TAVR:

Current Valve Types. Patient Selection

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August 2017
O Mendiz MD.

Medtronic: Proctor CoreValve, Speaker
AstraZeneca: Speaker
Terumo: Consultant
St Jude: Consultant
Phillips; Speaker
Cook: Consultant
Endologic; Consultant
<table>
<thead>
<tr>
<th></th>
<th>Sapien 3</th>
<th>Evolut Pro</th>
<th>Lotus</th>
<th>Portico</th>
<th>Symetis</th>
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<tbody>
<tr>
<td>High/Extreme Risk</td>
<td>+++</td>
<td>+++</td>
<td>Ongoing PMA</td>
<td>Ongoing PMA</td>
<td>Planned</td>
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<tr>
<td>Intermediate Risk</td>
<td>+++</td>
<td>Pending</td>
<td>Planned</td>
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<tr>
<td>Low Risk</td>
<td>Ongoing</td>
<td>Ongoing</td>
<td>Planned</td>
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<tr>
<td>Ao Valve-in-Valve</td>
<td>+++</td>
<td>+++</td>
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<tr>
<td>LGLO</td>
<td>+++</td>
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Modified from Popma J, TVT 2017
TAVR Systems. *Global Inventory*

- Sapien3
- EvolutR/Pro
- Symetis
- Lotus
- Portico
- Direct Flow
- Engager
- Jena Valve
- Centera
- Venus A Valve

### Current Industry Standards
- CE –approved;
- Increasing clinical use

### Other Systems
- Either: inactive, design modifications, or waiting for approval
TAVR Systems. *Global Inventory*

- Shanghai Valve
- Trinity
- Colibri
- Inovare
- Thubrikar
- Valve Medical
- Syntheon Verso
- Triskele
- BioValve
- MyVal
- HLT
- NVT (Nautilus)
- J-Valve
- Xeltis
- Zurich TEHV

All of the Rest!
TAVR limitations
Top 33% Surgical Risk
STS ≥ 4

Top 7% Surgical Risk
STS > 8

Extreme Risk

“Cohort C”

Two-thirds of patients will remain optimal surgical candidates

STS PROM < 4%
30-Day Mortality < 2-4%

SURGERY

NOTION

PARTNER IA
SURTAV

PARTNER II
A
CoreValve

PARTNER IB
CoreValve

PARTNER II
B
CoreValve

CoreValve

Low Risk

2017

Modified from Martin B Leon
In the next 10 years, TAVR growth will increase X4!

Source: Credit Suisse TAVI Comment - January 8, 2015. ASP assumption for 2024 and 2025 based on analyst model. Revenue split assumption in 2025 is 45% U.S., 35% EU, 10% Japan, 10% ROW

Courtesy Philippe Généreux
TAVR devices

Transfemoral TAVI devices

Balloon-expandable
- Edwards SAPIEN
  - SAPIEN XT
  - SAPIEN 3

Self-expanding
- CoreValve Evolut R
- ACURATE neo
- Portico
- CENTERA
- Biovalve

Differential deployment
- Lotus Direct Flow

Modified from Mohamed Chettibi
Majority of TAVR Procedures - Studies

Balloon Expandable
Edwards

Self-Expandable
CoreValve

Lotus

Symedics
Transfemoral TAVR Devices

Continues improvement of TAVRT procedures has been achieved by:

- Increasing technical success
- Reducing periprocedural complications:
  - Paravalvular leak
  - Vascular complications
  - Conduction disturbances
  - Stroke

A considerable body of evidence on this regards has been accumulated with new TAVR systems designed.
SAPIEN 3

- Balloon-expandable cobalt chromium frame
- Bovine pericardial intra-annular valve
- Outer skirt to reduce PVL
- Annular range: 16 – 28 mm
- 4 valve sizes: 20, 23, 26, 29 mm
- Axela Sheath: 14Fr compatible for all valve sizes including the 29 mm, for a 5.5 mm minimum vessel diameter
Edwards SAPIEN 3 Ultra System:
Axela Sheath

Revolutionary next-generation seamless expandable sheath

Transient expansion and active contraction for low profile entry/exit

<table>
<thead>
<tr>
<th>Valve Size</th>
<th>Sheath Size</th>
<th>Min. Vessel Diam</th>
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<tbody>
<tr>
<td>20 mm</td>
<td>14F</td>
<td>5.5 mm</td>
</tr>
<tr>
<td>23 mm</td>
<td>14F</td>
<td>5.5 mm</td>
</tr>
<tr>
<td>26 mm</td>
<td>14F</td>
<td>5.5 mm</td>
</tr>
<tr>
<td>29 mm</td>
<td>14F</td>
<td>5.5 mm</td>
</tr>
</tbody>
</table>

