
<td>Class III</td>
<td>18.0%</td>
</tr>
<tr>
<td>Class IV</td>
<td>10.0%</td>
</tr>
</tbody>
</table>

Rogers J., Thouravi V. TCT 2023
Intrepid – Mitral Valve

- Prosthesis anchors with multiple small cleats and a cork-like effect
- Symmetrical design eliminates need for rotational alignment
- Circular inner stent houses a 27 mm tri-leaflet bovine pericardial valve
- 42 & 48 mm valves in clinical evaluation; 54 mm valve in development
- ~35 Fr delivery system; 29 Fr coming

Transfemoral Transeptal INTREPID TMVR EFS 1-year (N=33)

Early and Late Clinical Outcomes

<table>
<thead>
<tr>
<th></th>
<th>30 Days</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>0.0%</td>
<td>6.7%</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>CV hospitalization</td>
<td>6.1%</td>
<td>22.3%</td>
</tr>
<tr>
<td>Re-operation (or re-intervention)</td>
<td>3.0%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Clinically significant valve thrombosis</td>
<td>0.0%</td>
<td>3.4%</td>
</tr>
<tr>
<td>MV endocarditis (definite)</td>
<td>0.0%</td>
<td>3.4%</td>
</tr>
<tr>
<td>MVARC major vascular complications</td>
<td>24.2%</td>
<td>24.2%</td>
</tr>
<tr>
<td>ASD closure performed</td>
<td>75.0%</td>
<td>–</td>
</tr>
</tbody>
</table>

Mitral Regurgitation

NYHA Functional Class

Apollo Pivotal Trial

Assessment by Multidisciplinary Heart Team
Unsuitable for approved transcatheter repair or surgical mitral valve therapies

Primary Cohort
N=250-550
(Primary or Secondary MR)

TMVR
Primary Endpoint:
All-Cause Mortality OR HF Hospitalization >30 days OR KCCQ Improvement <10 at 1 year vs. Performance Goal

Roll-in subjects

MAC Cohort
N= up to 300 (maximum)

TMVR
Primary Endpoint:
All-Cause Mortality OR HF Hospitalization at 1 year vs. Performance Goal

Study Chairman & Co-PIs
Michael Mack, David Adams, & Martin Leon

Cephea

• Dual disk circular design
• Anchoring via compression and radial forces
• Low-profile delivery system (Trans-septal 36-38 Fr)
• Fully repositionable and recapturable
Cephea™ EFS Phase 1 Experience

**Outcomes: Intra-procedural and 30-Day (n=10)**

<table>
<thead>
<tr>
<th>Procedural Events</th>
<th>N=10</th>
<th>30-Day Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
<td></td>
<td>Any mortality – no. (%)</td>
</tr>
<tr>
<td>Valve implanted</td>
<td>10 (100.0%)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Technical success (MVARC)</td>
<td>10 (100.0%)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Implant retrieved/abandoned</td>
<td>0 (0.0 %)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Procedural stroke</td>
<td>0 (0.0 %)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Emergency surgery</td>
<td>0 (0.0 %)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>ECMO required</td>
<td>0 (0.0 %)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Procedural mortality</td>
<td>0 (0.0 %)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>IASD Closures</td>
<td>0 (0.0 %)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

**Core Lab Echo Evaluation (n=10)**

- **MR Grade**
  - Baseline: 30% Grade 4+, 20% Grade 3+, 22% Grade 2+, 28% Grade 1+, 20% None
  - 1 Month: 80% Grade 4+, 78% Grade 3+, 22% Grade 2+, 20% Grade 1+, 0% None

- **NYHA Classification (n=10)**
  - Baseline: 33% Class 4, 44% Class 3, 7% Class 2, 10% Class 1
  - 30 Day: 20% Class 4, 70% Class 3, 10% Class 2, 11% Class 1

