NON SURGICAL TREATMENT OF CARDIAC DISEASE

PETER J SABIA, MD FACC
ASSOCIATES IN CARDIOLOGY
SILVER SPRING, MARYLAND
TOPICS

- ATRIAL SEPTAL DEFECT
- VSD
- IHSS
- PERCUTANEOUS AORTIC VALVE
- PERCUTANEOUS MITRAL VALVE
- LAA CLOSURE
- ABDOMINAL AORTIC ANEURYSM REPAIR
ATRIAL SEPTAL DEFECT
TYPES OF ASD
PRIMUM ATRIAL SEPTAL DEFECT
SINUS VENOSUS ASD
SECUNDUM ATRIAL SEPTAL DEFECT
INDICATIONS FOR CLOSURE

• Class 1- Closure of an ASD either percutaneously or surgically is indicated for right atrial and RV enlargement with or without symptoms. *(LoE: B)*

• Class 2a- Closure of an ASD, either percutaneously or surgically, is reasonable in the presence of:
  a. Paradoxical embolism. *(Level of Evidence: C)*
  b. Documented orthodeoxia-platypnea. *(LoE: B)*

Class 3- Patients with severe irreversible PAH and no evidence of a left-to-right shunt should not undergo ASD closure.
ASD with RVE and Flat IVS
THROMBUS
SURGICAL VIEW OF ASD
SURGICAL CLOSURE ASD
ASD DEVICES
ASD CLOSURE DEVICES
ASD CLOSURE
18mm Amplatzer Cribriform ASO
ECHO OF ASD CLOSURE
MULTIPLE ASD CLOSURE
ASD CLOSURE

• Preferential use for Ostium Secundum

• Out of 174 “intention to treat procedures”
  – 151 patients received a single device
  – 10 patients received > 1 device
  – 13 patients received no device (7.5%)
    • Defect > 40 mm : 5
    • Insufficient rim : 5
    • Three defects : 1
    • Multiple fenestrations : 1
    • Iliac vein access : 1
# ASD Adverse Events

## Table 1: Adverse Events - Pivotal Study

<table>
<thead>
<tr>
<th>Major Adverse Events</th>
<th>AMPLATZER Patients</th>
<th>Surgical Control Patients</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Arrhythmia requiring major treatment</td>
<td>2/442 (0.5%)</td>
<td>0/154 (0.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Device Embolization with surgical removal</td>
<td>3/442 (0.7%)</td>
<td>0/154 (0.0%)</td>
<td>0.57</td>
</tr>
<tr>
<td>Device Embolization with percutaneous removal</td>
<td>1/442 (0.2%)</td>
<td>0/154 (0.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Delivery System Failure</td>
<td>1/442 (0.2%)</td>
<td>0/154 (0.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Pericardial Effusion with tamponade</td>
<td>0/442 (0.0%)</td>
<td>3/154 (1.9%)</td>
<td>0.017</td>
</tr>
<tr>
<td>Pulmonary Edema</td>
<td>0/442 (0.0%)</td>
<td>1/154 (0.6%)</td>
<td>0.26</td>
</tr>
<tr>
<td>Repeat Surgery</td>
<td>0/442 (0.0%)</td>
<td>2/154 (1.3%)</td>
<td>0.066</td>
</tr>
<tr>
<td>Surgical Wound Adverse Events</td>
<td>0/442 (0.0%)</td>
<td>2/154 (1.3%)</td>
<td>0.066</td>
</tr>
<tr>
<td><strong>Total Major Adverse Events Patients</strong></td>
<td><strong>7/442 (1.6%)</strong></td>
<td><strong>8/154 (5.2%)</strong></td>
<td><strong>0.030</strong></td>
</tr>
</tbody>
</table>
VENTRICULAR SEPTAL DEFECT CLOSURE
Large perimembranous inlet VSD – no role for a device
Patient Selection for Device Closure of VSD

- Hemodynamically significant
- Qp/Qs > 1.5
- LA or LV enlargement
- Cardiomegaly on CXR
- Failure to thrive because of VSD
- Aortic valve rim 4 mm or more
- AV valve rim 4 mm or more
Different Amplatzer VSD Devices