SAPIEN 3 Ultra System and Axela Sheath are not approved for sale.
Paravalvular Leak (S3HR and S3i)

- **None**: 55.7% (n=425)
- **Trace**: 32.6% (n=462)
- **Mild**: 8.2% (n=131)
- **Mild-To-Moderate**: 3.5% (n=47)
- **≥Moderate**: 8% (n=8)
Evolut PRO is the Next Generation of EvolutR Valve

- Self-expanding Nitinol frame
- Porcine pericardial supra-annular valve
- Optimized sealing: extended skirt and more conformable frame
- Recapturable
- Annular range: 18 – 30 mm
- 4 valve sizes: 23, 26, 29, 34 mm
- 14Fr –equivalent profile, vessels ≥ 5.0 mm
- 34 mm system: 16Fr-equivalent, vessels ≥ 5.5 mm
Evolut PRO 30-Day Safety Outcomes

Forrest, et al., presented at ACC 2017

AKI, acute kidney injury; MVC, major vascular complication; PPI, permanent pacemaker implantation.
Evolut PRO Aortic Regurgitation at 30 Days

Percent of Evaluable Echocardiograms

- Evolut PRO
  - N=58

Categories:
- None/Trace
- Mild
- Moderate
- Severe

- None/Trace: 72.4%
- Mild: 27.6%
ACURATE neo

- Self-expanding Nitinol frame
- Porcine pericardial supra-annular valve
- Inner and outer pericardial skirts to minimize PVL
- Upper crown for supra-annular anchoring
- Lower crown minimizes protrusion into the LVOT
- Annular range: 21 – 27 mm
- 18Fr – sheath compatible, vessels ≥ 6.0mm
ACURATE neo

Acurate neo CE Mark Study  
N=89

- All-Cause Mortality: 3.4% (30 D), 22.5% (1 Yr)
- Stroke: 5.6% (30 D), 9.0% (1 Yr)
- Pacemaker: 9.0% (30 D), 10.1% (1 Yr)
- Mod/Severe PVL: 4.9% (30 D), 5% (1 Yr)

Abizaid, et al.
Lotus

- Mechanically-expanded Nitinol frame
- Bovine pericardial valve
- Adaptive seal designed to minimize PVL
- Repositionable and recapturable
- No rapid pacing needed to deploy
- Annular range: 20 – 27 mm
- 3 valve sizes: 23, 25, 27 mm
- 18Fr sheath, vessels ≥ 6.0 mm
**LOTUS Clinical Program**

**Primary Endpoint:** All-cause Mortality at 30 Days = 2.6%  
N=1014

**Key Secondary Endpoint:**  
Moderate/Severe Paravalvular Regurgitation at Hospital Discharge  
0.3% (N=996)

**Safety Endpoints at 30 Days (N=987)**  
- All-cause mortality: 2.2%  
- Cardiovascular mortality: 2.0%  
- Disabling stroke: 2.2%  
- LT/disabling bleeding: 2.2%  
- MI (>72h post-procedure): 0.3%  
- AKIN (stage 2 or 3): 1.7%  
- Newly implanted PPM: 30.0%  
- Pacemaker dependent at 30 days: 36.1% (site-reported)

**Valve Hemodynamics**  
Core-lab Adjudicated Data

- Mean Aortic Gradient (mmHg)
  - Baseline: 1.8 ± 0.5  
  - Discharge: 10.8 ± 4.6  
  - P < 0.001 vs baseline

- Mean Effective Orifice Area (cm²)
  - Baseline: 38.0 ± 15.5  
  - Discharge: 0.7 ± 0.2  
  - P < 0.001 vs baseline

**Aortic Valve Regurgitation**

- Percentage of Evaluable Echocardiograms
  - LOTUS Clinical Program
  - N=925
  - N=929
  - None
  - Trace
  - Mild
  - Moderate
  - Severe

Presented by Falk, PCR 2016.
Lotus

REPRISE II + Extended Cohort
N=250

- All-Cause Mortality: 4.0% (30 D), 11.6% (1 Yr)
- Stroke: 6.8% (30 D), 8.4% (1 Yr)
- Pacemaker: 28.9% (30 D), 32.5% (1 Yr)
- Mod/Severe PVL: 0.2% (30 D), 0.0% (1 Yr)
1-Month Moderate/Severe PVL