* n=9 (1 missed 1 Month visit)
AltaValve

- Supra-annular with minimally protrusion (<15 mm) into the left ventricle
- Anchoring is achieved by a nitinol frame that is oversized relative to the left atrium
- Orientation parallel to the outflow tract
- Transapical or transseptal approaches
- No interaction with the native mitral valve or apparatus

AltaValve

First Percutaneous AltaValve
May 2023
First 2 patients in MAC arm were treated with SAPIEN XT, all subsequent patients were treated with SAPIEN 3 valves.
Mitral Annular Calcification Score


Mitral Annular Calcification Score

**MITRAL II Pivotal Trial**

**Mitral Implantation of TRAnscatheter vaLves**

Severe MAC with Severe mitral stenosis or 3+mitral regurgitation or mixed ≥ moderated stenosis and ≥ moderate regurgitation.

- **Valve-in-MAC**
  - N=110
- **Natural History**
  - N=100
- **Transeptal**
  - MAC score ≥ 7

Primary End Point

All Cause Morality and Hospitalization for Heart Failure

Screen Failure

- 89.0% failure (n=203)
  - 32% Anatomical Reason
  - 35% Clinical Risk Exclusion
  - 22% Futility Marker

**Intrepid Global Pilot Study**

- 26.1%
- 37.3%
- 27.6%

- Native MV too large
- MV too small
- Concern for LVOT obstruction
- Enrollment

Meduri CU et al. JACC Card Interventions 2019;12:2402-2412
Screen Failure

Cephea™ EFS Phase 1 Screening

<table>
<thead>
<tr>
<th>Primary Screen Fail Reason</th>
<th>%</th>
<th>Future Cephea Device Generations to Address With:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large Annular Dimensions</td>
<td>34%</td>
<td>New valve design and sizes</td>
</tr>
<tr>
<td>Small Annular Dimensions</td>
<td>20%</td>
<td>Advanced delivery system</td>
</tr>
<tr>
<td>Septal Height</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td>neoLVOT</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>Anatomical Interference</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>Sealing/Seating</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>Inclusion/Exclusion</td>
<td>6%</td>
<td>Study Protocol modifications</td>
</tr>
</tbody>
</table>

Current Challenges of TMVR

Anatomic Challenges
- Sizing
- LVOT
- Various anatomies

Device Challenges
- Leaflet Thrombosis
- Need for AC
- Anatomical Interference

Procedure Challenges
- Complex Devices
- Expert Imaging
- Too high-risk patients
LVOT Obstruction Prevention

- Septal Reduction Strategies
- Anterior Leaflet Strategies

- Alcohol Septal Ablation
- Radiofrequency ablation
- SESAME Myotomy
- LAMPOON
- SITRAL
- BATMAN

Balloon-Assisted Translocation of the Mitral ANterior leaflet (BATMAN)
Surgical Implantation of TRanscatheter valve in mitral Annular caLcification (SITRAL)

- Orient the valve into standard surgical configuration
- Remove midportion of anterior leaflet A2 and septum if needed
- Teflon felt skirt to prevent PVL
- Securing sutures

Management algorithm

- Surgery/TEER Candidate
  - Yes
  - Surgery/TEER Candidate
  - No
  - TMVR Candidate
  - Yes
  - TMVR
  - No
  - High Risk LVOT
  - ViMAC Candidate
  - Other Factors
  - Modification
  - ViMAC +/- Modification
  - High Risk Surgery Medical Therapy
  - SITRAL

Re-assess
Back to our patient - Transeptal AltaValve

Transeptal AltaValve

Balloon Septostomy  Valve placement across the annulus  Cage deployment
Transeptal AltaValve

Device release

ASD Closure
Case 2

- 84-yo female with severe symptomatic MR, torrential TR, HFpEF (EF 60-65%) and SC-PPM
- Recurrent hospitalizations with HF exacerbation despite being on GDMT
- Underwent Mitral TEER with Mitraclip (NTx1)

