AP Valve 2017
Seoul, August 16th, 2017

New Mainstream TAVR
New Devices

Eberhard Grube, MD, FACC, FSCAI
University Hospital, Dept of Medicine II, Bonn, Germany
Stanford University, Palo Alto, California, USA

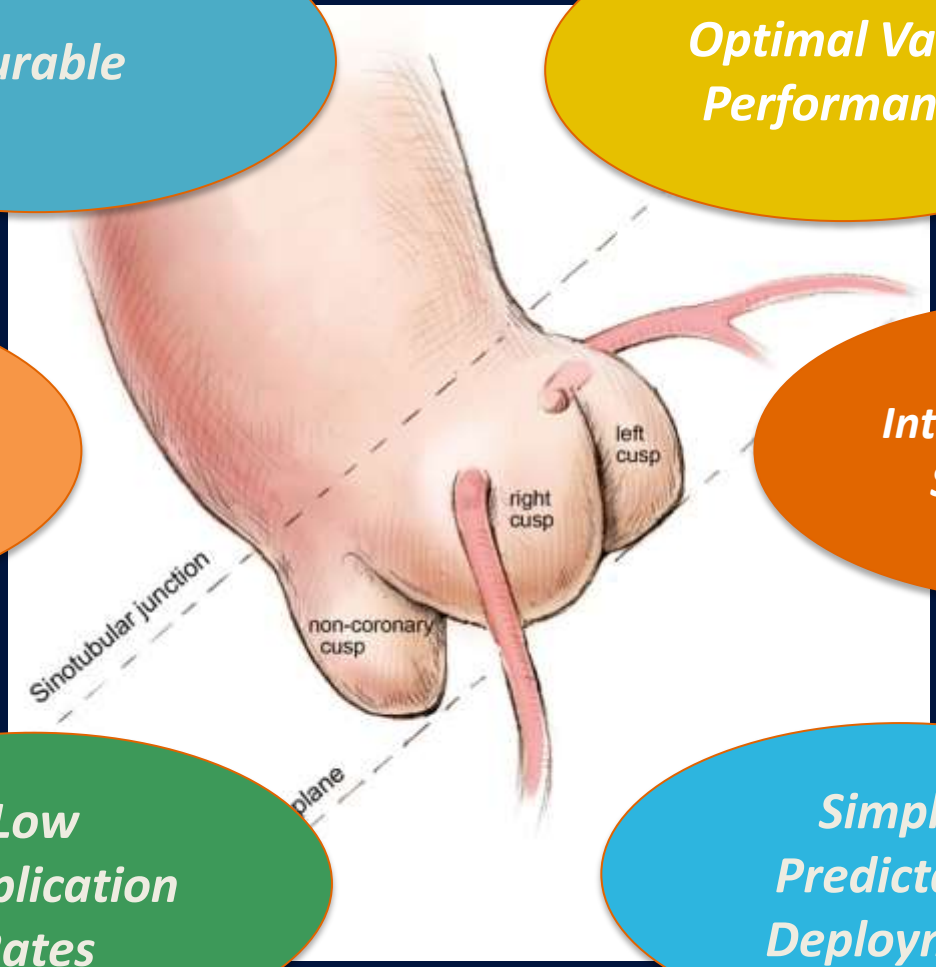
Eberhard Grube, MD

Physician Name	Company/Relationship
Speaker Bureau/Advisory Board:	Medtronic: C, SB, AB, OF LivaNova: C, SB, AB Highlife: AB, SB Boston Scientific: C, SB, AB
Equity Interest:	Millipede: E, SB, C, InSeal Medical: E, AB, Valtech: E, SB, Claret: E, AB Shockwave: E, AB Valve Medical: E, AB Mitraltech: E,AB Mitra/Trilign E, AB, SB

Key

G – Grant and or Research Support E – Equity Interests S – Salary, AB – Advisory Board
C – Consulting fees, Honoraria R – Royalty Income I – Intellectual Property Rights
SB – Speaker's Bureau O – Ownership OF – Other Financial Benefits

The Ideal Transcatheter Aortic Valve



Durable

Optimal Valve Performance

Low Profile for Transfemoral Delivery

Minimal Interference with Surrounding Structures

Low Complication Rates

Simple, Predictable Deployment

TAVR Systems

Global Inventory (#25)

- Sapien 3
- Evolut R
- Sy[illegible]
- [illegible]ve
- Centera
- Venus A Valve

Current Leaders!

- Shanghai Valve
- Trinity
- Colibri
- In[illegible]e
- T[illegible]
- [illegible]
- NVT (Nautilus)
- J - Valve
- Xeltis
- Zurich TEHV

Future Contenders?

So Many Choices

Transfemoral TAVR Devices

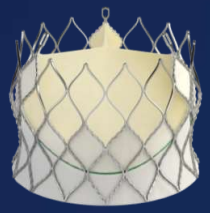
Iterative Device Design

- For the continued success of TAVR, complications specific to the therapy, such as paravalvular leak, vascular trauma, and conduction disturbances, should be mitigated.
- A considerable body of evidence has accumulated on new TAVR systems designed with this goal in mind. This presentation will provide an overview of the data.


Evolut R


SAPIEN 3


Lotus


CENTERA


Portico


ACURATE neo

SAPIEN 3

SAPIEN 3

Design Features

Clinical Trials

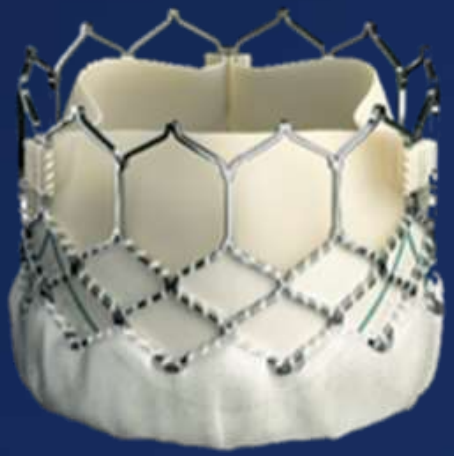
Long Term Follow-Up

Real World Experience

Design Iterations

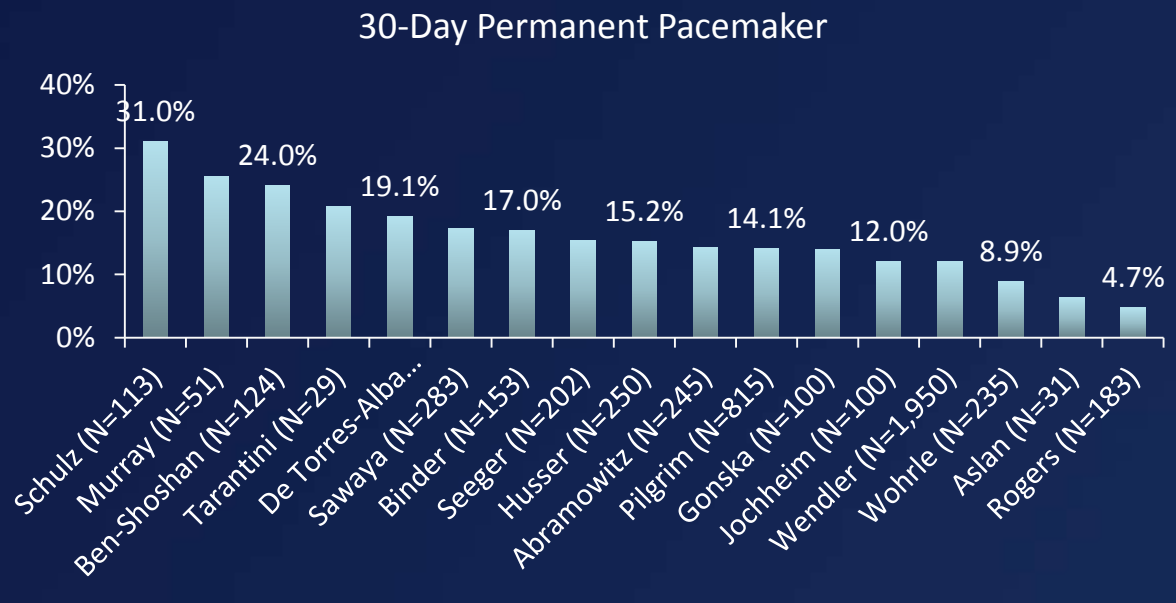
Clinical Program

- Balloon-expandable cobalt chromium frame
- Bovine pericardial intra-annular valve
- Outer PET fabric skirt to reduce PVL
- Annular range: 16 – 28 mm
  - 4 valve sizes: 20, 23, 26, 29 mm
- Expandable 14Fr (vessels ≥ 5.5 mm) or 16Fr (vessels ≥ 6.0 mm) delivery sheaths for TF delivery
  - 14Fr: 20, 23, 26 mm THVs
  - 16Fr: 29 mm THV



SAPIEN 3

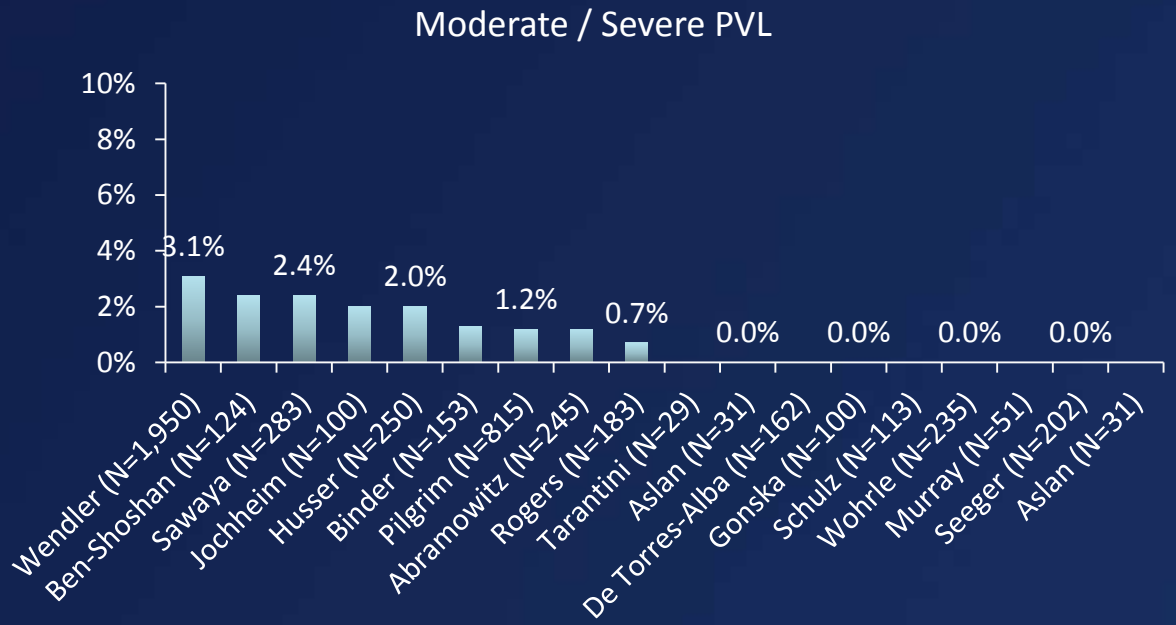
- Design Features
- Clinical Trials
- Long Term Follow-Up
- **Real World Experience**
- Design Iterations
- Clinical Program



