Next Innovation in Transcatheter Valve Intervention
New Valves and New Techniques

Eberhard Grube, MD, FACC, MSCAI
University Hospital, Dept of Medicine II, Bonn, Germany

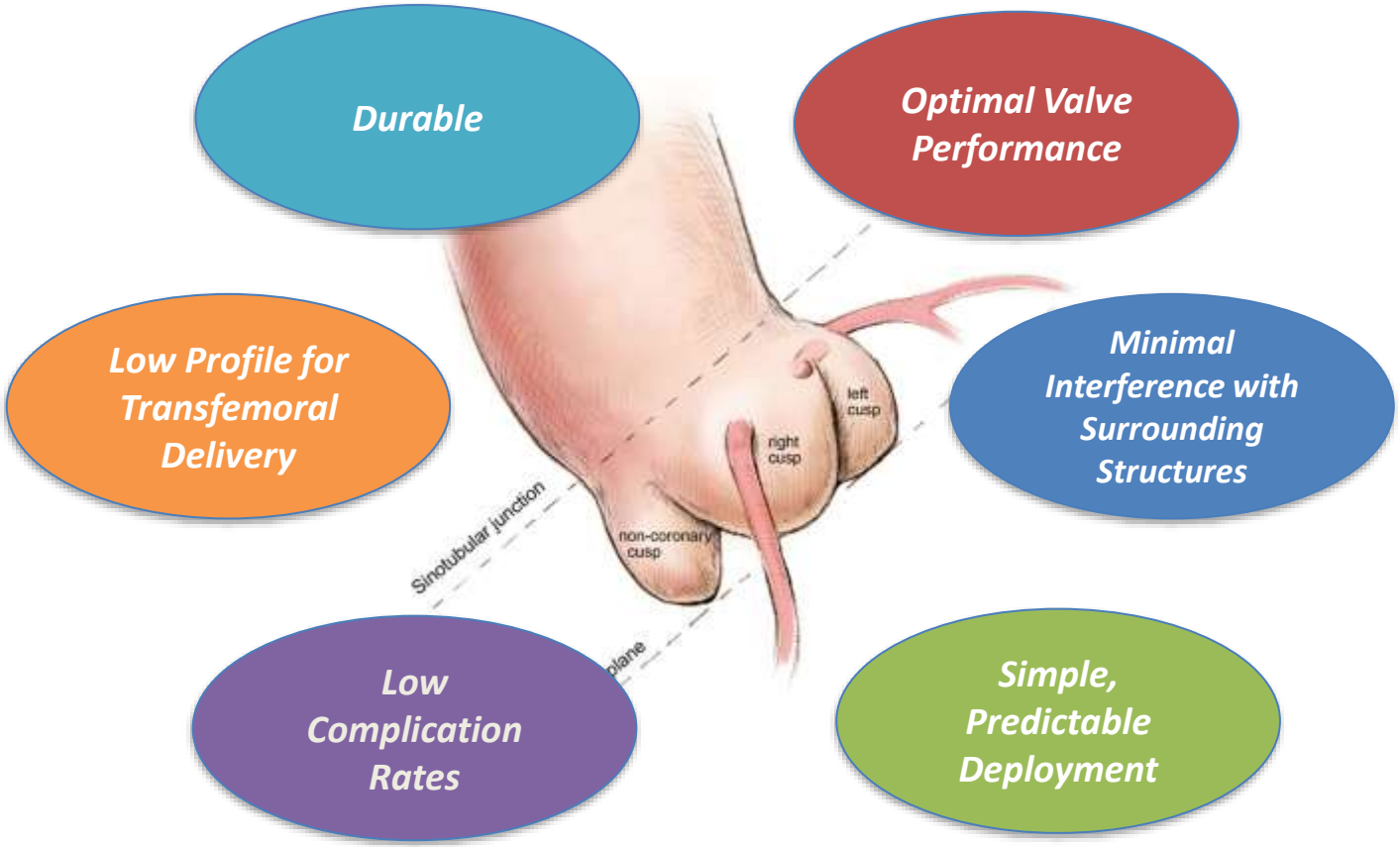
Financial Disclosure

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, Anteris

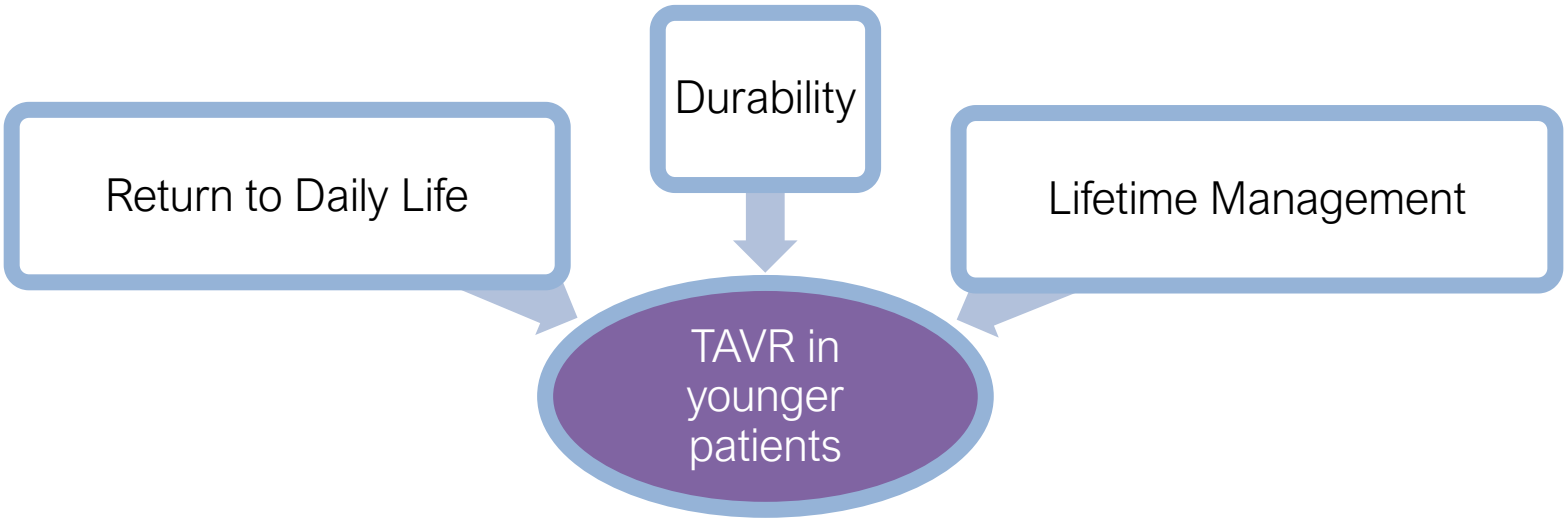
Equity Interest: Cardiovalve, Claret, Shockwave, Valve medical, CardioMech, Millipede, Imperative Care, Pi-Cardia, Ancora, Laminar, ReNiva Medical

The Ideal Transcatheter Aortic Valve



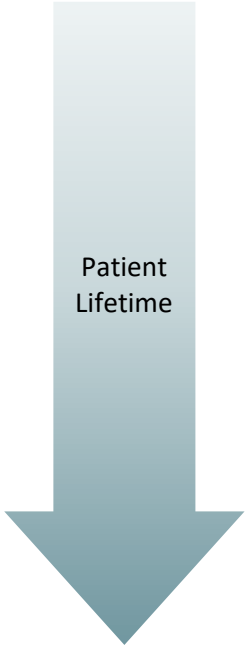
TAVR Device Selection
Priorities for the Future

Device selection in younger, low-risk patients will be driven by valve durability and performance of TAVR valves, lifetime management of patients, and getting patients back to their daily lives faster.