- **Muscular VSDs** being closed routinely by catheter techniques
- 4-18 mm sizes, waist 7 mm, discs = waist + 8 mm
- Waist should be 1 – 3 mm larger than VSD

Recent trend towards catheter closure of **Perimembranous VSDs**

The Heart Center at Nationwide Children’s Hospital
TEE Guidance for Apical VSD
Muscular VSD  
N=80

Technical Failure
Unable to cross the defect | 1
Defect too big | 2
Patient developed hypotension & bradycardia | 1
Device embolized to LV-surgical removal | 1
Catheter dislodgment, blood loss, death | 1
Cardiac perforation, death | 1

***Most SAE related to size of patient < 5.2Kg

The Heart Center at Nationwide Children’s Hospital
IHSS
Idiopathic Hypertrophic Subaortic Stenosis
IHSS Pathology
IHSS
IHSS - SAM
LVOT GRADIENT
ALCOHOL SEPTAL ABLATION
Septal Ablation

Alcohol Septal Ablation

Before

After
2D echocardiography

Identification of LV obstruction site and mechanisms (SAM-related/SAM-free) in order to delineate the target zone

- Septal thickness in the target zone ≥18 mm
  - MCE
    - Septal coronary branch accurately supplies target zone
    - Minimal potential area of necrosis
    - Alcohol septal ablation
  - Mismatch between septal coronary branch and target zone
    - Threatening opacification of the papillary muscle or the left or right ventricle wall
    - High-risk pattern (contrast extends beyond target zone, target zone is excessively large, or contrast extends to the right side of septum)

- Septal thickness in the target zone <18 mm
  - Surgical repair or replacement of mitral valve
  - Surgical myectomy

TAVI

TRANSVASCULAR AORTIC VALVE INTERVENTION.
Aortic Stenosis

Normal

Degenerative calcific  Bicuspid  Rheumatic
Figure 1. Disease Progression in Calcific Aortic Stenosis, Showing Changes in Aortic-Valve Histologic Features, Leaflet Opening in Systole, and Doppler Velocities.

In Panel A, the histology of the early lesion is characterized by a subendothelial accumulation of oxidized low-density lipoprotein (LDL), production of angiotensin (Ang) II, and inflammation with T lymphocytes and macrophages. Disease progression occurs by several mechanisms, including local production of proteins, such as osteopontin, osteocalcin, and bone morphogenic protein 2 (BMP-2), which mediate tissue calcification; activation of inflammatory signaling pathways, including tumor necrosis factor α (TNF-α), tumor growth factor β (TGF-β), the complement system, C-reactive protein, and interleukin-1β; and changes in tissue matrix, including the accumulation of tenasin C, and up-regulation of matrix metalloproteinase 2 and alkaline phosphatase activity. In addition, leaflet fibroblasts undergo phenotypic transformation into osteoblasts, regulated by the Wnt3–Lrp5–β catenin signaling pathway. Microscopic accumulations of extracellular calcification (Ca++) are present early in the disease process, with progressive calcification as the disease progresses and areas of frank bone formation in end-stage disease. The corresponding changes in aortic-valve anatomy are viewed from the aortic side with the valve open in systole (Panel B) and in Doppler aortic-jet velocity (Panel C).
The standard for critical AS RX is Surgical AVR

- Mechanical
- Tissue
- Stentless
- Homograft
- Ross
Lenox Hill Heart and Vascular Institute of New York

Edwards-Sapien

- Bovine pericardium Tri-leaflet configuration
- Mounted on a 14 mm long x 23 mm or 26 mm highly resistant stainless steel balloon expandable stent
- Delivery system 24F - 26F (ID)

ReValving® System CoreValve

- Single layer porcine pericardium
- Tri-leaflet configuration
- Nitinol frame self-expandable - Inflow: 26 and 29 mm – 20 to 27 mm annulus
- Delivery system 18F / 12F (OD)
TAVI
SAVI
CORE VALVE
The DFM AV Prosthesis European Clinical Trial

- Aortic orifice area in patients with a permanent implant

$P<0.001$ (repeated-measures ANOVA)

![Box plots showing changes in aortic orifice area over time](image)