Pacemakers

Weighted Average:

13.3%



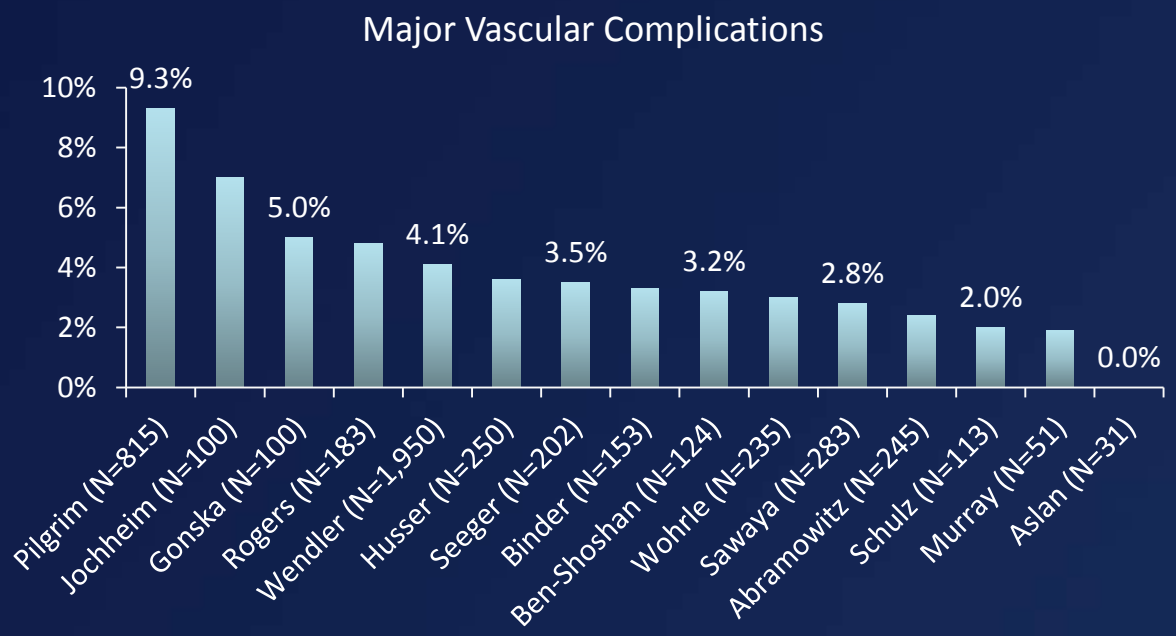
PVL

Weighted Average:

2.2%

SAPIEN 3

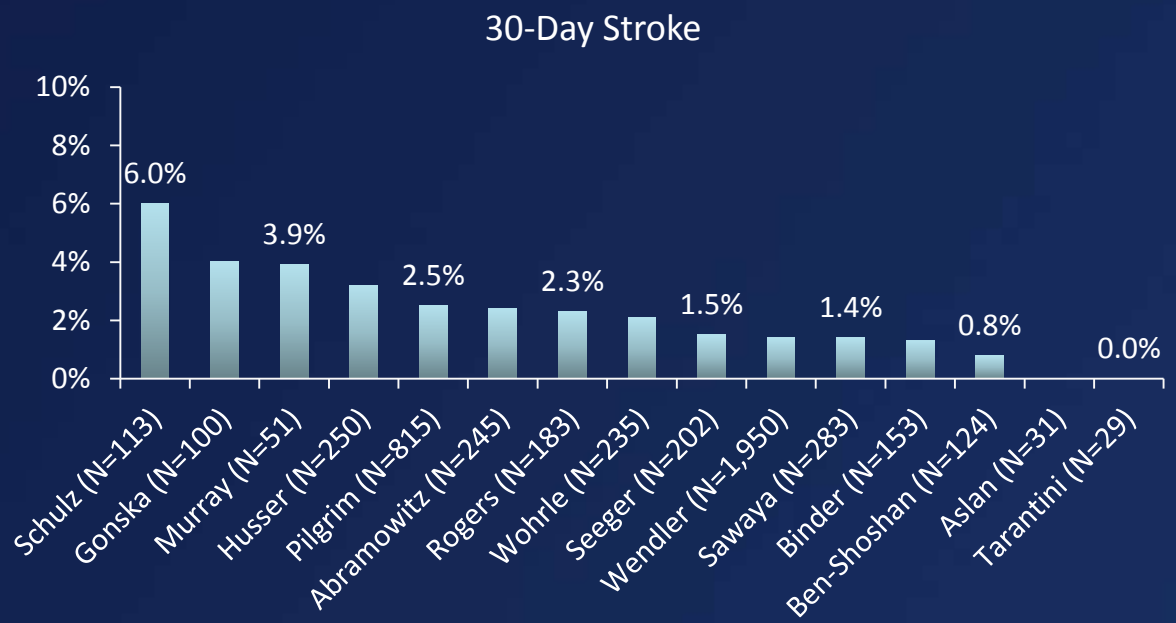
- Design Features
- Clinical Trials
- Long Term Follow-Up
- **Real World Experience**
- Design Iterations
- Clinical Program



MVCs

Weighted Average:

4.8%



All Stroke

Weighted Average:

1.9%

SAPIEN 3

- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- Design Iterations
- Clinical Program

SAPIEN 3 Ultra Delivery System

- On-balloon design removes valve alignment step
- Pusher is eliminated, reducing steps required during deployment

Axela Sheath

- 14Fr compatible for all valve sizes including the 29 mm, for a 5.5 mm minimum vessel diameter
- Seamless sheath design to maintain hemostasis
- Transient expansion and active contraction allows for low profile entry / exit

CENTERA

CENTERA

Design Features

Clinical Trials

Long Term Follow-Up

Real World Experience

Design Iterations

Clinical Program

- Self-expanding, contoured Nitinol frame
- Bovine pericardial valve
- Inner PET skirt to reduce PVL
- Repositionable and recapturable
- Fully pre-attached valve
- Motorized delivery system
- Annular range: 18 – 26 mm
  - 3 valve sizes: 23, 26, 29 mm
- 14Fr sheath for all valve sizes

CENTERA

- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- Design Iterations
- Clinical Program

The CENTERA Trial[1]

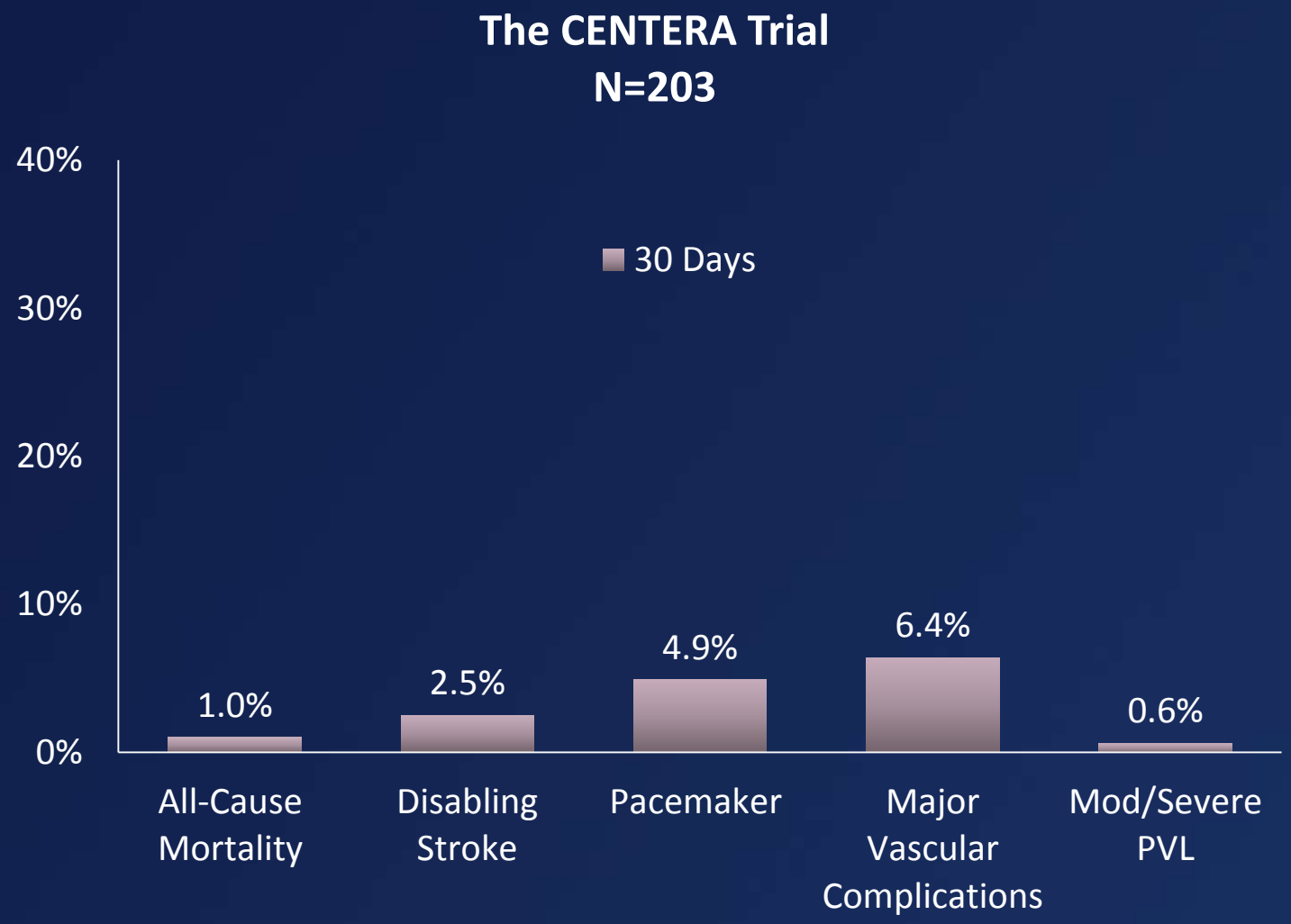
Single arm, observational
N = 203
STS: 6.1%
Age: 83 years
Female: 67.5%
Enrolled: March 2015-July 2016

Follow-up through 30 Days

[1]Tchetche, et al., presented at EuroPCR 2017

CENTERA

- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- Design Iterations
- Clinical Program