Next Generation THV design with a focus on Lifetime Management of Aortic Stenosis

Priorities for the Future



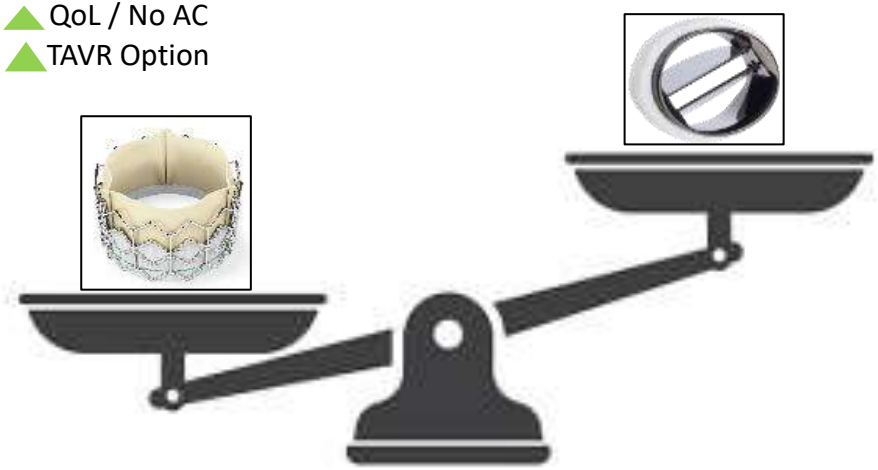
Optimize index procedure	Safety, reproducibility, low access profile, personalized valve sizing, PVL solution
Extend valve longevity	Novel tissue technology, valve design
Maintain coronary access	Short frame height, commissural alignment
Plan for THV-in-THV	Control of valve orientation relative to anatomy

The Heart Valve Conundrum

There is no perfect valve
Which is the best option for which patient?

Tissue
- ▼ Durability
- ▲ QoL / No AC
- ▲ TAVR Option

Mechanical
- ▲ Durability
- ▼ QoL / No AC
- ▼ TAVR Option



The "Ideal" Heart Valve

= One Procedure & Normal Lifestyle

The Durability Controversy

Until there is long-term (>10 years) reliable clinical and echo data treated with "modern era" transcatheter bioprosthetic valves, there will always be concerns regarding "durability"!

THVs have collected more rigorous durability data than any surgical valve until now !

The Evolution of Heart Valves

The promise...

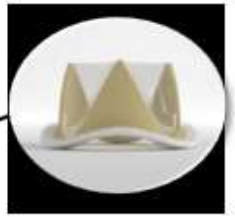
Non living

1960

Mechanical valves

Bioprosthetic valves

Synthetic permanent Polymer



Living

2020

Regenerative material/tissue engineered valve

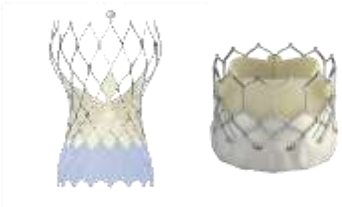
One valve for life!

TAVR Devices

Current Landscape

- Sapien 3/S3 Ultra
- Evolut R/PRO+

Current Industry Standard



- Acurate Neo 2
- Portico/Navitor
- My Val

Increasing Clinical Use/Next in Line

- Jena Valv/J Valve
- Venus A Valve

Rebooting and Increasing Momentum

- Direct Flow
- Engager
- Centera

Early ot Later Demise

Others!

- VitaFlow
- Taurus One
- Trinity
- Colibri
- Inovare
- Thubrikar
- HLT Meridian
- NVT
- Xeltis
- Zurich TEHV

TAVR Devices
Current Landscape

Self Expanding


Evolut R/Pro


Portico


ACURATE Neo2


Venus A


Jena Valve

Balloon Expandable


MyVal


SAPIEN 3/Ultra

Supra-Annular


Evolut R/Pro


Venus A


ACURATE Neo2


Jena Valve

Intra-Annular

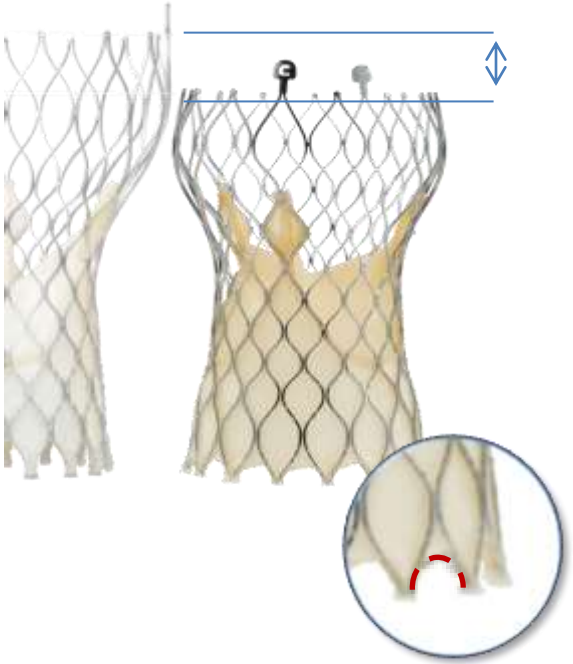

SAPIEN 3/Ultra


MyVal


Portico

Current "Standards" for TAVR

MDT Evolut R (PRO +) EW Sapien 3 Ultra



“Next in Line” for TAVR

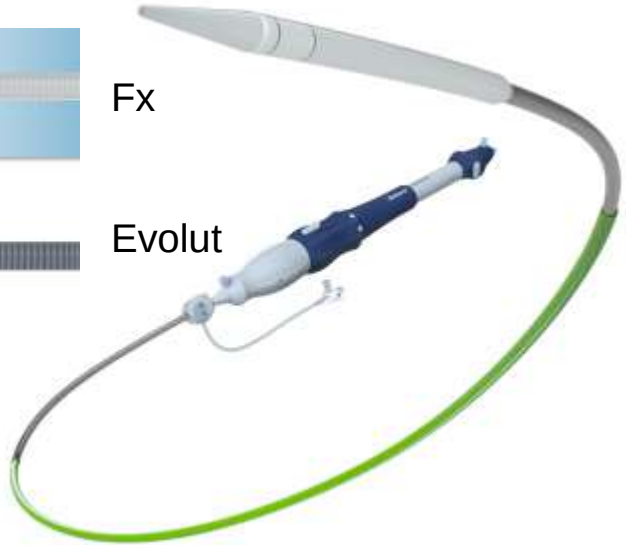
Evolut FX

WHAT'S NEW WITH FX?