- Baseline ($n=20$): $0.60$
- Post ($n=20$): $1.50$
- 30 Days ($n=13$): $1.57$
- 90 Days ($n=11$): $1.34$

$P<0.05$* for Baseline vs. Post
$P=n.s.$* for other comparisons

*Holm test
The PARTNER IDE Trial

Population: High Risk/Non-Operable Symptomatic, Critical Calcific Aortic Stenosis

Co-principal Investigators:
Martin B. Leon, MD Interventional Cardiology
Craig Smith, MD, Cardiac Surgeon
Columbia University

Two Trials: Individually Powered Cohorts (Cohorts A & B)

Cohort A
- n= up to 690 pts
- ASSESSMENT: Operability
  - Yes
  - Cohort A TA
  - 1:1 Randomization
  - Powered to be Pooled with TF
- Transfemoral VS Transapical
- AVR Control

Primary Endpoint: All Cause Mortality (Non-inferiority)

Cohort B
- n=350 pts
- ASSESSMENT: Operability
  - No
- Transfemoral VS Transapical
- AVR Control

Primary Endpoint: All Cause Mortality (Superiority)

ASSESSMENT: Transfemoral Access

Cohort A TF
- Powered Independently
- 1:1 Randomization
- Transfemoral VS AVR Control

Cohort A TA
- Powered to be Pooled with TF
- 1:1 Randomization
- Transapical VS AVR Control

Cohort B
- Not in Study
- 1:1 Randomization
- Transfemoral VS Medical Management Control

Total n= 1040

Update SEPT 2008
## PARTNERS TAVI VS MED

### Primary End Points

<table>
<thead>
<tr>
<th>End point</th>
<th>TAVI (%)</th>
<th>Standard (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-y all-cause death</td>
<td>30.7</td>
<td>50.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1-y all-cause death or repeat hospitalization</td>
<td>42.5</td>
<td>71.6</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### TAVI vs Standard Therapy Secondary End Points

<table>
<thead>
<tr>
<th>End point</th>
<th>TAVI (%)</th>
<th>Standard (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-d major stroke</td>
<td>5.0</td>
<td>1.1</td>
<td>0.06</td>
</tr>
<tr>
<td>30-d vascular comp</td>
<td>16.2</td>
<td>1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1-y cardiac death</td>
<td>19.6</td>
<td>41.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1-y major bleeding</td>
<td>22.3</td>
<td>11.2</td>
<td>0.007</td>
</tr>
</tbody>
</table>
Core Valve in Bicuspid Valve
Incompletely Deployed Core Valve
Valve in Valve
Figure 4. Deployment of 23 mm Sapien valve within pre-existing 21 mm Perimount valve. Delivery balloon has been prepped with 1 less milliliter of fluid.
TAVI Valve in Valve
MITRAL REGURGITATION
Perspective

- >250,000 cases of significant Mitral Regurgitation diagnosed annually in the US

- Current therapeutic options:
  - Medical management
    - Effective in symptom management
    - Ineffective in treating underlying pathophysiology or disease progression
  - Surgical Repair or Replacement (Standard of Care)
    - Effective yet invasive with associated morbidity
    - Only ~20% of patients with significant MR undergo MV surgery

- Unmet need for an effective less invasive option
Catheter-Based Mitral Valve Repair
MitraClip® System
EVEREST II Randomized Clinical Trial

Study Design

279 Patients enrolled at 37 sites

- Significant MR (3+-4+)
- Specific Anatomical Criteria

Randomized 2:1

Device Group
MitraClip System
N=184

Control Group
Surgical Repair or Replacement
N=95

Echocardiography Core Lab and Clinical Follow-Up:
Baseline, 30 days, 6 months, 1 year, 18 months, and annually through 5 years
EVEREST II RCT: Primary Endpoints
Per Protocol Cohort

Safety
Major Adverse Events
30 days

Device Group, n=136
- 9.6%
- $p_{SUP} <0.0001$

Control Group, n=79
- 57.0%

Met superiority hypothesis
- Pre-specified margin = 6%
- Observed difference = 47.4%
- 97.5% LCB = 34.4%

Effectiveness
Clinical Success Rate*
12 months

Device Group, n=134
- 72.4%
- $p_{NI} =0.0012$

Control Group, n=74
- 87.8%

Met non-inferiority hypothesis
- Pre-specified margin = 31%
- Observed difference = 15.4%
- 95% UCB = 25.4%