[1]Tchetche, et al., presented at EuroPCR 2017

Evolut R

Evolut R

Design Features

Clinical Trials

Long Term Follow-Up

Real World Experience

Design Iterations

Clinical Program

- 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 R

- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- Design Iterations
- Clinical Program

Evolut R CE Study[1,2,3]

Single arm, observational
N = 60
STS: 7.0 ± 3.7%
Age: 82.8 ± 6.1 yrs
Female: 66.7%
Enrolled: Oct 2013-July 2014

Follow-up through 2 yrs

Evolut R US IDE Study[4,5]

Single arm, observational
N = 241
STS: 7.4 ± 3.4%
Age: 83.3 ± 7.2 years
Female: 68.5%
Enrolled: Sept 2014-July 2015

Follow-up through 1 yr

[1]Manoharan, et al., *J Am Coll Cardiol Intv* 2015; 8: 1359-67;[2]Manoharan, et al., presented at TCT 2015; [3]Brecker, et al., presented at TCT 2016; [4]Popma, et al., *J Am Coll Cardiol Intv* 2017; 10:268-75; [5]Popma, et al., presented at TCT 2016

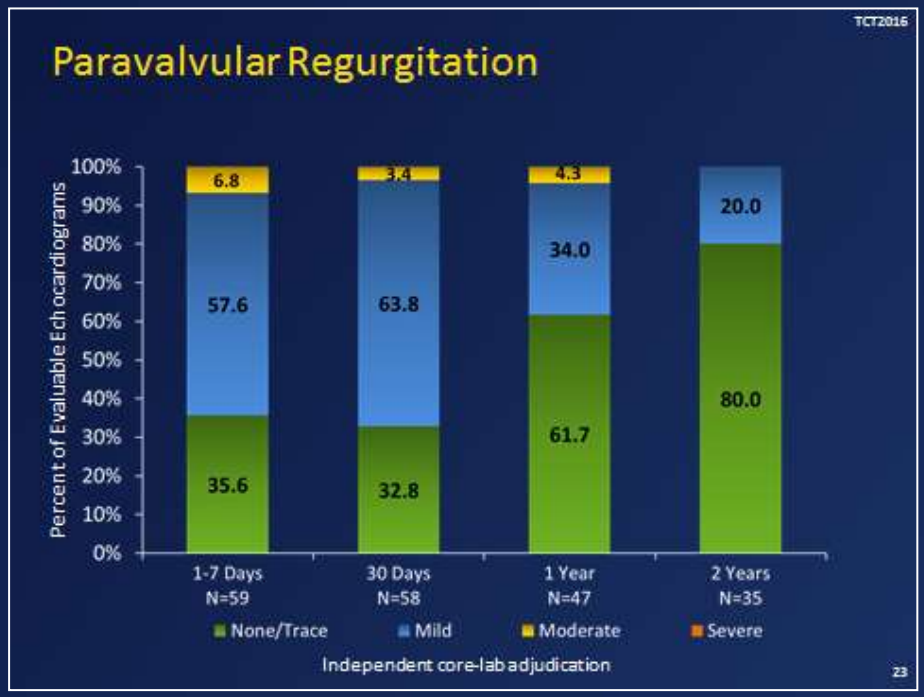
Evolut R

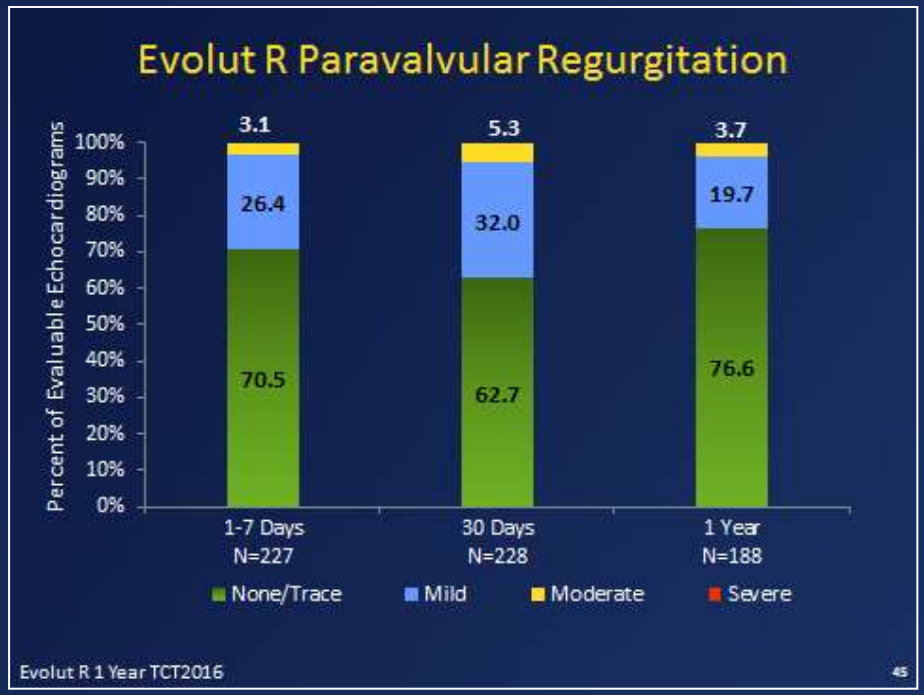
- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- Design Iterations
- Clinical Program

Evolut R CE Study
N=60

Both cohorts demonstrate an increase in the % of patients with none/trace PVL over time

Evolut R US Study
N=241





[1]Brecker, et al., presented at TCT 2016; [2]Popma, et al., presented at TCT 2016

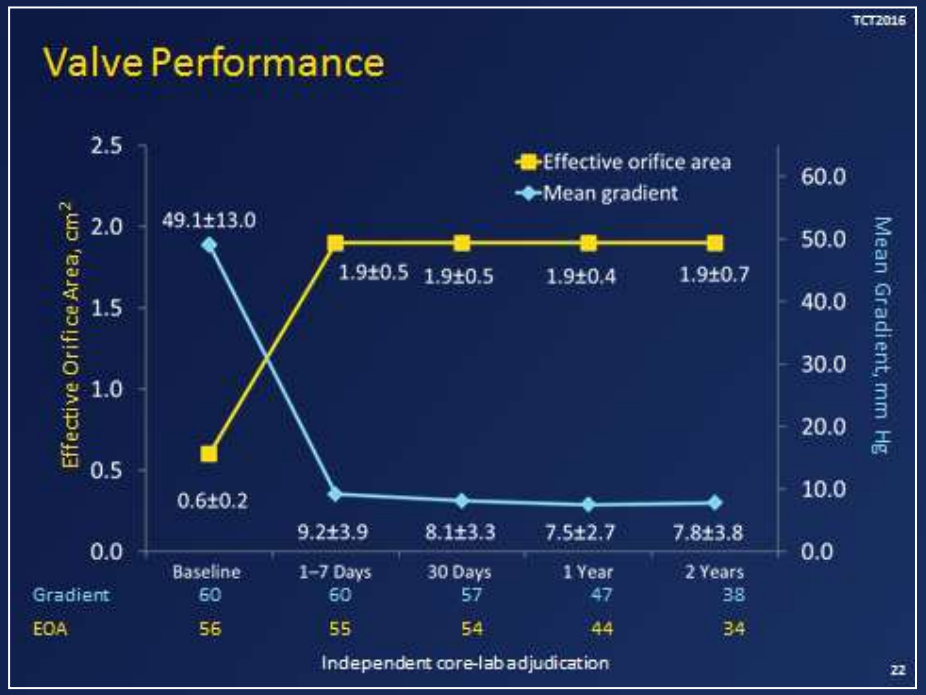
Evolut R

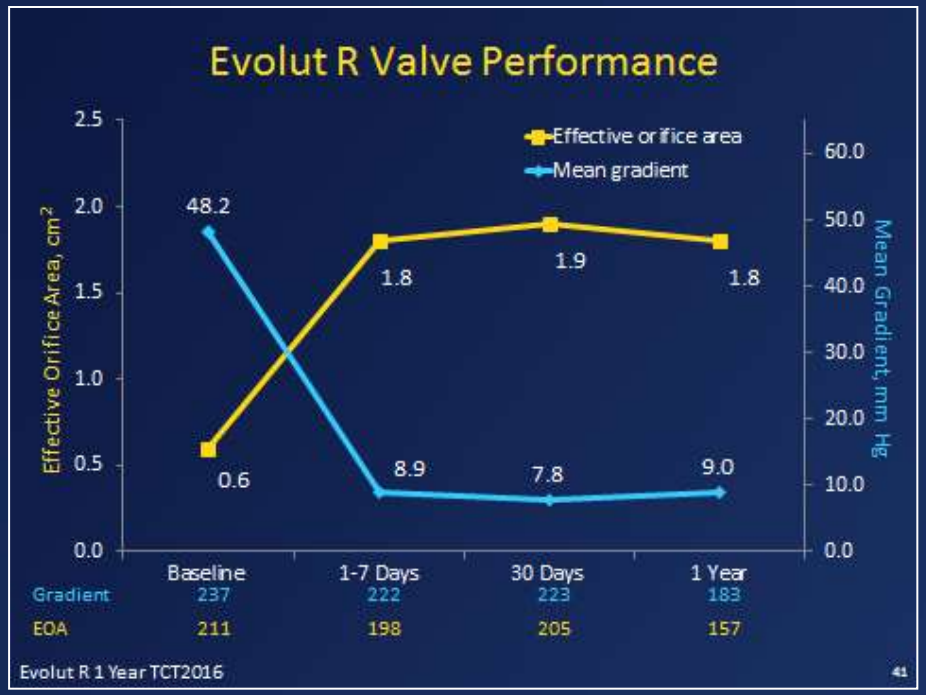
- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- Design Iterations
- Clinical Program