Case 2

- Remains symptomatic despite Mitral TEER with Mitraclip
- On stable dose of Torsemide
- NYHA III
- High surgical risk
- Right heart catheterization:
  - RA - mean 9mmHg (V 15mmHg)
  - RV - 49/1 mmHg (ED 11mmHg)
  - PA - 46/18/28 mmHg
  - PCWP - 10mmHg
Tricuspid Valve

Torrential TR

Deep Transgastric
Background

- Tricuspid regurgitation is estimated to affect >1.5 million people in the U.S.
- Yearly incidence of about 200,000 patients in the US and >300,000 patients in Europe
- Limited medical therapy options – diuretics
- Severity easily underestimated
- Volume overload well tolerated for years

35 US Community/Academic Hospitals >714,000 patients

<table>
<thead>
<tr>
<th>VHD Type</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR</td>
<td>7.1%</td>
</tr>
<tr>
<td>MR</td>
<td>6.5%</td>
</tr>
<tr>
<td>AS</td>
<td>4.1%</td>
</tr>
<tr>
<td>AR</td>
<td>2.3%</td>
</tr>
<tr>
<td>MS</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

Prevalence of significant VHD

Brennan et al. ACC 2022

Tricuspid Regurgitation

Primary
- Congenital
- Infection
- Inflammation
- Carcinoid
- Radiation

Secondary
- Pulmonary Hypertension
- RV Myopathy
- RV Volume
- High output
- Idiopathic

10%* 90%
Secondary Tricuspid Regurgitation

Annular dilation and flattening of the normal “saddle-shaped” configuration

Nishimura et al. Heart 2018;104:798-806

Survival with Tricuspid Regurgitation
Community population (N=1,095)

Isolated TR survival

Survival Plot

Survival with Tricuspid Regurgitation
VA study (N=5,223) over 4 years

Nath et al. JACC 2004; 43(3): 405-9

Tricuspid Valve Surgery - Outcomes

• STS ACSD Registry
• 18 years or older
• Isolated Tricuspid valve repair or replacement
• July 1, 2017 – June 30, 2023
• 13,587 procedures at 842 participating sites
• ~2,000 cases per year

**Long-term Survival - Isolated TR Surgery**

Longitudinal echocardiography database (N=3,276)

---

**Surgical Intervention Indications**

- Left sided surgery, severe TR (I)
- Left sided surgery, progressive TR in the context of either 1) tricuspid annular dilation (tricuspid annulus end diastolic diameter >4.0 cm) or 2) prior signs and symptoms of right-sided HF (IIA)
- Severe primary or secondary TR on GDMT (IIA)
- Asymptomatic severe primary TR with RV dilation or RV systolic dysfunction (IIB)
- Symptomatic severe TR with hx of prior surgery and absence of severe pulmonary hypertension or severe RV systolic dysfunction (IIB)

No class I recommendation for isolated TR
Tricuspid Regurgitation is Prevalent but Rarely Treated with Surgery

**1.6M**

Moderate to severe TR prevalence

<8k

Surgical procedures annually

---

**ECHO - Tricuspid Regurgitation Severity**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>MILD</th>
<th>MODERATE</th>
<th>SEVERE</th>
<th>MASSIVE</th>
<th>TORRENTIAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vena Contracta width (biplane average)</td>
<td>&lt;3 mm</td>
<td>3-6.9 mm</td>
<td>7 mm - 13 mm</td>
<td>14-20 mm</td>
<td>≥21 mm</td>
</tr>
<tr>
<td>EROA by PISA</td>
<td>&lt;20 mm²</td>
<td>20-39 mm²</td>
<td>40-59 mm²</td>
<td>60-79 mm²</td>
<td>≥80 mm²</td>
</tr>
<tr>
<td>3D Vena Contracta Area or Quantitative Doppler EROA</td>
<td>-</td>
<td>-</td>
<td>75-94 mm²</td>
<td>95-114 mm²</td>
<td>≥115 mm²</td>
</tr>
</tbody>
</table>