* Freedom from the combined outcome of
death, MV surgery or re-operation for MV
dysfunction, MR >2+ at 12 months

LCB = lower confidence bound
UCB = upper confidence bound
**EVEREST II RCT: Primary Safety Endpoint**

**Per Protocol Cohort**

<table>
<thead>
<tr>
<th>30 Day MAE, non-hierarchical</th>
<th># Patients experiencing event</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Device Group (n=136)</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
</tr>
<tr>
<td>Major Stroke</td>
<td>0</td>
</tr>
<tr>
<td>Re-operation of Mitral Valve</td>
<td>0</td>
</tr>
<tr>
<td>Urgent / Emergent CV Surgery</td>
<td>0</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>0</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>0</td>
</tr>
<tr>
<td>Deep Wound Infection</td>
<td>0</td>
</tr>
<tr>
<td>Ventilation &gt;48 hrs</td>
<td>0</td>
</tr>
<tr>
<td>New Onset Permanent Atrial Fib</td>
<td>0</td>
</tr>
<tr>
<td>Septicemia</td>
<td>0</td>
</tr>
<tr>
<td>GI Complication Requiring Surgery</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>All Transfusions ≥2 units*</td>
<td>12 (8.8%)</td>
</tr>
</tbody>
</table>

**TOTAL % of Patients with MAE**

- **Device Group**: 9.6%
- **Control Group**: 57.0%

\[p<0.0001^*\]

\[(95\% \text{ CI 34.4\%, 60.4\%})\]

*p<0.0001 if include Major Bleeding only*
LAA CLOSURE
Non-Valvular Atrial Fibrillation

- 500,000 strokes/year in U.S.
- Up to 20% of ischemic strokes occur in patients with atrial fibrillation

Stroke 22(18), 1991
Non-Valvular Atrial Fibrillation Warfarin Use in AF Patients by Age

- Only 55% of AF patients with no contraindications have evidence of warfarin use in previous 3 months
- Other studies cite warfarin use 17-50%
- Elderly patients with increased absolute risk least likely to be taking warfarin; Contraindications 30-40%

Ann Int Med 131(12), 1999
LAA Thrombus

LAA containing blood clot
WATCHMAN LAA Closure Device in situ

- Plane of maximum diameter distal to ostium
- Fixation barbs engage LAA wall
LAA Closure
LAA Closure Device
PROTECT AF Trial Endpoints

- **Primary Efficacy Endpoint**
  - All stroke: ischemic or hemorrhagic
    - deficit with symptoms persisting more than 24 hours or
    - symptoms less than 24 hours confirmed by CT or MRI
  - Cardiovascular and unexplained death: includes sudden death, MI, CVA, cardiac arrhythmia and heart failure
  - Systemic embolization

- **Primary Safety Endpoint**
  - Device embolization requiring retrieval
  - Pericardial effusion requiring intervention
  - Cranial bleeds and gastrointestinal bleeds
  - Any bleed that requires ≥ 2uPRBC

- NB: Primary effectiveness endpoint contains safety events
## Intent-to-Treat

### Primary Safety Results

**Randomization allocation (2 device : 1 control)**

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Events (no.)</th>
<th>Total pt-yr</th>
<th>Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>900 pt-yr</td>
<td>48</td>
<td>554.2</td>
<td>8.7 (6.4, 11.3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Events (no.)</th>
<th>Total pt-yr</th>
<th>Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>312</td>
<td>4.2</td>
<td>(2.2, 6.7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rel. Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.08 (1.18, 4.13)</td>
</tr>
</tbody>
</table>

### Intent-to-Treat - Event-free probability

**Device vs. Control**

- **Control**
  - Days: 730
  - Event-free probability: 0.9

- **Watchman**
  - Days: 1,095
  - Event-free probability: 0.8
EVAR
ENDOVASCULAR ANEURYSM REPAIR
ABDOMINAL AORTIC ANEURYSM
SURGICAL REPAIR

Abdominal Aortic Aneurysm (AAA) Open Surgical Repair
How to Fix an Aneurysm

Aorta (cross-section)