**TAVI Clinical Trials**

<table>
<thead>
<tr>
<th>% Patients with Mod/Severe PVL</th>
<th>1-Month Mod/Severe PVL</th>
</tr>
</thead>
<tbody>
<tr>
<td>CoreValve ADVANCE³</td>
<td>13,1</td>
</tr>
<tr>
<td>CoreValve High Risk²</td>
<td>9,0</td>
</tr>
<tr>
<td>Evolut R³</td>
<td>3,4</td>
</tr>
<tr>
<td>Portico CE Study⁴</td>
<td>4,0</td>
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<tr>
<td>SAPIEN 3 EU⁵</td>
<td>3,5</td>
</tr>
<tr>
<td>SAPIEN 3 PARTNER II S3⁶</td>
<td>3,8</td>
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<tr>
<td>Direct Flow DISCOVER⁷</td>
<td>1,2</td>
</tr>
<tr>
<td>LOTUS REPRISE II &amp; EXT⁸</td>
<td>0,6</td>
</tr>
<tr>
<td>LOTUS RESPOND*⁹</td>
<td>0,3</td>
</tr>
</tbody>
</table>

N=696  N=356  N=58  N=75  N=113  N=1504  N=81  N=177  N=694

## Lotus Edge

<table>
<thead>
<tr>
<th>First Generation LOTUS VALVE</th>
<th>LOTUS Edge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery System</td>
<td>Pre-shaped</td>
</tr>
<tr>
<td>Sheath</td>
<td>18F</td>
</tr>
<tr>
<td>Locking Verification</td>
<td>Multiple views</td>
</tr>
<tr>
<td>Valves Sizes</td>
<td>23, 25, 27 mm</td>
</tr>
<tr>
<td>CE Mark Indication</td>
<td>Transfemoral, Transaortic</td>
</tr>
<tr>
<td>Deployment</td>
<td>Controlled Mechanical</td>
</tr>
</tbody>
</table>
**Depth Guard Deployment Technology**

*Limit depth of implant with LOTUS Edge*

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**Optimizing Valve Deployment:**

- Anchors early during deployment
- Minimizes depth of valve frame reducing LVOT interaction
- Enables more predictable placement
DepthGuard technology: Improved PPM rates w/o sacrificing PVL

RESPOND: 0% severe PVL; 0.3% moderate PVL
RESPOND Extension: 0% moderate or severe PVL
- Self-expanding Nitinol frame
- Intra-annular bovine pericardial valve
- Porcine pericardium sealing cuff
- Resheathable and recapturable
- Rapid pacing is not required for full deployment
- Annular range: 19 – 27 mm
- 4 valve sizes: 23, 25, 27, 29 mm
- 18Fr sheath for 23 and 25 mm and 19Fr for 27 and 29 mm
Manoharan, et al., presented at TVT 2016
Direct Flow

- Designed for Improved Outcomes
  - Non-metallic, double-ring design conforms to anatomy for a better seal
  - “Fine-tunable”
  - Early valve assessment during positioning
  - Adjustable at the annulus site
  - Fully repositionable and retrievable
INTRA-DILATATION is different from POSTDILATATION: after this stage the valve is still completely repositionable and retrievable.
JenaValveTF System allows for treatment of aortic stenosis and pure regurgitation

- Anatomical alignment for reliable positioning and good seal
- Cusp fixation prevents coronary ostia occlusion even in low coronary offtake
Impact of Experience and New devices on Vascular Complications

Paravalvular Leak
TAVI: 30-day All-cause Mortality

8.4% for CoreValve Extreme Risk N=489
7.0% for SAPIEN TVT HR N=12182
5.1% for SAPIEN PARTNER IIB N=276
4.4% for LOTUS REPRISE II + Ext N=249
3.5% for SAPIEN XT PARTNER IIB N=284
3.3% for CoreValve High Risk N=390
2.9% for Portico CE Study N=103
2.2% for SAPIEN 3 PARTNER II S3 HR N=583
1.3% for Direct Flow DISCOVER N=75
1.1% for SAPIEN 3 PARTNER II S3i N=1076
0.0% for Evolut R CE Study N=60

References:
Which device for each patient?

- There are few head-to-head RCT comparing TAVR devices.

- Most of the cases can be done with one TAVR device System. The one you are familiar with (and have evidence for that).

- Specific anatomical situation may arise the need of different devices.

- In summary, you have to have experience with 2-3 different TAVR devices.
Borderline Sizing

- Frequently, clinicians encounter cases where the annular dimensions fall between two valve sizes for a specific system.
- In such instances, the availability of different systems can be of considerable benefit.
Calcium Quantification and Location

- LVOT calcifications has been identified as the most important anatomic predictor of aortic root rupture during balloon-expandable TAVR.
- An alternative solution is to use a self-expanding or mechanically expandable valve for these patients.