Example:

Hahn et al. JACC Cardiol Imag. 2019; 12(3):469-90
Tricuspid Valve Nomenclature

Hahn et al. JACC Cardiol Imag. 2021;14(7):1299-305

The Big 5 for Success
G-A-L-I-O

GAPS
Small <7 mm
Moderate 7-10 mm
Large >10 mm

ANATOMY
# Leaflets
Leaflet length
Leaflet mobility
Coaptation planes

LEADS
Location
Impingement
Interaction

IMAGING
TEE windows
Shadowing
ICE
Horizontal heart

OTHER
Right Ventricle
Pulmonary Vascular
Left Sided Heart

Courtesy of Dr. Hamid
Anatomical Success Predictors

<table>
<thead>
<tr>
<th>EASY</th>
<th>MEDIUM</th>
<th>HARD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small (&lt;7mm) gaps</td>
<td>Moderate (&gt;7 but &lt;=10mm) gaps</td>
<td>Large (&gt;10mm) gaps</td>
</tr>
<tr>
<td>Septo-anterior jet location</td>
<td>Septo-posterior location</td>
<td>Thick and/or severely restricted leaflets</td>
</tr>
<tr>
<td>Favorable leaflet annular index</td>
<td>Type III or IV leaflet morphology</td>
<td>Antero-posterior jet location</td>
</tr>
<tr>
<td>Type I/II leaflet morphology</td>
<td>CIED in commissure and/or not a jet location “Non-hostile”</td>
<td>Poor echo visualization (role for ICE)</td>
</tr>
<tr>
<td></td>
<td>Minimal leaflet restriction</td>
<td>Hostile CIED</td>
</tr>
<tr>
<td></td>
<td>Focal primary disease</td>
<td>Horizontal heart (role for ICE)</td>
</tr>
</tbody>
</table>

Transcatheter Tricuspid Landscape

[Diagram showing various transcatheter tricuspid valve devices]
TRILUMINATE -
Enrollment and Treatment Pathway

- Symptomatic Severe Tricuspid Regurgitation
  and Intermediate or greater risk for TV surgery

Subjects Approved by Eligibility Committees for:
- Suitable Anatomy
- Adequate management
- No severe Pulmonary Hypertension

- Ability to reduce TR to moderate or less

Randomize 1:1

TriClip Device (N=175)
Medical Therapy (N=175)

12-month follow up

TriClip G4 Delivery System

- Four Implant Sizes
  - G4 NT
  - G4 NTW
  - G4 XTW
  - G4 XT

- Controlled Grasper Actuation
  - Optimize \& maintain grasping

- Delivery System
  - Precision delivery for accurate results in complex conditions
  - Near-LC torque response and stability with a high support delivery system

- Steering Guide Catheter
  - Gain the height you need over the valve
  - Maintain coaxial position during steering and positioning
  - Easily navigate away from the target by changing perpendicularity to the tricuspid valve
  - Navigate across all lines of potential with minimal shearing

- Detail Curve
  - Tricuspid optimized curve placement for direct access

65

66
30-day Adverse Events

<table>
<thead>
<tr>
<th>Variable</th>
<th>TRILUMINATE™ Pivotal RCT (Device Arm) N=172</th>
<th>TRILUMINATE™ Pivotal SA N=99</th>
<th>bRIGHT N=111</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause Mortality</td>
<td>0.6%</td>
<td>0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Cardiovascular Mortality</td>
<td>0.6%</td>
<td>0%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Endocarditis Requiring Surgery</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>New-onset Renal Failure</td>
<td>1.2%</td>
<td>0%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Non-elective CV Surgery, TVRS For Device-related AE</td>
<td>0%</td>
<td>0%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Major Bleeding*</td>
<td>5.1%</td>
<td>5%</td>
<td>7.2%</td>
</tr>
<tr>
<td>Single Leaflet Device Attachment (SLDA)</td>
<td>7.0%</td>
<td>7.5%</td>
<td>3.8%</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.6%</td>
<td>0%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Device Embolization</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Device Thrombosis</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>New CRT/CRT-D/I/ICD/Permanent Pacemaker</td>
<td>0.6%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