Stent graft released from catheter (catheter is slowly pulled back)

Abdominal aortic aneurysm

Plaque

Catheter inserted into leg artery

Common iliac artery (to leg)

Catheter needed for other side

Blood flows through stent graft

Endovascular stent graft in place
EVAR DEVICES
EVAR BEFORE AND AFTER RESULT
### 1 YEAR SURVIVAL

#### Study name

<table>
<thead>
<tr>
<th>Study name</th>
<th>Odds ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fairman 08 (VALOR)</td>
<td>0.741</td>
<td>0.440</td>
<td>1.247</td>
<td>0.259</td>
</tr>
<tr>
<td>Matsumura 08</td>
<td>0.531</td>
<td>0.221</td>
<td>1.276</td>
<td>0.157</td>
</tr>
<tr>
<td>Buz 08</td>
<td>0.591</td>
<td>0.090</td>
<td>3.864</td>
<td>0.583</td>
</tr>
<tr>
<td>Dick 08</td>
<td>2.143</td>
<td>0.756</td>
<td>6.074</td>
<td>0.152</td>
</tr>
<tr>
<td>Doss 05</td>
<td>0.148</td>
<td>0.016</td>
<td>1.358</td>
<td>0.091</td>
</tr>
<tr>
<td>Kasirajan 03</td>
<td>0.250</td>
<td>0.020</td>
<td>3.100</td>
<td>0.280</td>
</tr>
<tr>
<td>Kokotsakis 07</td>
<td>0.900</td>
<td>0.072</td>
<td>11.254</td>
<td>0.935</td>
</tr>
<tr>
<td>Najibi 02</td>
<td>0.438</td>
<td>0.070</td>
<td>2.728</td>
<td>0.376</td>
</tr>
<tr>
<td>Nienaber 99</td>
<td>0.076</td>
<td>0.004</td>
<td>1.594</td>
<td>0.097</td>
</tr>
<tr>
<td>Patel 08</td>
<td>0.918</td>
<td>0.404</td>
<td>2.090</td>
<td>0.839</td>
</tr>
<tr>
<td>Overall</td>
<td>0.734</td>
<td>0.526</td>
<td>1.023</td>
<td>0.068</td>
</tr>
</tbody>
</table>

**I² = 0%**

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J Am Coll Cardiol, 2010; 55:986-1001
THE END

THANK YOU
LAA CLOSURE
30 DAY SURVIVAL

J Am Coll Cardiol, 2010; 55:986-1001
HOW TO FIX AN ANEURYSM

1. Small radiopaque markers provide top (proximal) orientation of graft material. Long radiopaque marker aligns with contralateral limb.

2. Anterior contralateral limb orientation

3. Posterior contralateral limb orientation

4. Lateral contralateral limb orientation

5. Balloon expansion/graft sealing sites
MULTIPLE ASD CLOSURE
MULTIPLE ASD CLOSURE
Getting Carried Away ???

Two infants with Swiss Cheese VSDs

Top Panels: 11 mo/old with 8mm, 6mm, & 8mm AMVSDO

Left Panel: 2 y/o with 6mm & 8mm AMVSDO. Also has 3 ASOs: 11, 9, & 6mm
IHSS ECHO

ALCOHOL SEPTAL ABLATION

1: Pre-ablation (septal artery visible)
2: Ablation (balloon in septal artery)
3: Post-ablation (septal artery no longer visible)
IHSS / SAM
IHSS - SAM
CONTRAST LOCALIZATION IHSS
ABNORMAL LOCATION OF CONTRAST IN IHSS
Non-Valvular Atrial Fibrillation
Adequacy of Anticoagulation in Clinic

Low INR <1.6

Therapeutic
INR 2-3

High INR >3.2

Efficacy ↓ 4-fold

Bungard: Pharmacotherapy 20:1060, 2001
Non-Valvular Atrial Fibrillation
Stroke Pathology

• Major fatal bleed with age >75 = 3%/year (30% over 10 years)
• Intracranial hemorrhage
  – 0.3-0.5%/100 patient-years
  – 3% in INR >4.0
  – 10% if INR >4.5