- Nosecone redesign
- More flexible capsule
- Single spine shaft
- Optimized stability layer
- ***Three radiopaque inflow markers***
  - Located just adjacent to Commissures
  - Positioned at 3mm target depth

Fx

Evolut

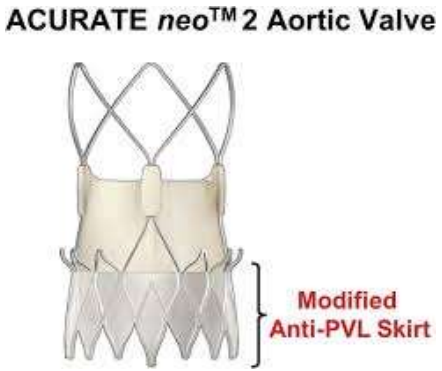


"Next in Line" for TAVR

Acurate neo 2

The next device iteration, Acurate neo 2, has design goals for improved PVL performance and other features including:

- ***Inner and outer pericardial skirts***
- Design updates for improved conformability in irregular, calcified anatomy
- New radiopaque positioning marker



Reducing PVL with the next-generation valve iteration is necessary in order for the Acurate neo 2 to become a viable option for TAVR patients.

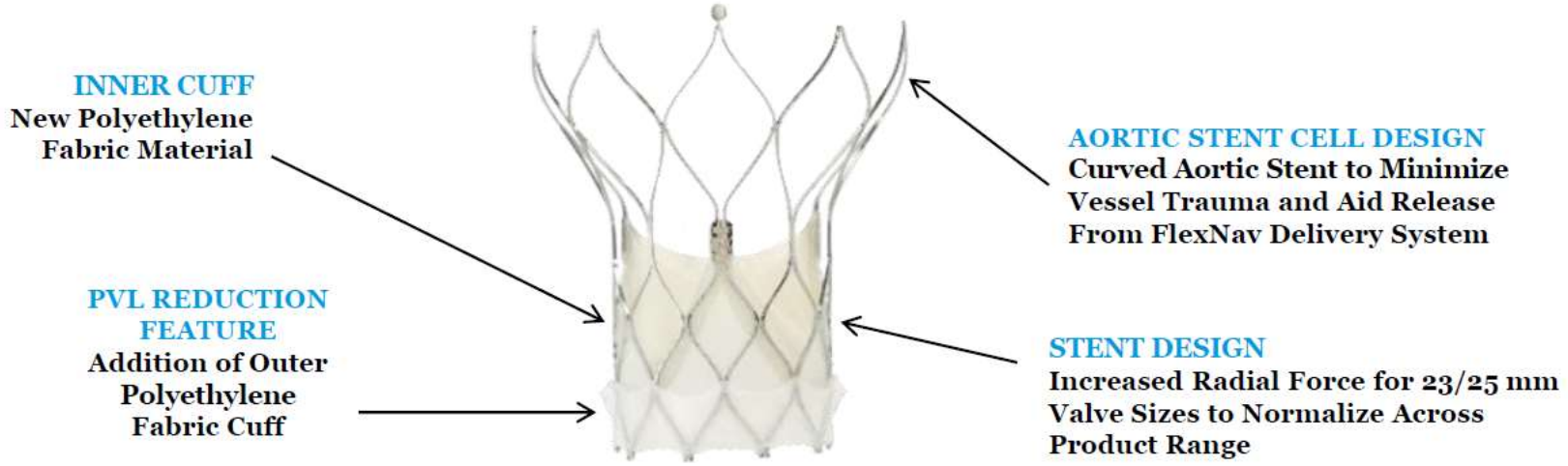
Lanz, Presented at TCT 2019

"Next in Line" for TAVR

Navitor

Future developments from the Portico platform include ***additional studies on the FlexNav delivery system*** and further investigation of the Navitor valve.

The Navitor study is a prospective, multicenter single-arm study to support CE Mark or FDA approval in high- or extreme-surgical risk patients. The study is currently enrolling, and 30-day results are expected to be presented in 2020.