*Defined as bleeding ≥ Type 3 based on a modified Bleeding Academic Research Consortium (BARC) definition
Reduction in TR Severity

Physiologic Remodeling
QOL Improvement

No waning effect

![Graph showing QOL Improvement](adapted from Adams D, Sorajja P, et al. TCT 2023)

**FDA Approves TriClip TEER Device for Tricuspid Repair**

**ABBOTT RECEIVES FDA APPROVAL FOR TRICLIPTM, FIRST-OF-ITS-KIND DEVICE TO REPAIR LEAKY TRICUSPID HEART VALVE**

*Updated: The approval was based on positive data from the TRIUMPH trial, which included a highly symptomatic population.

**Breaking News**

**FDA Update: Agency Approves Abbott TriClip to Treat TR**

*Apr 02, 2024*

**ACC News Story**

First-in-human 2017

1st Triluminate case

August 28th, 2019

Last Triluminate case

April 2nd, 2024

1st commercial case

April 4th, 2024
CLASP II TR trial

Roll-in cohort of up to first 3 patients per site

Patients with symptomatic severe TR despite medical therapy

Multidisciplinary Heart Team Assessment

- 2:1 PASCAL System + OMT
- OMT alone

Primary endpoint (24 months)
Composite endpoint including all-cause mortality, RVAD implantation or heart transplant, tricuspid valve intervention, heart failure hospitalizations, and Quality of Life improvement (measured by KCCQ score)

CLASP II TR trial — Roll in Cohort
Enrollment and procedural characteristics

Roll-in patients
N=73
Pending visit n=2
Missed visit n=1
Withdraw n=1
30-day follow up n=68

% (n/N) or Mean ± SD (N)

Successful implant rate
84.4 (54/64)
PASCAL Ace
88.9 (56/63)
Mean number of devices implanted
1.5 ± 0.6
Device time (implant insertion to guide sheath removal), mins
148.2 ± 71.9
Length of hospital stay (procedure to discharge), days
1.7 ± 1.5
Discharged to home
100%

CLASP II TR trial – Roll in Cohort
TR reduction and quality of life improvement

83.0% improved by ≥ 1 TR grade, 62.3% by ≥ 2 grades, and 73.6% reached ≤ moderate TR at 30 days

CLASP II TR trial – Roll in Cohort
Major adverse events

<table>
<thead>
<tr>
<th>CEC-adjudicated MAEs, N=69*</th>
<th>30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (n)</td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0 (0)</td>
</tr>
<tr>
<td>New need for renal replacement therapy</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Major cardiac structural complications</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Non-elective tricuspid valve re-intervention, percutaneous or surgical</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Severe bleeding</td>
<td>2.9 (2)</td>
</tr>
<tr>
<td>Major access site and vascular complications</td>
<td>0 (0)</td>
</tr>
<tr>
<td>SLDA[T]</td>
<td>5.8 (4)</td>
</tr>
<tr>
<td>Composite MAE rate</td>
<td>8.7 (6)</td>
</tr>
</tbody>
</table>

Other events
- All-cause mortality: 0
- Heart failure hospitalization: 0

Orthotopic Replacement

**EVOQUE**

**INTREPID**

**VDYNE**

EVOQUE Tricuspid Valve Replacement System

Unique valve design engages leaflets, chords, and annulus to achieve secure placement.

Atraumatic anchors compatible with pre-existing leads and respect the native anatomy.

Conforming frame designed to achieve optimal retention force.

Multiple sizes offer treatment for a broad range of tricuspid pathologies and anatomies (44, 48 and 52 mm).