Evolut R CE Study
N=60

Very low gradients remained stable to 2 yrs

Evolut R US Study
N=241

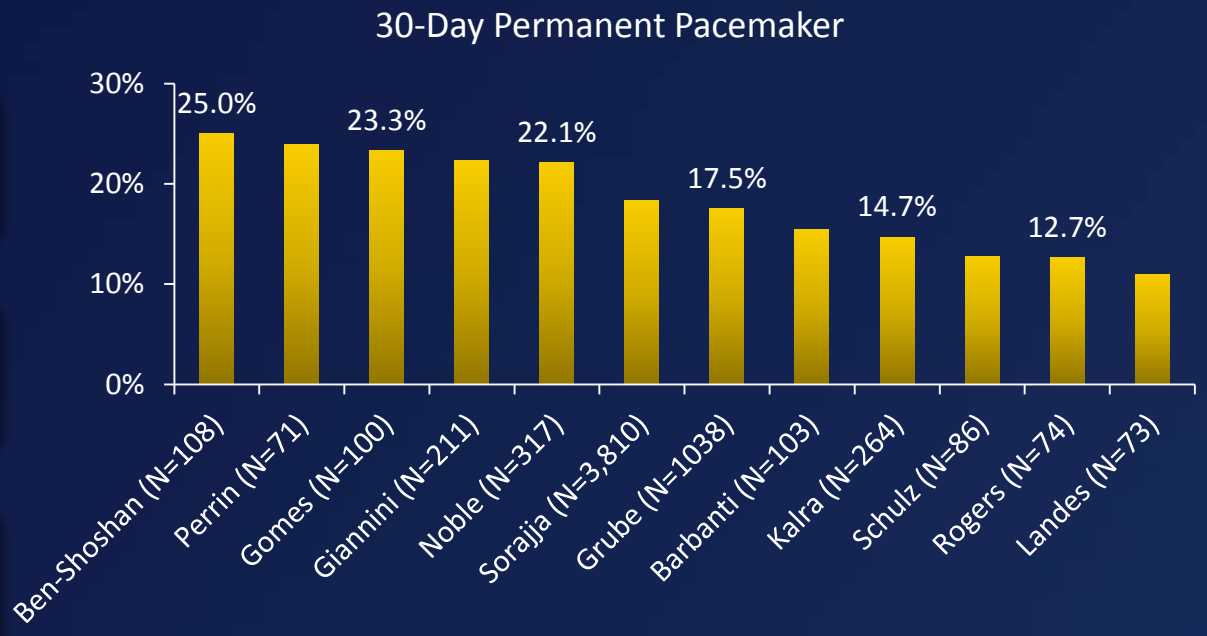




[1]Brecker, et al., presented at TCT 2016; [2]Popma, et al., presented at TCT 2016

Evolut R

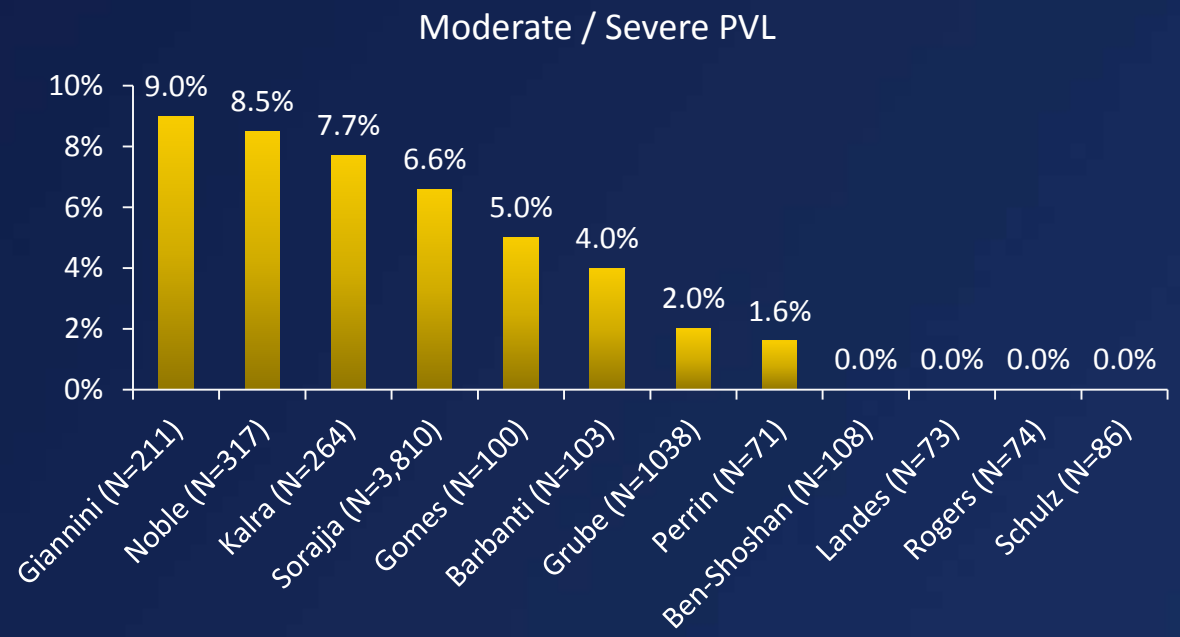
- Design Features
- Clinical Trials
- Long Term Follow-Up
- **Real World Experience**
- Design Iterations
- Clinical Program



Pacemakers

Weighted Average:

18.3%



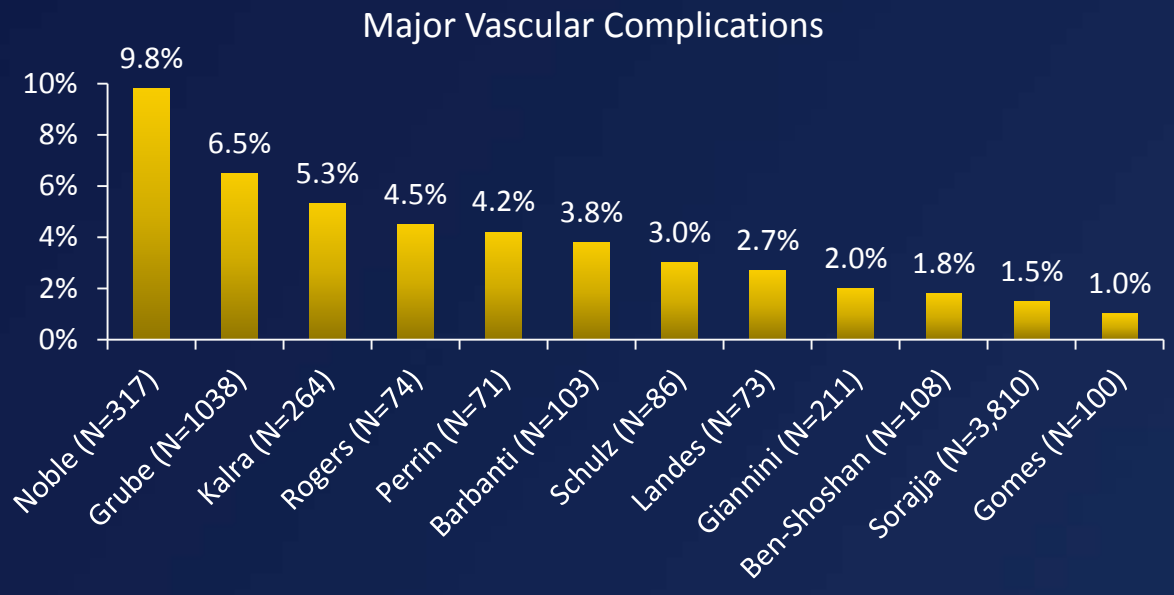
PVL

Weighted Average:

5.7%

Evolut R

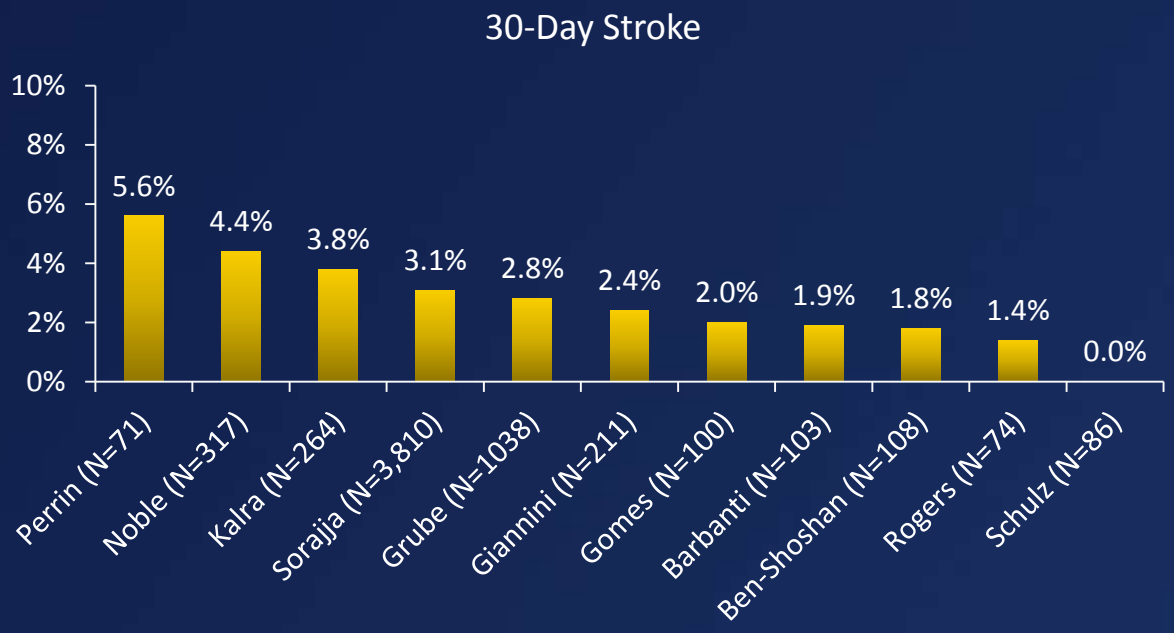
- Design Features
- Clinical Trials
- Long Term Follow-Up
- **Real World Experience**
- Design Iterations
- Clinical Program



MVCs

Weighted Average:

3.1%



All Stroke

Weighted Average:

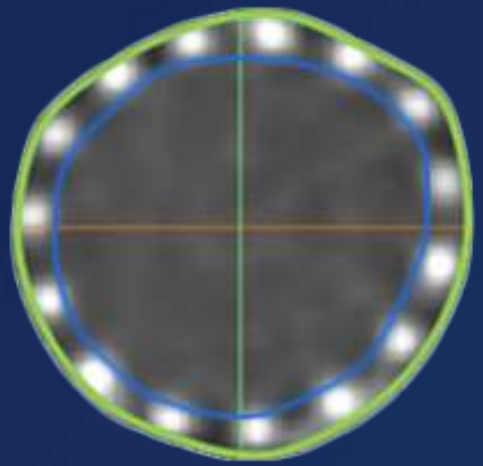
3.0%

Evolut PRO

- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- **Design Iterations**
- Clinical Program

Evolut PRO

- Evolut R with an added pericardial tissue wrap
- Provides greater surface area contact with native annulus
- Reduces “open spaces” between frame struts
- Enhances healing response due to pericardial tissue properties and increased surface contact



Evolut R

- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- **Design Iterations**
- Clinical Program

US Evolut PRO Study[1]