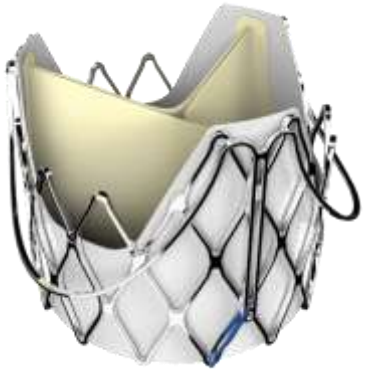


Fontana, Presented at TCT 2019

“Rebooting” or Increasing Momentum

JENA Valve

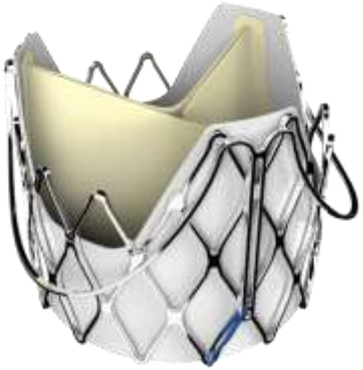
J Valve



VENUS A Valve

On The Horizon

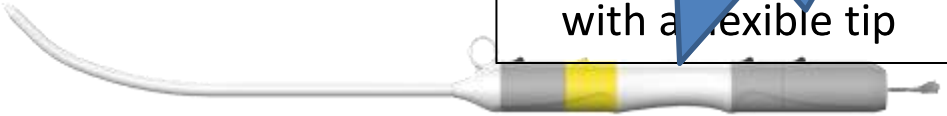
J - Valve



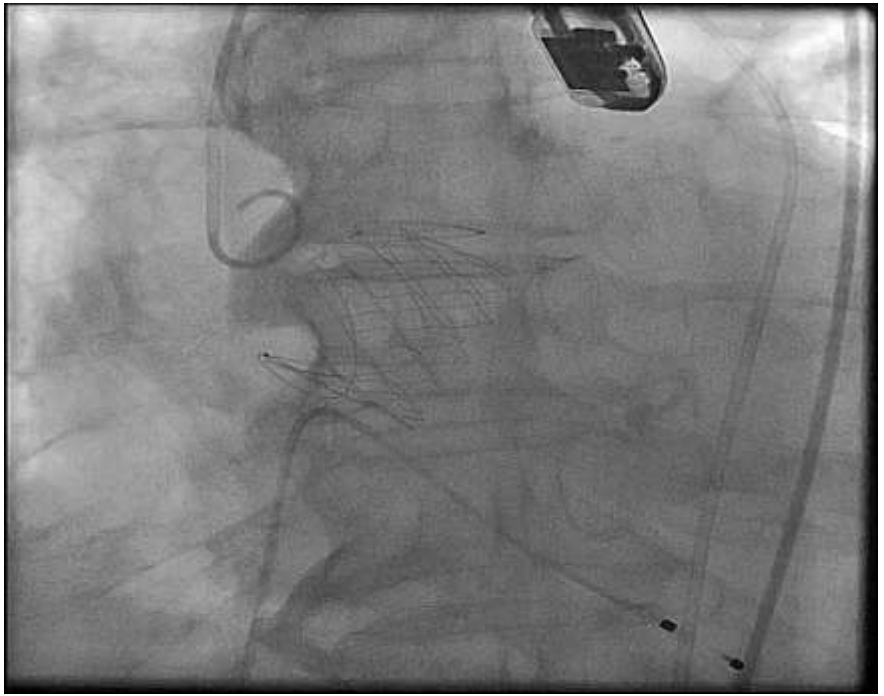
J-Valve Ausper

- Porcine pericardial tr eaflet valve
- Nitin l short ndin frame
  for tra fe
- ***Nitin ly***
  op s with
  na e
  ative
  le
- ss elivery catheter
  with a exible tip

CFDA
Approved
2017



Final Aortogram

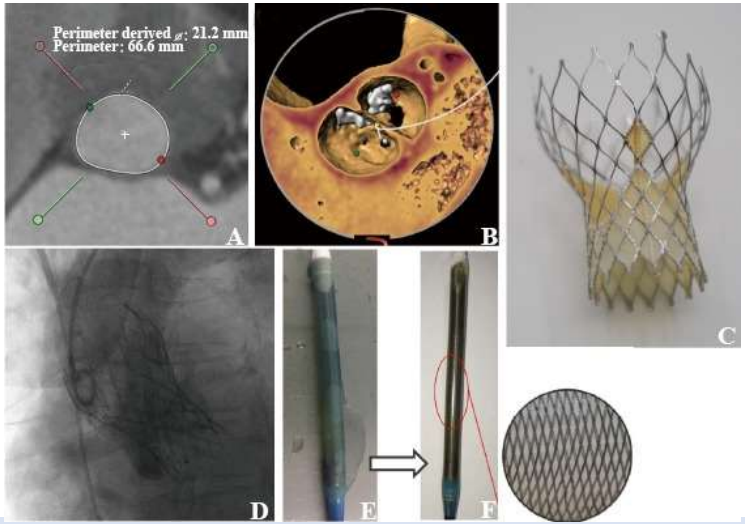


Courtesy Mark Hensey MD

Rebooting / Increasing Momentum

Venus A and Venus A-Plus

The Venus A platform (Chinese FDA approved) includes a self-expanding valve with supra-annular leaflets, and the second-generation Venus A-Plus includes a reinforced shaft and capsule in the delivery ***system to allow retrievability and repositioning.***



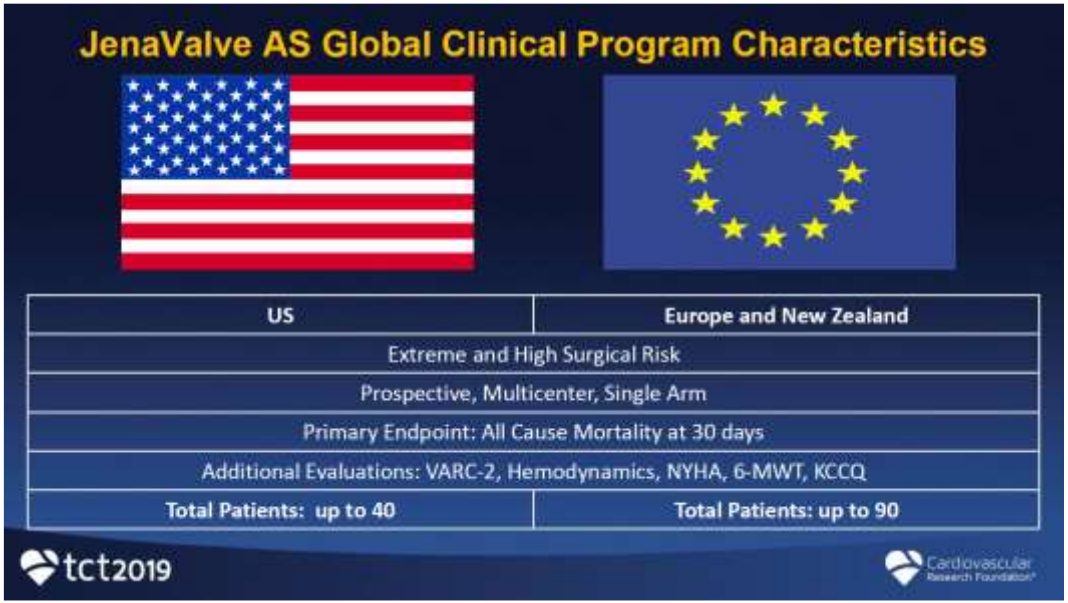
Rebooting / Increasing Momentum

Jena Trilogy™ Valve

Jena Trilogy™ has:

- ***Locator clips that align with sinuses and set implant depth and avoid low implants***
- **Self-expanding nitinol frame**
- **18-Fr equivalent Coronatix catheter delivery**

JenaValve

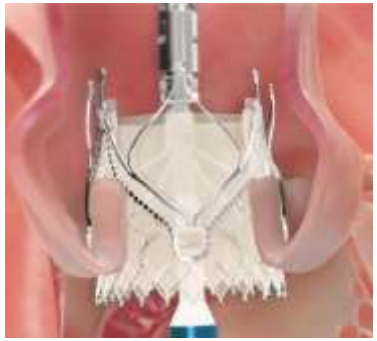


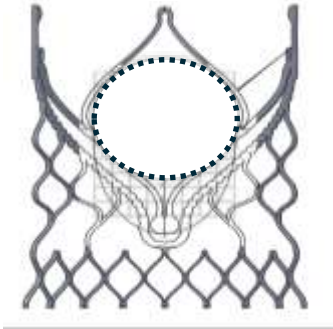
JenaValve Trilogy™ Frame Design with Locator Technology