28F transfemoral delivery system with multiple planes of flexion and depth control.
TRISCEND II Trial Design

- Screening and Enrollment
  - Eligibility Confirmed by Independent Review Committee
- EVOQUE + OMT
  - Pre-procedure OMT continued ≥ 3 months post-implant
  - Concomitant procedures not permitted
- OMT Alone
  - Pre-study OMT continued (primarily oral diuretics)
- Annual Follow-up Through 5 Years

- Day 30
  - Primary Safety
- Month 6
  - Primary Effectiveness
- Year 1
  - Hierarchical Outcomes

TRISCEND II: Two-Part Study Design Based on the Breakthrough Designation

- ‘First 150’
  - First 150 patients randomized and treated

- Total Cohort
  - N = 400
  - All-randomized patients
  - Enrolled, follow-up ongoing

Primary Endpoints

<table>
<thead>
<tr>
<th>First 150</th>
<th>Total Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety (30 Days)</td>
<td>✓</td>
</tr>
<tr>
<td>• Composite MAE rate</td>
<td>✓</td>
</tr>
<tr>
<td>Effectiveness (6 Months)</td>
<td>✓</td>
</tr>
<tr>
<td>• TR grade reduction</td>
<td>✓</td>
</tr>
<tr>
<td>• Hierarchical composite of KCCQ, NYHA and 6MWD</td>
<td>✓</td>
</tr>
</tbody>
</table>

Hierarchical Composite (1 Year)

1. All-cause mortality
2. RVAD implant or heart transplant
3. LV surgery or intervention
4. Annualized heart failure hospitalization
5. KCCQ, NYHA, 6MWD

Prespecified analysis
TRISCEND II 30-Day Results

<table>
<thead>
<tr>
<th>CEC-Adjudicated Major Adverse Events</th>
<th>EVOQUE + OMT N=95 % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular mortality</td>
<td>3.2 (3)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1.1 (1)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>New need for renal replacement therapy</td>
<td>1.1 (1)</td>
</tr>
<tr>
<td>Severe bleeding*</td>
<td>10.5 (10)</td>
</tr>
<tr>
<td>Non-elective TV re-intervention</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Major access site and vascular complication</td>
<td>3.2 (3)</td>
</tr>
<tr>
<td>Major cardiac structural complication</td>
<td>2.1 (2)</td>
</tr>
<tr>
<td>Device-related pulmonary embolism</td>
<td>1.1 (1)</td>
</tr>
<tr>
<td>Arrhythmia and conduction disorder requiring permanent pacing</td>
<td>14.7 (14)</td>
</tr>
<tr>
<td>Composite MAE Rate*</td>
<td>27.4 (26)</td>
</tr>
</tbody>
</table>

TR Grade at 6 Months

![Graph showing TR Grade comparison between EVOQUE + OMT and OMT Alone at baseline and 6 months.](image)
Changes in KCCQ at 30 days and 6 months

Baseline Mean KCCQ Score

- 30 Days: 50.6 (n=82)
- 6 Months: 50.7 (n=79)

EVOQUE + OMT
OMT Alone

Δ = 15.8
Δ = 17.8

Large Improvement

MCID

Change in NYHA and 6 MWT

Patients per NYHA Class (%)

Baseline
EVOQUE + OMT (n=80)
OMT Alone (n=61)

Class IV: 75.0, 21.3
Class III: 60.3, 29.3
Class II: 29.3
Class I: 1.3

6 Months
EVOQUE + OMT (n=80)
OMT Alone (n=61)

Class IV: 50.0, 40.8
Class III: 50.0
Class II: 29.3
Class I: 1.3

Change from Baseline in 6MWD (Meters)

30 Days
EVOQUE + OMT (n=80)
OMT Alone (n=61)

Δ = 9.8
Δ = 10.0

6 Months
EVOQUE + OMT (n=80)
OMT Alone (n=61)

Δ = 31.9
Δ = 33.3

Kodali S. TCT 2023
FDA Approves First Transcatheter Tricuspid Valve Replacement Device