Brass. Stroke 28(12), 1997
VanWalraven: JAMA 288, 2002
Non-Valvular Atrial Fibrillation Stroke Pathology

- Insufficient contraction of LAA leads to stagnant blood flow
- Culprit: embolization of LAA clot
- 90% of thrombus found in LAA
- TEE-based risk factors
  - Enlarged LAA
  - Reduced inflow and outflow velocities
  - Spontaneous Echo contrast

Johnson: Eur J Cardiothoracic Surg 17, 2000
Fagan: Echocardiography 17, 2000
### Intent-to-Treat

#### All Stroke

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Device</th>
<th>Events (no.)</th>
<th>Total pt-yr</th>
<th>Rate (95% CI)</th>
<th>Control</th>
<th>Events (no.)</th>
<th>Total pt-yr</th>
<th>Rate (95% CI)</th>
<th>RR (95% CI)</th>
<th>Non-inferiority</th>
<th>Superiority</th>
</tr>
</thead>
<tbody>
<tr>
<td>600 pt-yr</td>
<td>14</td>
<td>409.3</td>
<td>3.4 (1.9, 5.5)</td>
<td>8</td>
<td>223.6</td>
<td>3.6 (1.5, 6.3)</td>
<td>0.96</td>
<td>(0.43, 2.57)</td>
<td>0.927</td>
<td>0.488</td>
<td></td>
</tr>
<tr>
<td>900 pt-yr</td>
<td>15</td>
<td>582.9</td>
<td>2.6 (1.5, 4.1)</td>
<td>11</td>
<td>318.1</td>
<td>3.5 (1.7, 5.7)</td>
<td>0.74</td>
<td>(0.36, 1.76)</td>
<td>0.998</td>
<td>0.731</td>
<td></td>
</tr>
</tbody>
</table>

#### Event-free probability

- **Watchman**
- **Control**

**ITT cohort: Non-inferiority criteria met**

Randomization allocation (2 device:1 control)

900 patient-year analysis

### Event-free probability

- 0 days: 1.0
- 365 days: 0.99
- 730 days: 0.95
- 1095 days: 0.90

- 244 days: 22
- 463 days: 22
- 147 days: 12
- 270 days: 12
- 52 days: 92
- 92 days: 92

![Graph showing event-free probability over time]
PROTECT AF Summary

• PROTECT AF trial was a randomized, controlled, statistically valid study to evaluate the WATCHMAN device compared to warfarin.

• Hemorrhagic stroke risk is significantly lower with the device (91%).

• All cause stroke and all cause mortality risk are equivalent to that with warfarin (26 and 39%).

• Early safety events, specifically pericardial effusion.
Specific Safety Endpoint Events

- Pericardial effusions – largest fraction of safety events in device group
- Stroke events – most serious fraction of safety events in control group
- Bleeding events were also frequent
FDA SAFETY DATA

• Major Safety End Points:
  – AF (%) CAP (%) p
  7.7  3.7  .007

• Procedure/device-related events at 7 d
  5.0  2.2  .019

• Serious pericardial effusions at 7 d

• Procedure-related stroke
  0.9  0.0  .039
EVEREST II Randomized Clinical Trial
Key Inclusion/Exclusion Criteria

**Inclusion**
- Candidate for MV Surgery
- Moderate to severe (3+) or severe (4+) MR
  - Symptomatic
    - >25% EF & LVESD ≤55mm
  - Asymptomatic with one or more of the following
    - LVEF 25-60%
    - LVESD ≥40mm
    - New onset atrial fibrillation
    - Pulmonary hypertension

**Exclusion**
- AMI within 12 weeks
- Need for other cardiac surgery
- Renal insufficiency
  - Creatinine >2.5mg/dl
- Endocarditis
- Rheumatic heart disease
- MV anatomical exclusions
  - Mitral valve area <4.0cm²
  - Leaflet flail width (≥15mm) and gap (≥10mm)
  - Leaflet tethering/coaptation depth (>11mm) and length (<2mm)

ACC/AHA Guidelines
JACC 52:e1-e142, 2008
EVEREST II Randomized Clinical Trial
Primary Endpoints

Safety
- Major Adverse Event Rate at 30 days
- Per protocol cohort
- Superiority hypothesis