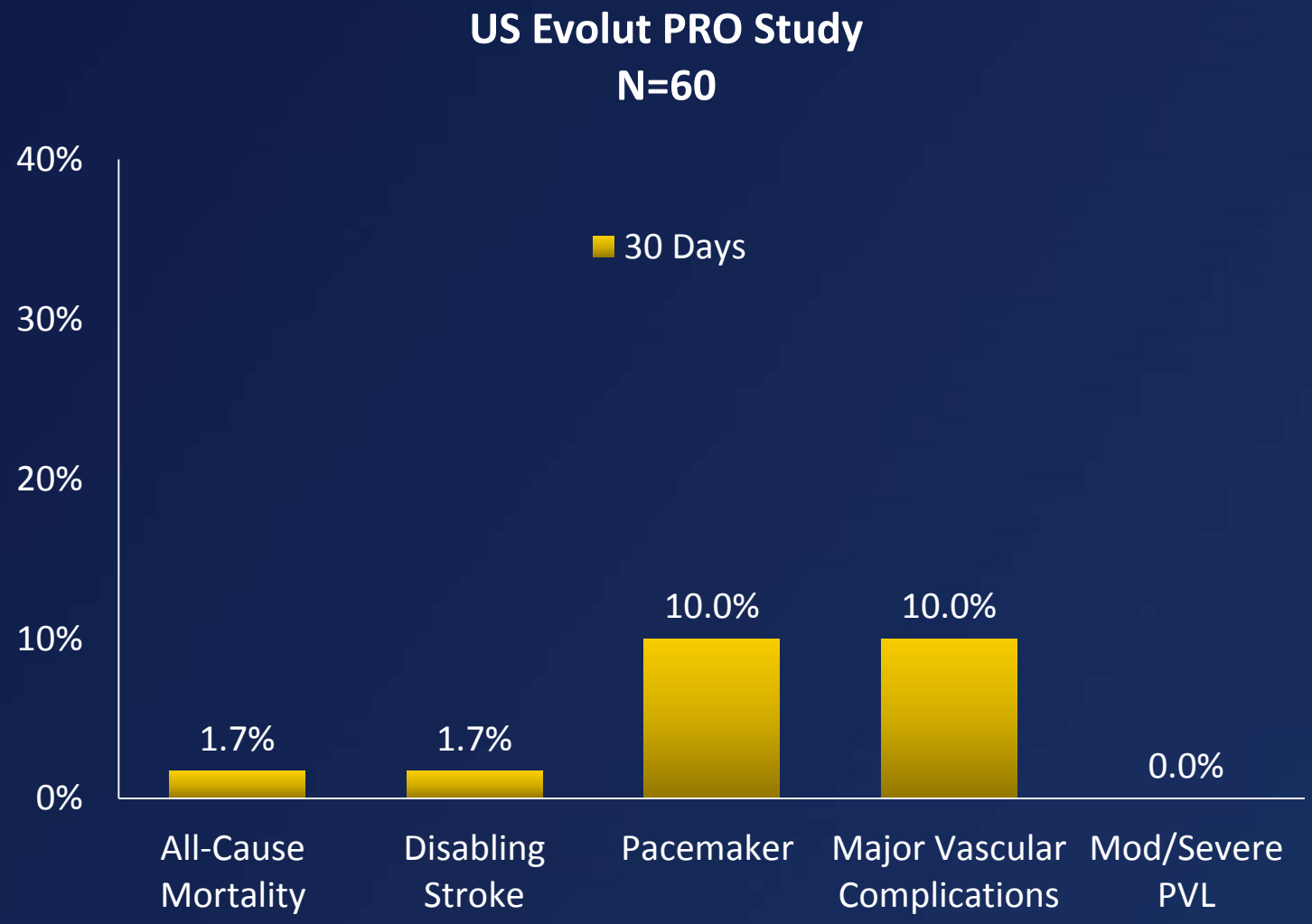
Single arm, observational
N = 60
STS: 6.4%
Age: 83 years
Female: 65%

Follow-up through 30 Days

[1]Forrest, et al., presented at ACC 2017

Evolut R

- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- **Design Iterations**
- Clinical Program



[1]Forrest, et al., presented at ACC 2017

Lotus

Lotus

Design Features

Clinical Trials

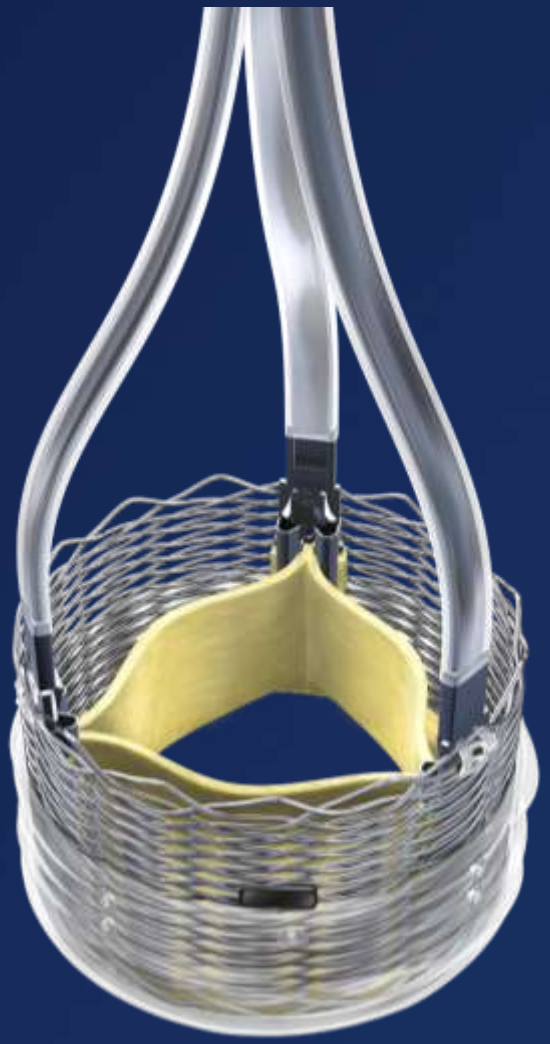
Long Term Follow-Up

Real World Experience

Design Iterations

Clinical Program

- Mechanically-expanded braided 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

- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- Design Iterations
- Clinical Program

REPRISE I

Single arm, observational
N = 11

Follow-up through 4 Years

REPRISE II + Extended Cohort[1]

Single arm, observational
N = 250
STS: 6.5%
Age: 84 yrs
Female: 52.4%

Follow-up through 2 Years

REPRISE III[2]

Randomized 2:1
Lotus vs. CoreValve
N = 912

Follow-up through 1 Year

[1]Meredith, et al., presented at PCR London Valves 2016; [2]Feldman, et al., presented at EuroPCR 2017

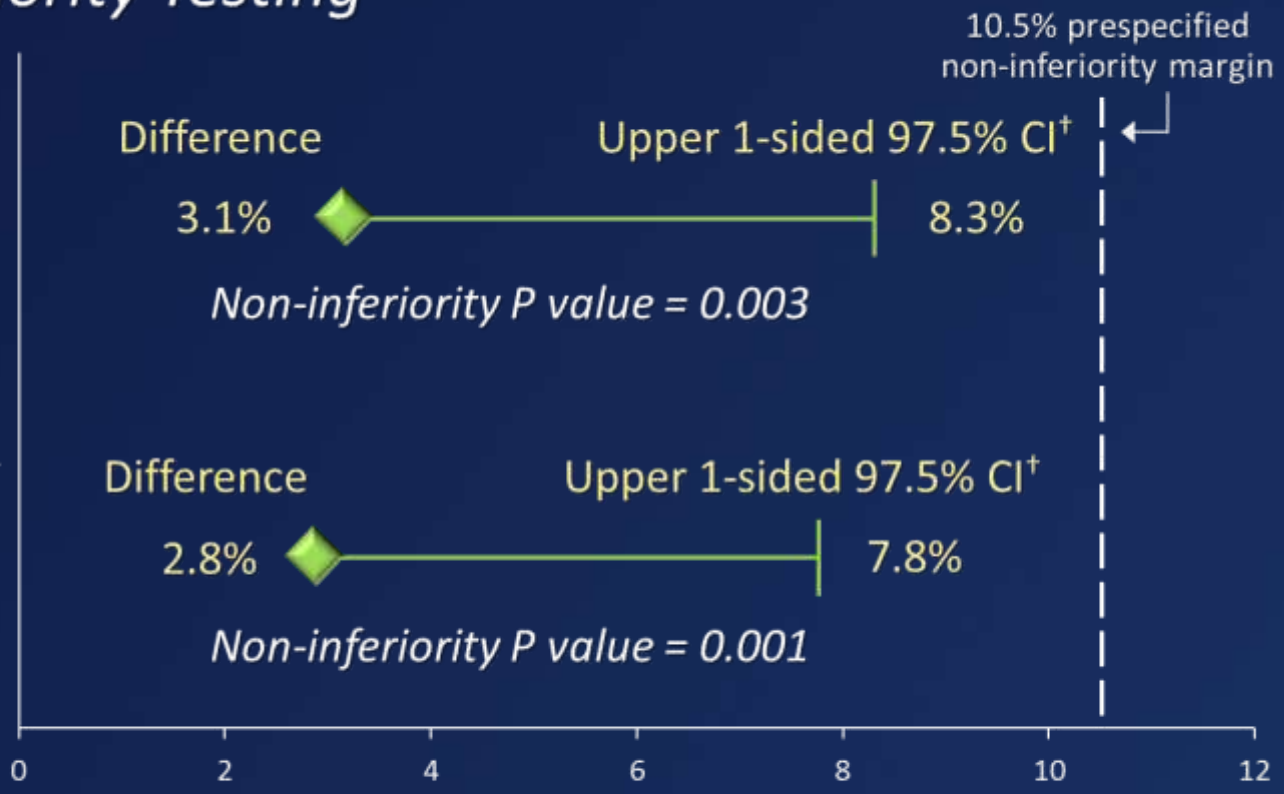
Lotus

REPRISE III
Lotus Valve System

- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- Design Iterations
- Clinical Program

Primary Composite Safety Endpoint*

Non-Inferiority Testing



*Death, stroke, life-threatening/major bleed, major vascular complications, stage 2/3 AKI at 30 days

→ *Non-inferiority criteria met for primary safety endpoint*

‡ Primary analysis set
† Upper 1-sided CI and *P* value are derived from the Farrington-Manning test