A Unique Design for Securing and Sealing Valve in Native Anatomy

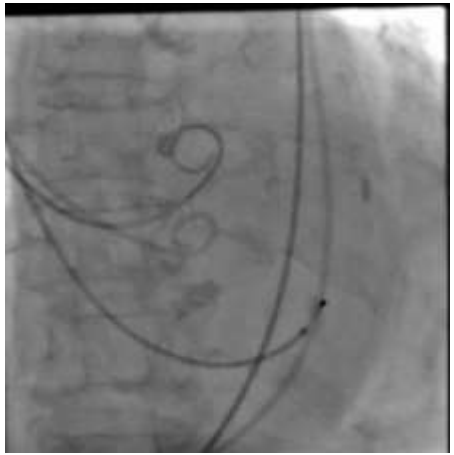
- **Aligns THV with Native Cusps (Commissural Alignment) by Design**
- Locators “Clip” onto Native Leaflets Forming a Natural Seal and Stable Securement

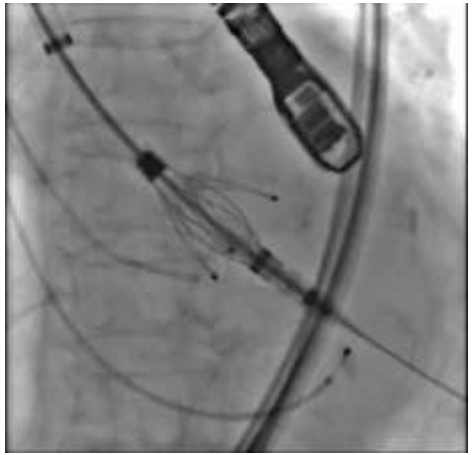
- **Large-Open Cells Provides Access to Low Coronaries**
- 24 Diamond-Shaped Cells Provide Annular Conformability and Sealing