Effectiveness
- Clinical Success Rate
  - Freedom from the combined outcome of
    - Death
    - MV surgery or re-operation for MV dysfunction
    - MR >2+ at 12 months
- Per protocol cohort
- Non-inferiority hypothesis

Pre-Specified MAEs
- Death
- Major Stroke
- Re-operation of Mitral Valve
- Urgent / Emergent CV Surgery
- Myocardial Infarction
- Renal Failure
- Deep Wound Infection
- Ventilation >48 hrs
- New Onset Permanent Atrial Fib
- Septicemia
- GI Complication Requiring Surgery
- All Transfusions ≥2 units
EVEREST II RCT: Patient Flow
Per Protocol Cohort: Analysis of Device Performance

Randomized Cohort
n=279

Device Group
n=184

Treated
n=178

Acute Procedural Success
Not Achieved
n=41

Acute Procedural Success
Achieved
n=137

30 days
n=136
99% Clinical Follow-up

12 months
n=134
98.5% Clinical Follow-up
98% Echo Follow-up

Control Group
n=95

Treated
n=80
(86% MV repair)

Acute Procedural Success (APS) = MR ≤ 2+ at discharge

30 days
n=79
99% Clinical Follow-up

12 months
n=74
94% Clinical Follow-up
92% Echo Follow-up
EVEREST II RCT: Summary

- Safety & effectiveness endpoints met
  - Safety: MAE rate at 30 days
    - MitraClip device patients: 9.6%
    - MV surgery patients: 57%
  - Effectiveness: Clinical Success Rate at 12 months
    - MitraClip device patients: 72%
    - MV Surgery patients: 88%

- Clinical benefit demonstrated for MitraClip System and MV surgery patients through 12 months
  - Improved LV function
  - Improved NYHA Functional Class
  - Improved Quality of Life

- Surgery remains an option after the MitraClip procedure
MITRAL ANNULOPLASTY

- Percutaneous Mitral Annuloplasty for Functional Mitral Regurgitation:

- **This was a single-arm evaluation of percutaneous mitral annuloplasty performed via the coronary sinus with the CARILLON Mitral Contour System.**

- Patients with dilated cardiomyopathy, moderate to severe functional mitral regurgitation (MR), an ejection fraction <40%, and a 6-minute walk distance between 150 and 450 m were enrolled in the study.

- The outcome measures were echocardiographic MR grade, exercise tolerance, New York Heart Association class, and quality of life, and they were assessed at baseline and 1 and 6 months.

- *Circulation* 2009;120:326-333
MITRAL ANNULOPLASTY RING
MITRAL ANNULOPLASTY

• The study enrolled 48 patients,
• 18 did not receive the device.
• Of the 18 patients, 3 had coronary sinus perforation or dissection. In 13 patients, the device was recaptured due to slippage of the distal anchor (n = 3) and due to coronary artery compromise or insufficient reduction in MR (n = 10).
• 1 patient died during follow-up and there were 3 myocardial infarctions in the periprocedural phase. No device migration or late infarctions were seen. The major adverse event rate was 13% at 30 days.
• At 6 months, the severity of MR reduction on quantitative echocardiographic measures ranged from 22% to 32%. There was significant improvement in the 6-minute walk distance (from 307 m at baseline to 403 m at 6 months, p < 0.001) and quality of life, measured by the Kansas City Cardiomyopathy Questionnaire (47 ± 16 points at baseline to 69 ± 15 points at 6 months, p < 0.001).
MITRAL ANNULOPLASTY

• The study demonstrates safety, efficacy, and feasibility of percutaneous mitral annuloplasty.
• The initial enthusiasm for coronary sinus–based percutaneous mitral annuloplasty waned once the variability in the relation of coronary sinus to the mitral annulus and the risk of coronary artery compromise were recognized.
• This study is provocative since the procedure was performed with reasonable safety, and there are some data to suggest efficacy in reducing MR and improvement in clinical status. This is a rapidly evolving field, and further refinement in the device and better preprocedural imaging will further improve safety and reduce the number of unsuccessful procedures. Larger controlled studies will be warranted to confirm the clinical improvement and assess long-term implications of percutaneous mitral annuloplasty before it can be used in routine clinical practice.