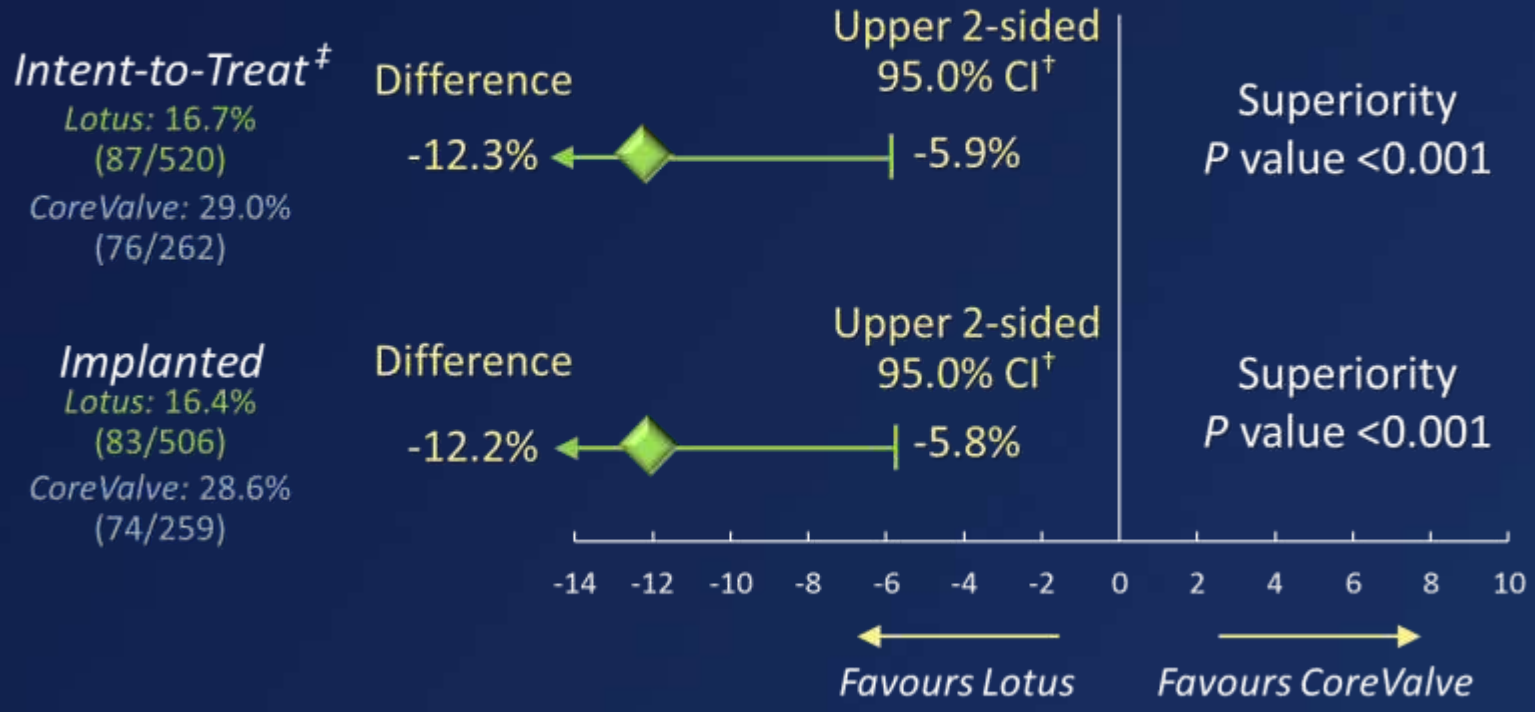
Lotus

REPRISE III
Lotus Valve System

- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- Design Iterations
- Clinical Program

Primary Effectiveness – Superiority

Death, Disabling Stroke, ≥ Moderate PVL at 1 Year

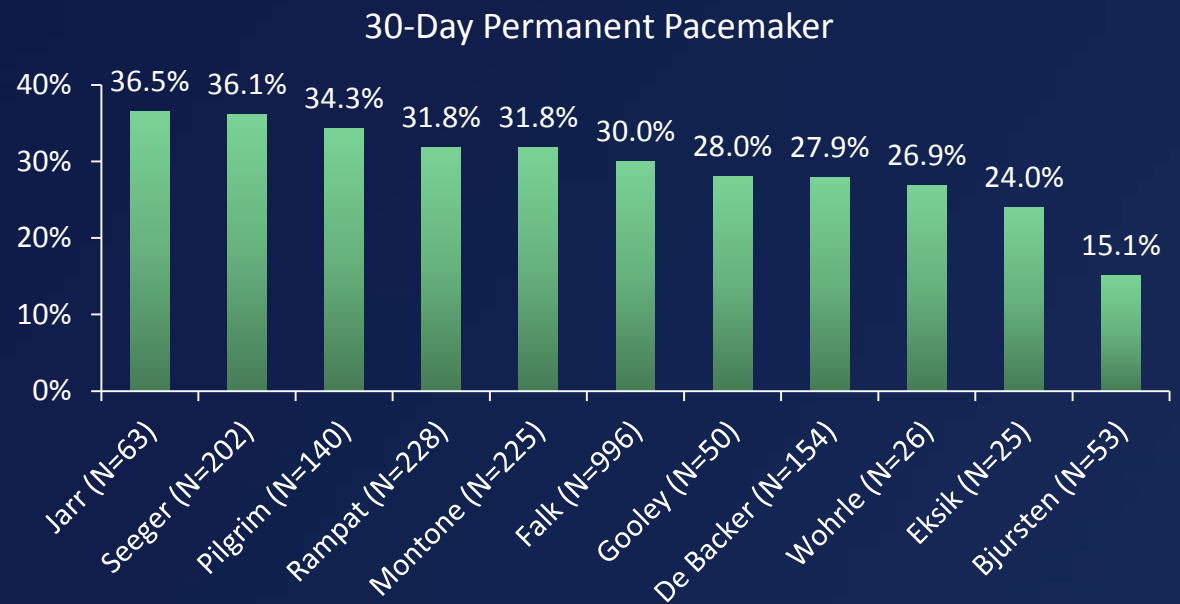


→ *Superiority achieved for primary effectiveness endpoint*

‡ Primary analysis set
† Superiority *P* value and 95% CI are derived from the Chi-square test

Lotus

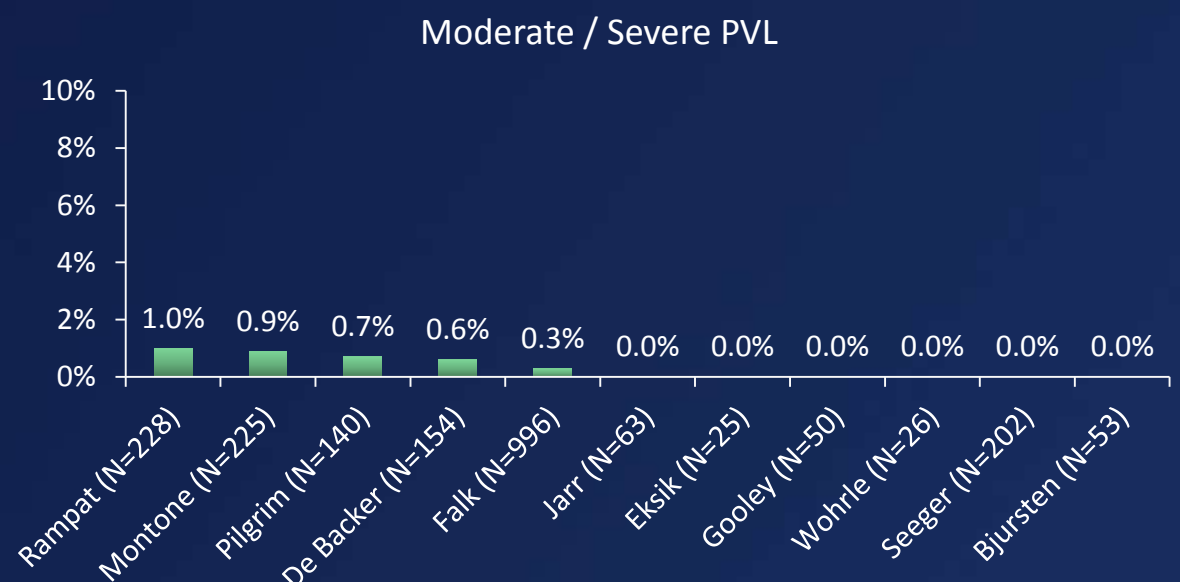
- Design Features
- Clinical Trials
- Long Term Follow-Up
- **Real World Experience**
- Design Iterations
- Clinical Program



Pacemakers

Weighted Average:

30.7%



PVL

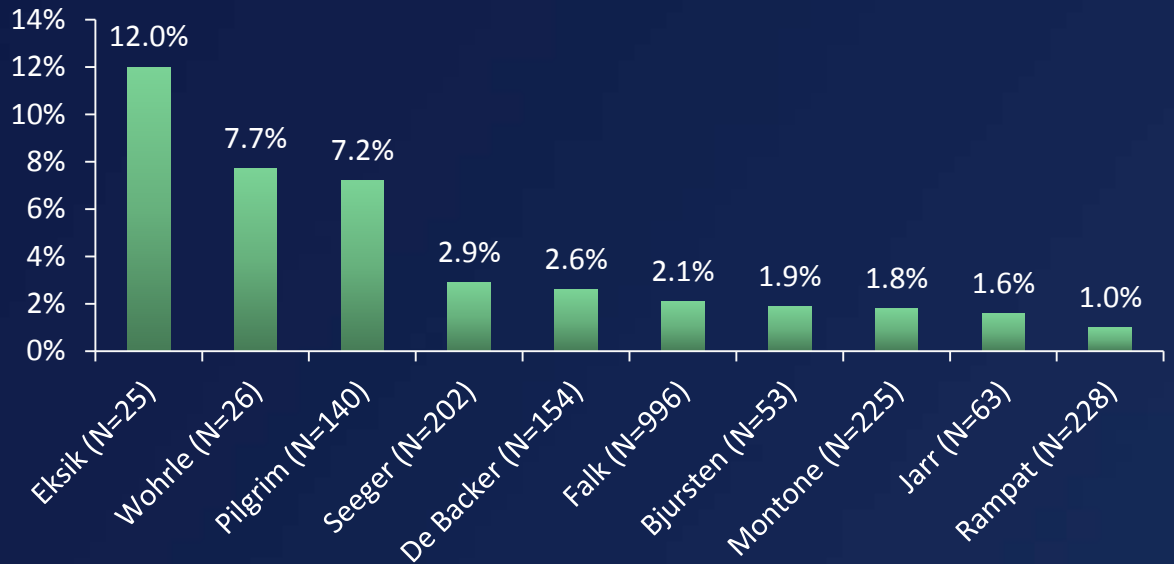
Weighted Average:

0.4%

Lotus

- Design Features
- Clinical Trials
- Long Term Follow-Up
- **Real World Experience**
- Design Iterations
- Clinical Program