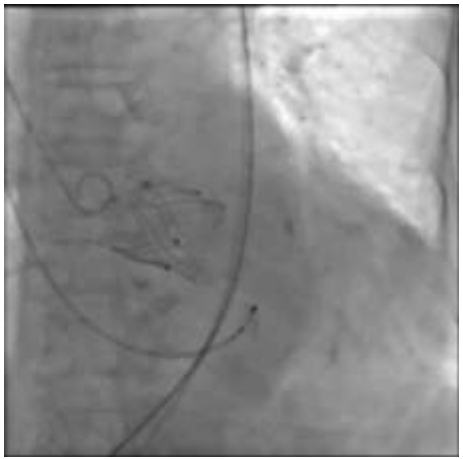


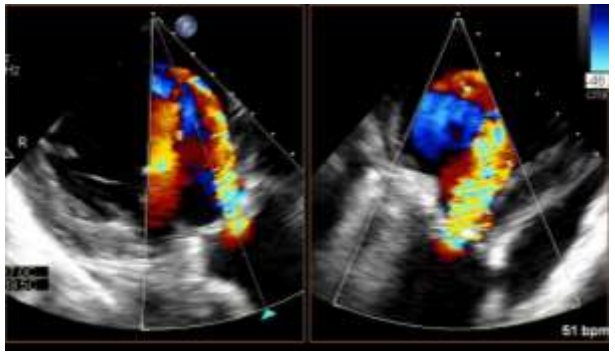


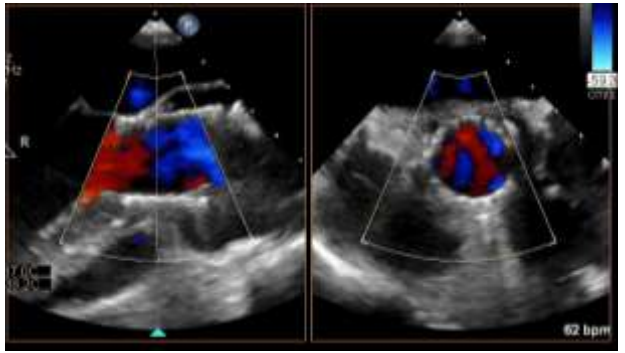
Transfemoral Jena Valve
Case Example



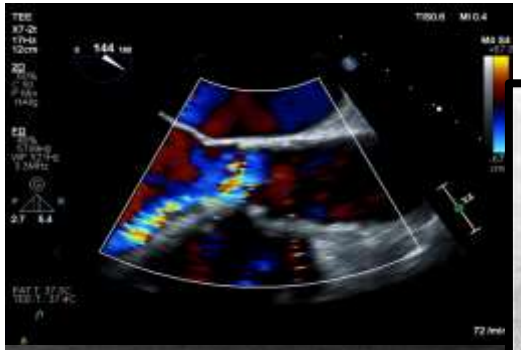


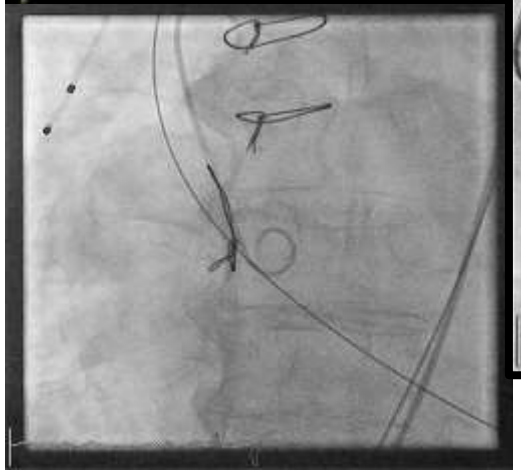


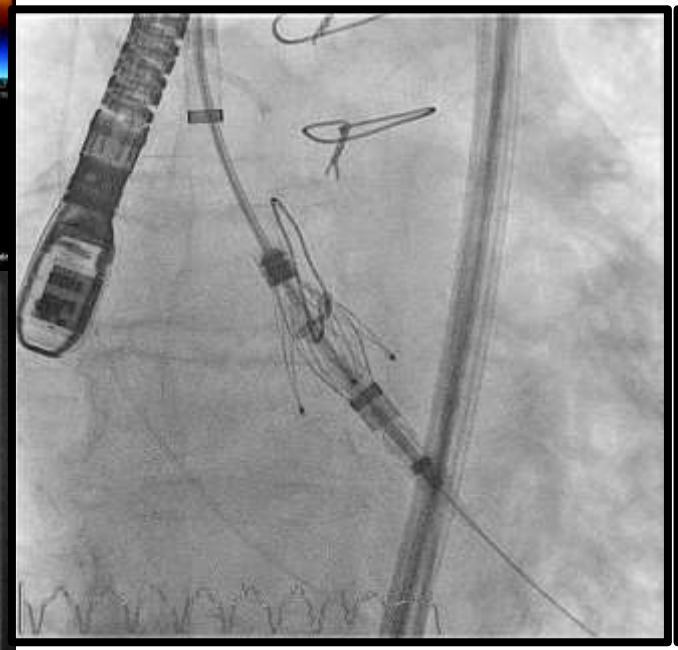


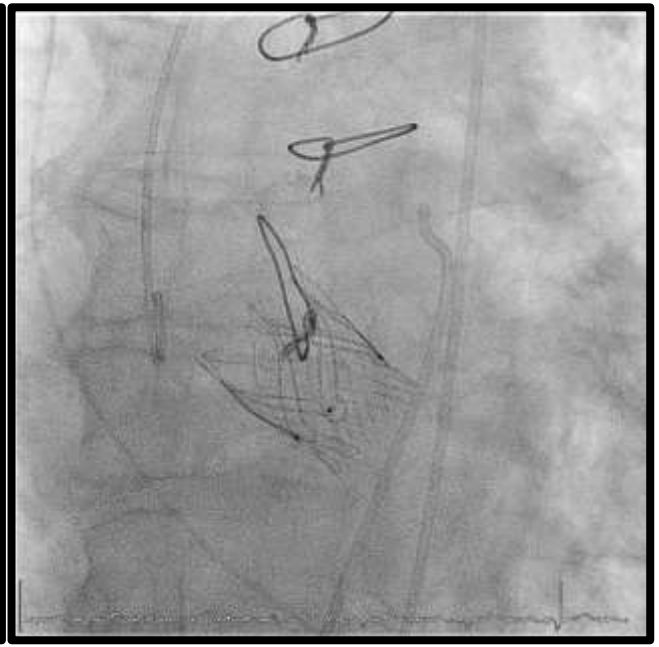


Jena Valve Transfemoral TAVR System to Treat Aortic Regurgitation in a Degenerated Freestyle Surgical Aortic Valve with Unfavorable Anatomy









Aortic Regurgitation

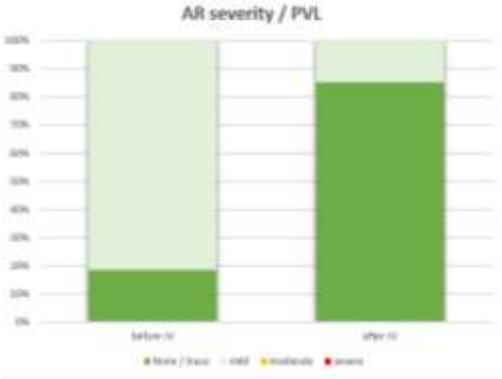
ALIGN – AR Trial Global Clinical Program

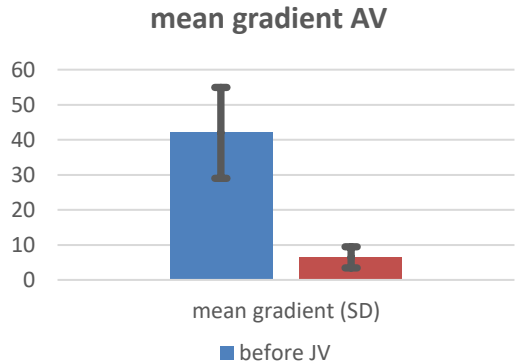
Parameter	US AR Study (N=23)	Yoon et al. Results (N=331)
Age, mean	73 ± 13	75 ± 12
All-Cause Mortality, %	4.3%	10.9%
Conversion to SAVR, %	0.0%	3.6%
Stroke, %	0.0%	16.6%
Acute Kidney Injury Stage 2 or 3, %	0.0%	8.2%
Life Threatening/Major Bleeding	2.3%	11.8%
New Permanent Pacemaker, %	30.4%	18.2%
Coronary Obstruction, %	0.0%	1.5%
Device Success	91%	74%
THV Mean Gradient, mmHg	4.5	9.3

Jena Valve Trilogy – first results after commercial implants for AS
Results

- First 27 patients have been treated with the TF JenaValve Trilogy system *commercially* for Aortic Stenosis!

• **Technical success (VARC-3):**	**100%**	-	
• **Device success (VARC-3) at 30 days:**	**96.3%**		1 death
• **Performance as indicated:**	**100%**	-	
• **Permanent Pacemaker Implantation**	**0%**		



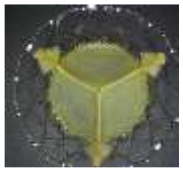


- These data suggest that treatment of severe Aortic Stenosis using the **Trilogy JenaValve system is safe and effective**.
- Coronary Alignemnent by design, bigger studies / registers needed.

Aortic Valve Therapies: The Future?

Alternative Materials

New tissue processes and novel materials are actively being researched, and this research may address shortcomings of current bioprosthetic valves.



New tissue process

Tissue based biomaterial

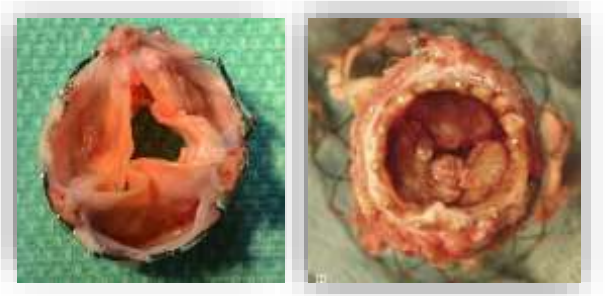
Synthetic permanent polymer

Biodegradable polymer/in situ tissue engineering

Regenerative material/tissue engineered valve

Aortic Valve Therapies: The Future?
Bioprosthesis Durability

Surgical explants – failed TAVR valves



Balloon-expandable Self-expanding

In the future, new bioprosthetic valve platforms will be introduced and tested with 'hopefully' improved durability profiles!

It's all about the leaflets and material science innovation!

- Edwards X4 RESILIA tissue valve
- Anteris DurAVR transcatheter valve
- Foldax TRIA heart valve

SAPIEN X4 Transcatheter Heart Valve System

RESILIA tissue

- ***Offers enhanced anti-calcification technology and enables dry storage***
- Maintains bovine pericardial leaflets matched for thickness and elasticity

Enhanced PET outer skirt

- Designed to further minimize PVL
- Maintains low profile access

Novel frame and leaflet design

- ***Enables adjustable sizing while maintaining valve performance over the deployment diameter range***
- Maintains high radial strength cobalt chromium balloon-expandable design

Low frame height and large cells

- Facilitates future coronary access

Courtesy P Yadav MD

SAPIEN X4: Provides Adjustable Valve Sizing

SAPIEN 3 Ultra

4 valve sizes (3 mm increments)

20 mm

23 mm

26 mm

29 mm

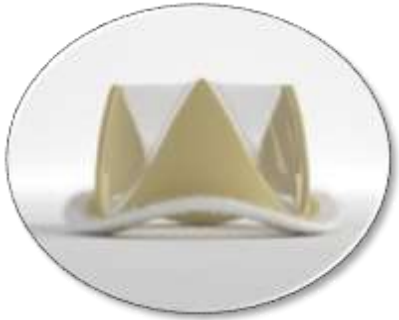
SAPIEN X4

3 valve sizes, 16 unique deployment diameters (0.5 mm increments)