(UPDATED) Edwards Lifesciences says there are “favorable trends” in hard outcomes among patients who have completed 1-year follow-up.

by L.A. McDonald | FEBRUARY 02, 2024

FDA Update: Agency Approves EVOQUE System For TR

Feb 02, 2024

ACC News Story

The U.S. Food and Drug Administration (FDA) has approved the EVOQUE tricuspid valve replacement system for the treatment of tricuspid regurgitation (TR). According to an Edwards press release, “It is the first transcatheter therapy to receive [FDA] approval for the treatment of [TR] and is “indicated for the improvement of health status in patients with symptomatic severe TR despite optimal medical therapy, for whom tricuspid valve replacement is deemed appropriate by a heart team.”

Edwards' EVOQUE Valve Replacement System First Transcatheter Therapy to Earn FDA Approval for Tricuspid Valve

Irvine, CA – (BUSINESS WIRE) – Edwards Lifesciences Corporation (NYSE: EW) today announced the company’s EVOQUE tricuspid valve replacement system is the first transcatheter therapy to receive U.S. Food and Drug Administration (FDA) approval for the treatment of tricuspid regurgitation (TR). The EVOQUE system is indicated for the improvement of health status in patients with symptomatic severe TR despite optimal medical therapy (OWT), for whom tricuspid valve replacement is deemed appropriate by a heart team.

Intrepid - Tricuspid Valve

Intrepid - Tricuspid Valve houses a 29 mm tri-leaflet valve delivery system - 29Fr system in a conformable outer stent anchors without leaflet capture or need for rotational alignment across three sizes (43, 46, 50 mm). The presence of pacing leads between the two stent frames may allow for future pacemaker implantation in an early feasibility trial.
VDYNE Valve

- Side-delivery technology – vertical folding
- 28Fr Transfermoral Delivery catheter
- Double-frame nitinol prosthesis that houses a 30mm porcine trileaflet valve
- Five valve sizes to treat a broader range of patient anatomies (perimeter up to 180mm)
- Securement mechanisms at RVOT, ventricular free wall and posterior septum - (<10% oversizing)
- Flexible - repositionable and retrievable
- No ventricular exclusions - indifferent to ventricular size or shape

VDYNE Early Feasibility Study

1st Vdyne EFS case
April 1st, 2024
Heterotopic Valve Implantation

**Indications**
- Patients unsuitable for TEER/TTVR
- Large gaps, RV dysfunction, Pacer induced TR, large annulus size
- Advanced TV disease

**Challenges:**
- Ventricularization of RA
- Large & variable SVC/IVC size may require custom-made devices
- Impact of severe RV failure on LV
- Worsening Cardiac Output
- Valve/Device Thrombosis
- Long-term anticoagulation
- Treatment effect durability

Pacer wire manipulation

<table>
<thead>
<tr>
<th>GAPS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ANATOMY</td>
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</tr>
<tr>
<td>LEADS</td>
<td></td>
</tr>
<tr>
<td>IMAGING</td>
<td></td>
</tr>
<tr>
<td>OTHER</td>
<td></td>
</tr>
</tbody>
</table>
After 2\textsuperscript{nd} Clip Deployment

![Image of echocardiogram after 2nd clip deployment]

IntraCardiac Echocardiogram

![Image of echocardiogram showing intracardiac view]

46 of 48
Wire release

Key Points

- Valvular heart is frequent in aging population – increased complexity
- Surgery “not an option” – age, co-morbidities, anatomical factors
- Transcatheter therapies have potential to provide options
- TMVR, TTVR are not TAVR (yet!)
- Improved imaging - ECHO, CT and MRI
- Improved devices respecting anatomy and minimizing interaction
- Multiple dedicated devices at various stages
- Many patients referred for clinical trials are currently excluded
Thank you!
Konstantinos.voudris@allina.com
@kvoudris