Major Vascular Complications

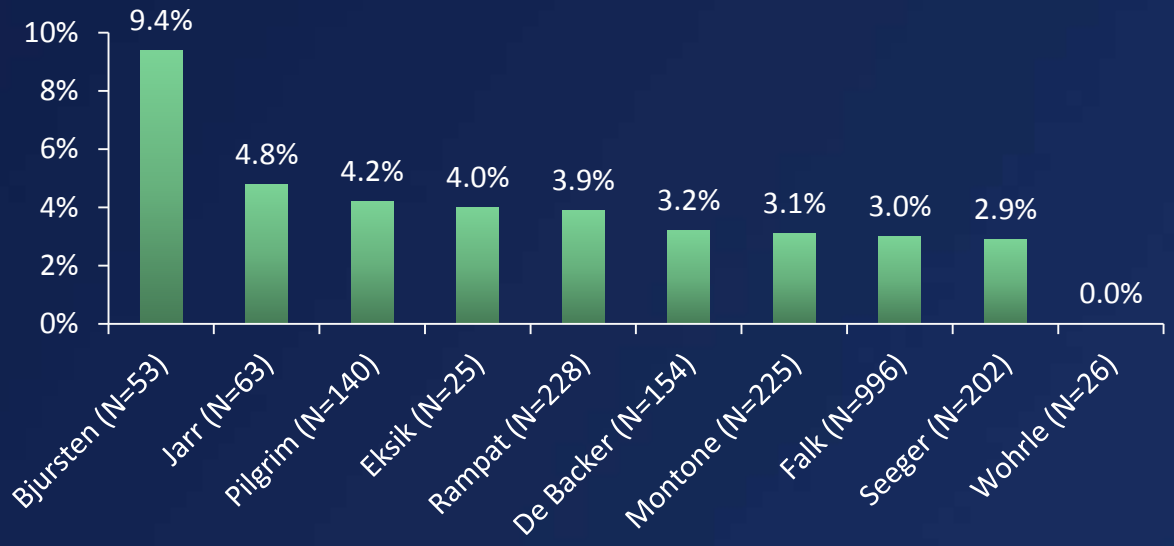


MVCs

Weighted Average:

2.5%

30-Day Stroke



All Stroke

Weighted Average:

3.3%

Portico

Portico

Design Features

Clinical Trials

Long Term Follow-Up

Real World Experience

Design Iterations

Clinical Program

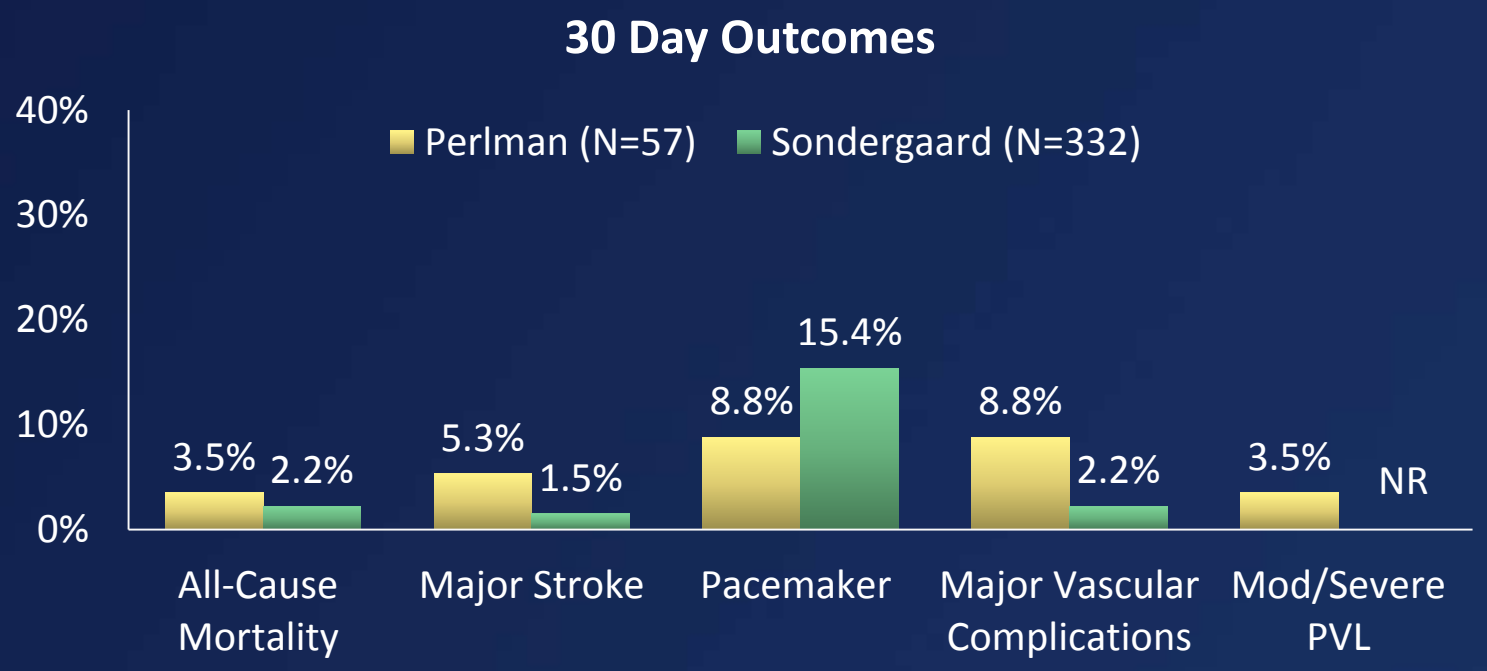
- Self-expanding Nitinol frame
- Intra-annular bovine pericardial valve
- Porcine pericardium sealing cuff
- Resheathable and recapturable
- Rapid pacing is not required for full deployment
- Annular range: 19 – 27 mm
  - 4 valve sizes: 23, 25, 27, 29 mm
- 18Fr sheath for 23 and 25 mm THVs
- 19Fr for 27 and 29 mm THVs

Portico

- Design Features
- Clinical Trials
- Long Term Follow-Up
- **Real World Experience**
- Design Iterations
- Clinical Program

Real-world outcomes in 389 patients have been reported

Study	Type	N	STS (%)	Age (Yrs)
Perlman[1]	Multicenter: Canada	57	7.7 ± 5.7	80.8
Sondergaard[8]	Portico I Study	332	5.6	82.9



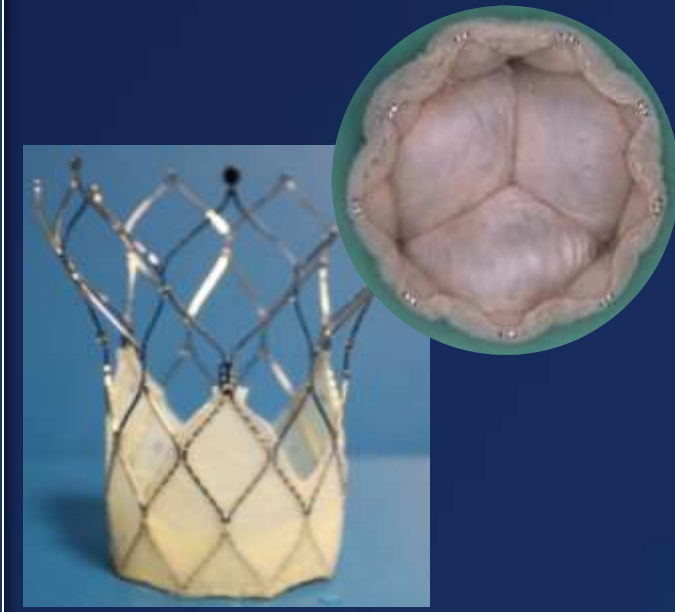
[1]Perlman, et al., *EuroIntervention* 2017; 12:1653-59; [2]Sondergaard, et al., presented at EuroPCR 2016

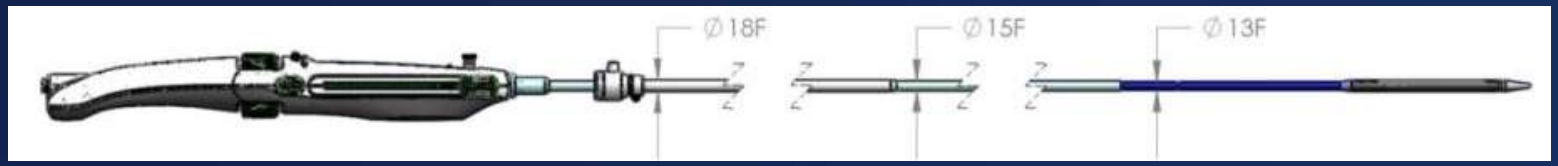
Portico

- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- **Design Iterations**
- Clinical Program

Next Generation Valve and Delivery System

- Enhanced low profile delivery and e-sheath compatibility
- Advanced placement accuracy
- Improved handle ease of use and ergonomics
- Enhanced valve stability
- Advanced PVL sealing feature
- Expanded valve size offering





[1]Pichard, et al., presented at TCT 2016

ACURATE neo

ACURATE neo

Design Features

Clinical Trials

Long Term Follow-Up

Real World Experience

Design Iterations

Clinical Program

- 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
  - 3 valve sizes: S, M, L
- 18Fr –sheath compatible, vessels ≥ 6.0mm

ACURATE neo

- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- Design Iterations
- Clinical Program

Acurate neo CE Mark Study[1]

Single arm, observational
N = 89
STS: 7.5%
Age: 83.7 yrs
Female: 65.2%

Follow-up through 1 Year

[1]Abizaid, et al., presented at CRT 2015

ACURATE neo

- Design Features
- Clinical Trials
- Long Term Follow-Up
- **Real World Experience**
- Design Iterations
- Clinical Program