Bioprosthesis Durability

Foldax TRIA Heart Valves

TRIA Heart Valves with Polymer Leaflets
[Siloxane poly (urethane-urea) Elastomer]



Surgical Aortic Valve (SAVR)

Surgical Mitral Valve (SMVR)

Transcatheter Aortic Valve (TAVR)

Robotic manufacturing

Foldax TRIA Heart Valve

Summary

- ***New polymer technology engineered to potentially last a patient's lifetime***
- Eliminate use of animal-sourced tissue
- Surgical valve results >1 year published
- TRIA TAVR designed for ease of implant
- Chronic ovine study demonstrated:
  - Accurate deliverability
  - Excellent hemodynamics to 90 days
  - No calcification
  - Coronary re-access

Bioprosthesis Durability

Anteris Dur AVR Transcatheter Valve

TISSUE = ACELLUAR, DETOXIFIED (wo glutaraldehyde), and wo CALCIFICATION

3D SHAPE

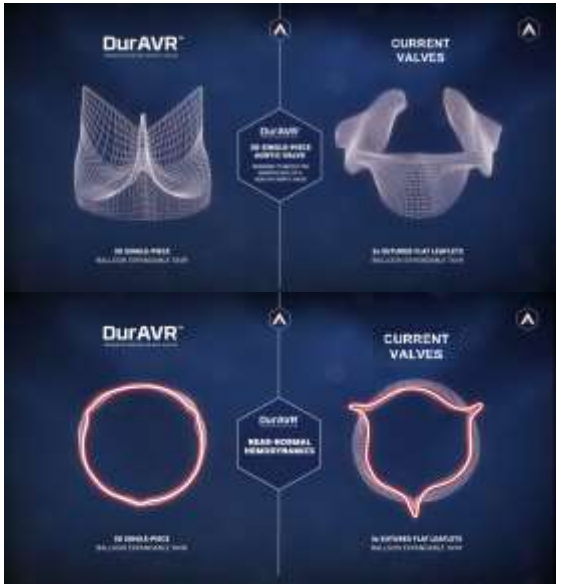
SINGLE-PIECE CONSTRUCTION

PVL SOLUTION (PET skirt)

BALLOON-EXPANDABLE, LARGE CELL

SUPRA-ANNULAR

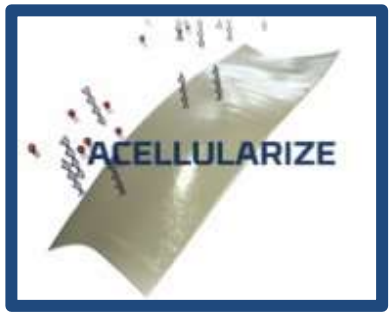
COMMISSURAL ALIGNMENT

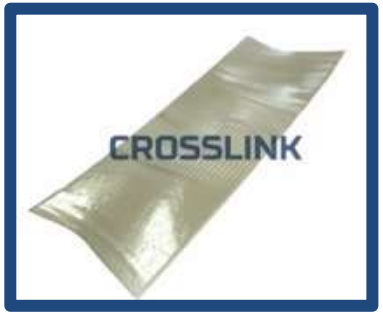


Single-piece 3D shape

ADAPT Anti-Calcification Tissue Process

Creates Accellular Tissue to Reduce Immune Response





Process removes DNA, phospholipids, alpha gal epitope

DurAVR THV Leaflet Technology
Designed to Mimic Native Valve Shape

Novel 3D Single-Piece Design

Design Goals:

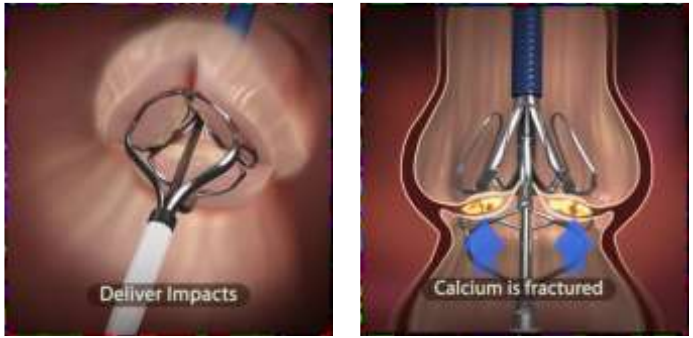
- *To **restore** near normal **hemodynamic function***
- *For **better coaptation** and **less leaflet stress***

New Technologies

AV Remodeling Therapies

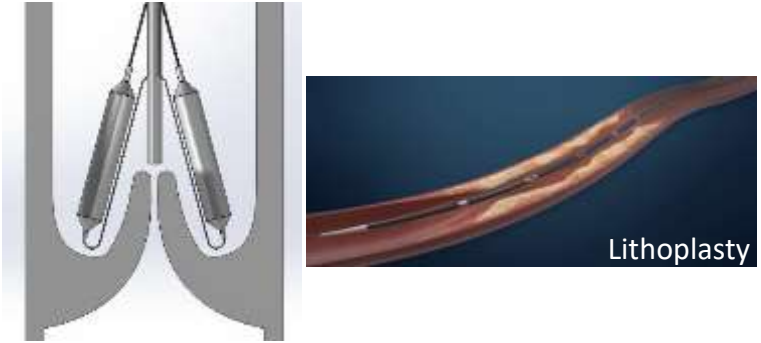
Technologies and devices are being developed that ***disrupt calcifications on the leaflets to restore leaflet function.*** Clinical trials are needed to assess the safety and hemodynamic benefits of these devices**.**

Leaflex AVRT



- Mechanical shock waves fracture leaflet calcium and improve leaflet mobility
- Can be used as stand-alone, bridge to TAVR/SAVR, or preparation for TAVR (especially bicuspid valves)

Lithoplasty for aortic leaflet restoration



- Electro-hydraulic lithotripsy in a balloon
- Constant, ultra-low pressure
- Sonic pressure waves crack calcium