EuroIntervention 2016;12:Y22-Y27
Coronary artery occlusion is a rare but devastating complication. Nevertheless, the availability of recapturable and repositionable TAVR systems should be considered in cases where the possibility of coronary occlusion is considered significant.
Successful PCI after TAVR requires guide catheter access to the coronary arteries.

The smallest cell will accept a 12Fr catheter.

The tapered shape at the height of the ostia diminishes the chances for coronary complications.
Valve-in-Valve
Aortic Root angulation

- Highly angulated aortic root anatomy “vertical annulus” or “horizontal aorta” can render TAVR implantation extremely challenging.
- The availability of deflectable delivery catheters, such as the Edwards Certitude and Commander systems, should be used in this most angulated anatomies.
Bicuspid Valve
RESPOND Bicuspid Analysis: PVL at Discharge
As-treated population (N=996)

Lotus Valve

<table>
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<tr>
<th></th>
<th>Bicuspid</th>
<th>Non-bicuspid</th>
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<tbody>
<tr>
<td>Percentages</td>
<td>69.0</td>
<td>81.2</td>
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<tr>
<td>P-values</td>
<td>NS</td>
<td>P=NS</td>
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</table>

Core lab adjudicated data

Presented by Blackman, PCR 2016.

- Severe
- Moderate
- Mild
- Trace
- None
TAVR With Early vs. New-Generation Devices in Bicuspid Aortic Valve Stenosis

A. Annulus Rupture

- Incidence (%)
  - Sapien XT: 4.6
  - CoreValve: 0.0
  - Sapien 3: 1.1
  - Lotus: 0.0

  *p for overall = 0.07*
  *p = 0.04*

B. Second Valve Implantation

- Incidence (%)
  - Sapien XT: 1.1
  - CoreValve: 10.7
  - Sapien 3: 1.1
  - Lotus: 0.0

  *p = 0.007*
  *p = 0.005*

C. New Permanent Pacemaker

- Incidence (%)
  - Sapien XT: 9.2
  - CoreValve: 16.1
  - Sapien 3: 17.6
  - Lotus: 9.1

  *p = 0.10*

D. Device Success

- Incidence (%)
  - Sapien XT: 85.1
  - CoreValve: 77.7
  - Sapien 3: 94.5
  - Lotus: 72.7

  *p = 0.001*

*p for overall = 0.07*
V-in-V

- In small surgical valves, a device with supra anular position (and with high implantation) is hemodynamically favored.
- In cases at risk for malposition (i.e. stentless) a repositionable THV is favored.
- In cases at risk for coronary obstruction a device with leaflet clipping mechanism (i.e. Jena) or a fully repositionable device (i.e. Evolute, Lotus).

Courtesy Danny Dvir, TVT 2017
Percutaneous Access for TAVR

Contralateral Balloon Occlusion

Prostar 10XL
## Vascular Considerations

<table>
<thead>
<tr>
<th></th>
<th>Sapien 3</th>
<th>Evolut</th>
<th>Lotus</th>
<th>Portico</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sheath Size</strong></td>
<td>14/16 E</td>
<td>14 Fr</td>
<td>18 F →</td>
<td>18 F</td>
</tr>
<tr>
<td></td>
<td>16 Fr Pro/34</td>
<td>14 Fr E</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Iliofemoral Diameter</strong></td>
<td>5.5 mm</td>
<td>5.0 mm</td>
<td>5.5 mm</td>
<td>5.5 mm</td>
</tr>
<tr>
<td></td>
<td>6.0 mm (29)</td>
<td>Pro 5.5 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Aortic Tortuosity</strong></td>
<td>+++</td>
<td>18 Fr Sheath</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Aortoventricular Angle &gt; 70°</strong></td>
<td>+++</td>
<td>Direct Aortic Access</td>
<td>+++</td>
<td>NR</td>
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<tr>
<td>“Horizontal” Aorta</td>
<td></td>
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Modified from Popma J, TVT 2017
New TAVR Systems

- There is no a single “perfect” TAVR system; design optimization involves tradeoffs (e.g. external cuff to reduce PVR increases profile and potentially PPM rate).

- There are strong subjective opinions regarding features – which is more important; PVR prevention, ultra-low profile, low PPM rate, retrievable and repositionable, etc.

- Significant operator experience is necessary to formulate thoughtful impressions – difficult to be an expert with more than 3 TAVR systems.
JIM@Favaloro Symposium Joint Session:

Chair: E. Grube – O. Mendiz

Live Cases from San Raffaello Hospital Milán, Italy
Operators: Antonio Colombo, Azeem Latib, Alaide Chieffo

See you in Buenos Aires
Thank you for your Attention