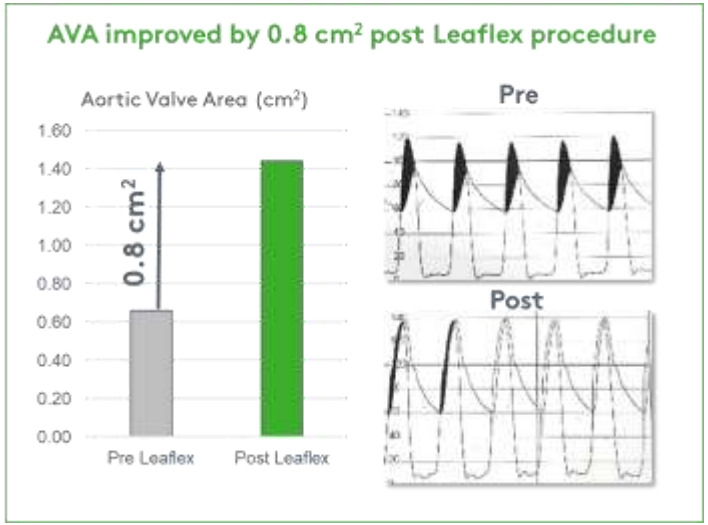
[1]Hill, presented at TCT 2017, [2]Leon, presented at TCT 2016

Aortic Valve Remodeling Therapies

Leaflex aortic valve scoring device to improve aortic valve flexibility and reduce stenosis

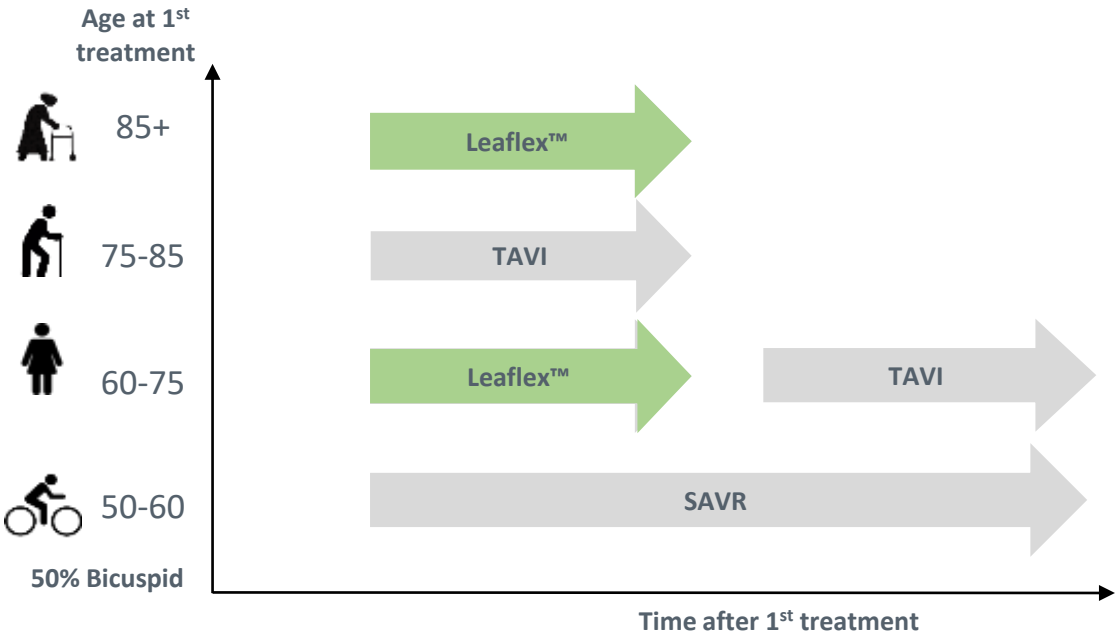
Pre-clinical studies w surgically excised human valves

Human feasibility experiences



Younger AS Patients: Therapy Sequencing

TAVR or SAVR "First"…

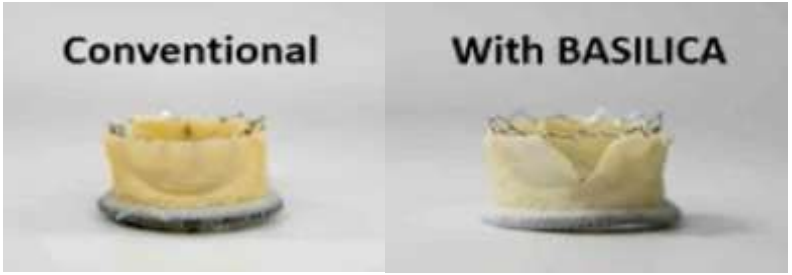


- *Younger patients will likely require multiple treatments or still go to surgery*
- *Leaflex can be used to avoid or defer TAVR*

TAVR I LIFETIME MANAGEMENT

New Techniques for Valve-in-Valve Procedures (BASILICA/SHORTCUT)

ShortCut

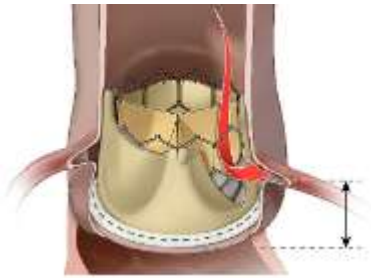


Aortic Valve Remodeling – ShortCut Catheter

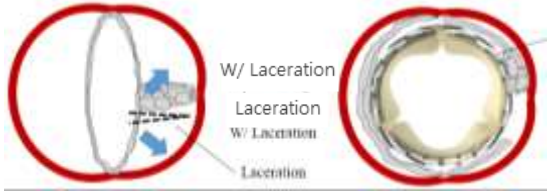
Dedicated valve leaflet splitting device

A simple device to split leaflets may open **2 significant indications for TAVI**

Splitting leaflets to enable Valve-in-Valve



"Tricuspidization" of Bicuspids pre-TAVI



TAVR Newcomers

Caveats to Consider…

- **There is no single "perfect" TAVR system** - *design optimization involves tradeoffs and compromises (e.g. external cuff to reduce PVR adds profile)*
- **Strong subjective opinions regarding features** – *which is more important… PVR prevention, ultra-low profile, low PPM rate, retrievable and repositionable, BE vs. SE, etc*.
- **Significant operator experience necessary to formulate thoughtful impressions** – *difficult to be an expert with more than ~3 TAVR systems*
- **Future TAVR systems should be expected to treat <u>ALL</u> patients with AS** (esp. lower risk and BAV)!

TAVR Newcomers & New Techniques

What's Hot?

- **Meaningful new versions of Sapien and Evolut** – *the industry leaders continue to iterate and innovate!*
- **Rapid emergence of other TAVR systems** – *approved in EU and coming to US (AcurateNeo2, and Navitor)*
- **New TAVR systems from CHINA are entering the clinical marketplace** *(Venus A+ and J-Valve)*
- **TAVR newcomers are developing novel device designs** (*dry leaflet technology, PVL prevention, ultra-low profiles)*
- **Tissue engineering concepts are quickly evolving** and may *spark a future round of improved valve leaflet designs*
- **New Techniques for Lifetime Managament and AV Remodeling are increasingly being used**

WE ARE ALL ONE WORLD, ONE MISSION OF MAKING LIFE BETTER, SAFER AND HEALTHIER TO ALL

THANK YOU AND
BE SAFE!