Real-world outcomes in over 1,000 patients have been reported

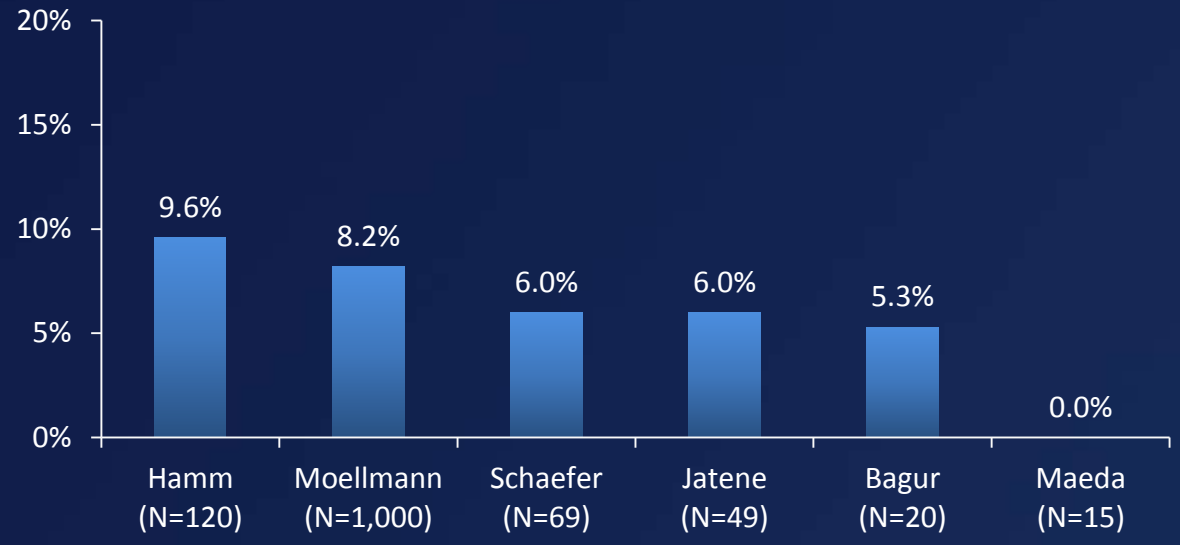
Study	Type	N	STS (%)	Age (Yrs)
Maeda[1]	Single Center: Osaka	15	7.5 ± 3.1	83.3
Bagur[2]	Multicenter: Canada	20	4.7 ± 2.3	82.7
Jatene[3]	Multicenter: Sao Paulo	49	6.1 ± 2.8	82.4
Schaefer[4]	Multicenter: Germany	69	5.6 ± 3.8	81.4
Hamm[5]	Single Center: Bad Neustadt	120	NR	81.4
Moellmann[6]	SAVI TF Registry	1000	6.0 ± 5.6	81.1

[1]Maeda, et al., *Circ J* 2015;79:1037-43; [2]Bagur, et al., *Catheter Cardiovasc Interv* 2016; epub; [3]Jatene, et al., *Catheter Cardiovasc Interv* 2016; epub; [4]Schaefer, et al., *Eur J Cardiothorac Surg* 2016; 50:368-73; [5]Hamm, et al., *EuroIntervention* 2017; epub; [6]Moellmann, et al., presented at TCT 2016

ACURATE neo

- Design Features
- Clinical Trials
- Long Term Follow-Up
- **Real World Experience**
- Design Iterations
- Clinical Program

30-Day Permanent Pacemaker

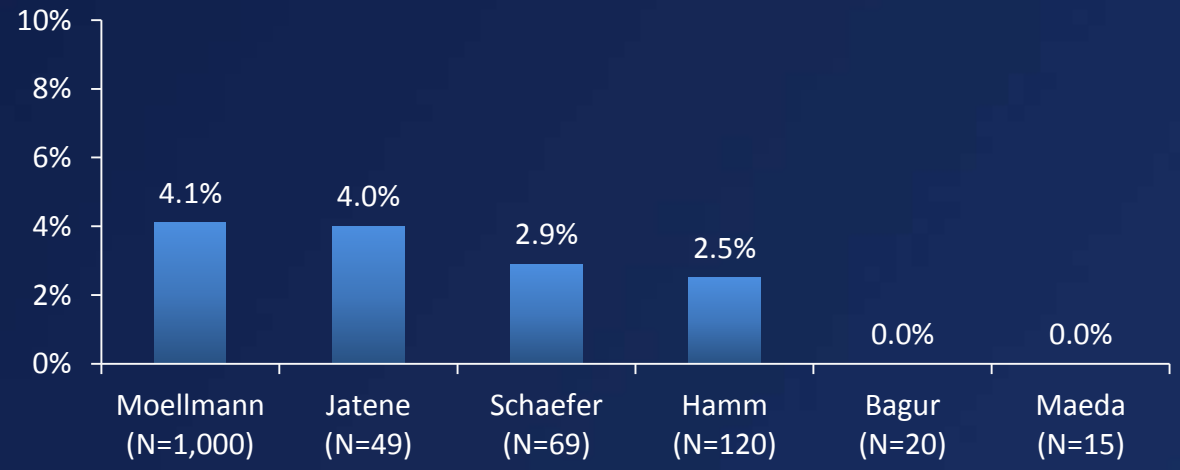


Pacemakers

Weighted Average:

8.0%

Moderate / Severe PVL



PVL

Weighted Average:

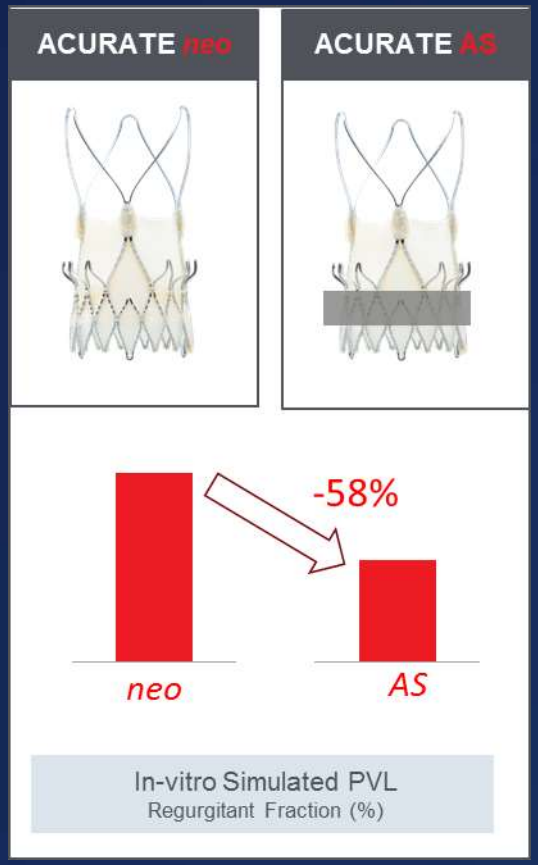
3.8%

ACURATE neo

- Design Features
- Clinical Trials
- Long Term Follow-Up
- Real World Experience
- Design Iterations
- Clinical Program

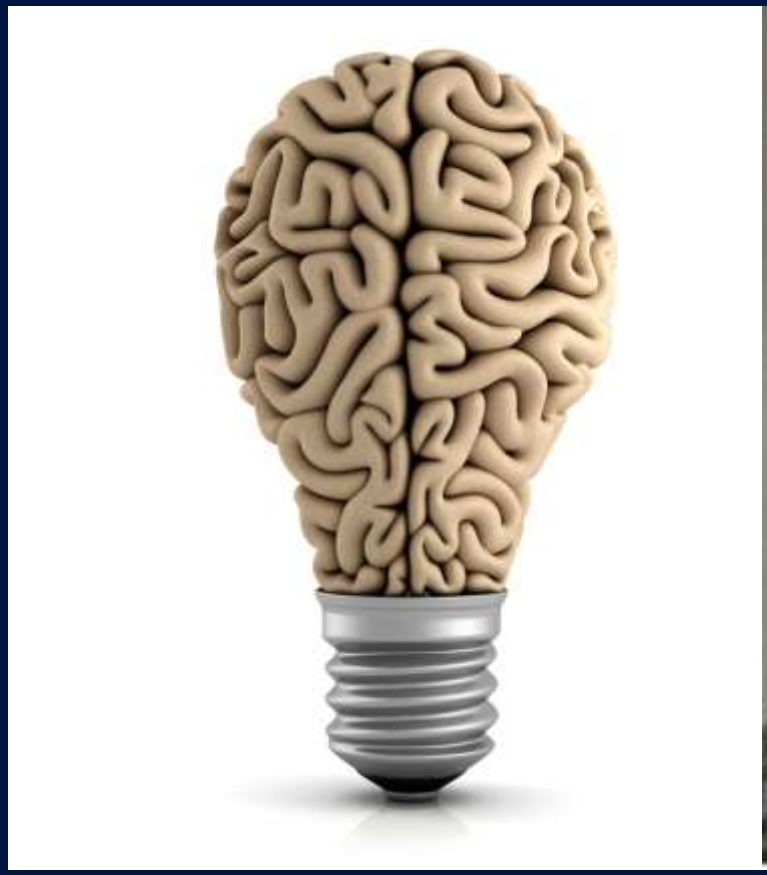
ACURATE neo AS

- ACURATE neo with modified skirt material
- Expected reduction of PVL
- CE mark trial ongoing, 30 of 120 patients are enrolled



[1]Walther, et al., presented at TVT 2017

What lies Ahead?



Venus A-Valve System

- Self-expanding frame
- Porcine pericardial valve
- Supra-annular leaflets
- 23, 26, 29 and 32mm
- Higher radial force

Venibri

- Preloaded in the delivery system, reduced profile

- Reduce aldehyde residue, decrease tissue calcification

- Dry tissue, half of the thickness as the fresh tissue
- Total recovery in 20s
- The new version will be retrievable

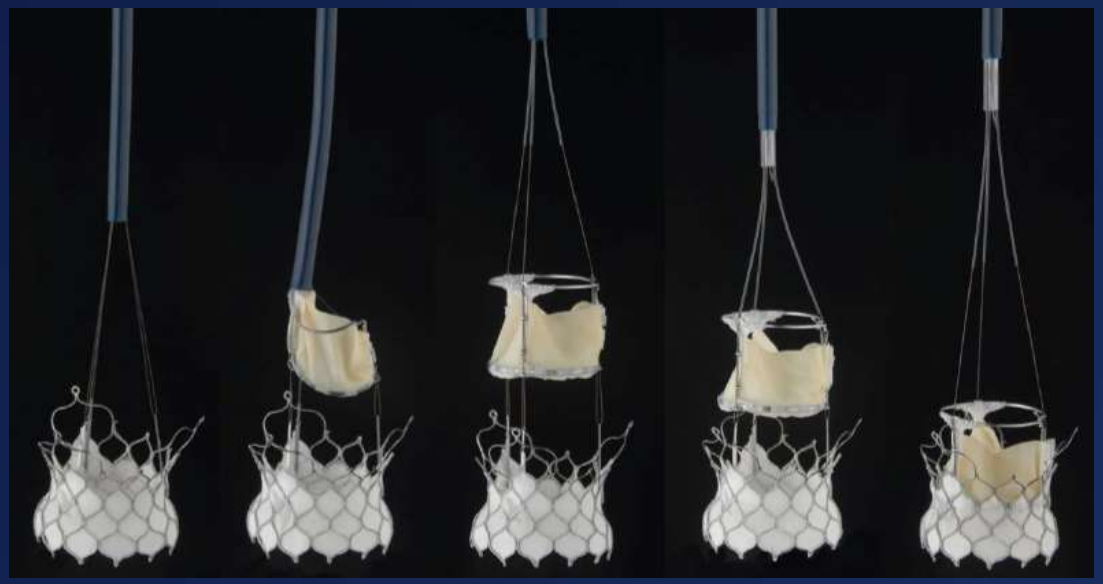
Valve Medical

- Frame and leaflets are introduced separately
- *In-situ* docking (valve to frame in ascending Ao)
- 12 Fr delivery
- Bovine pericardium
- Not crimped

Assembled Device

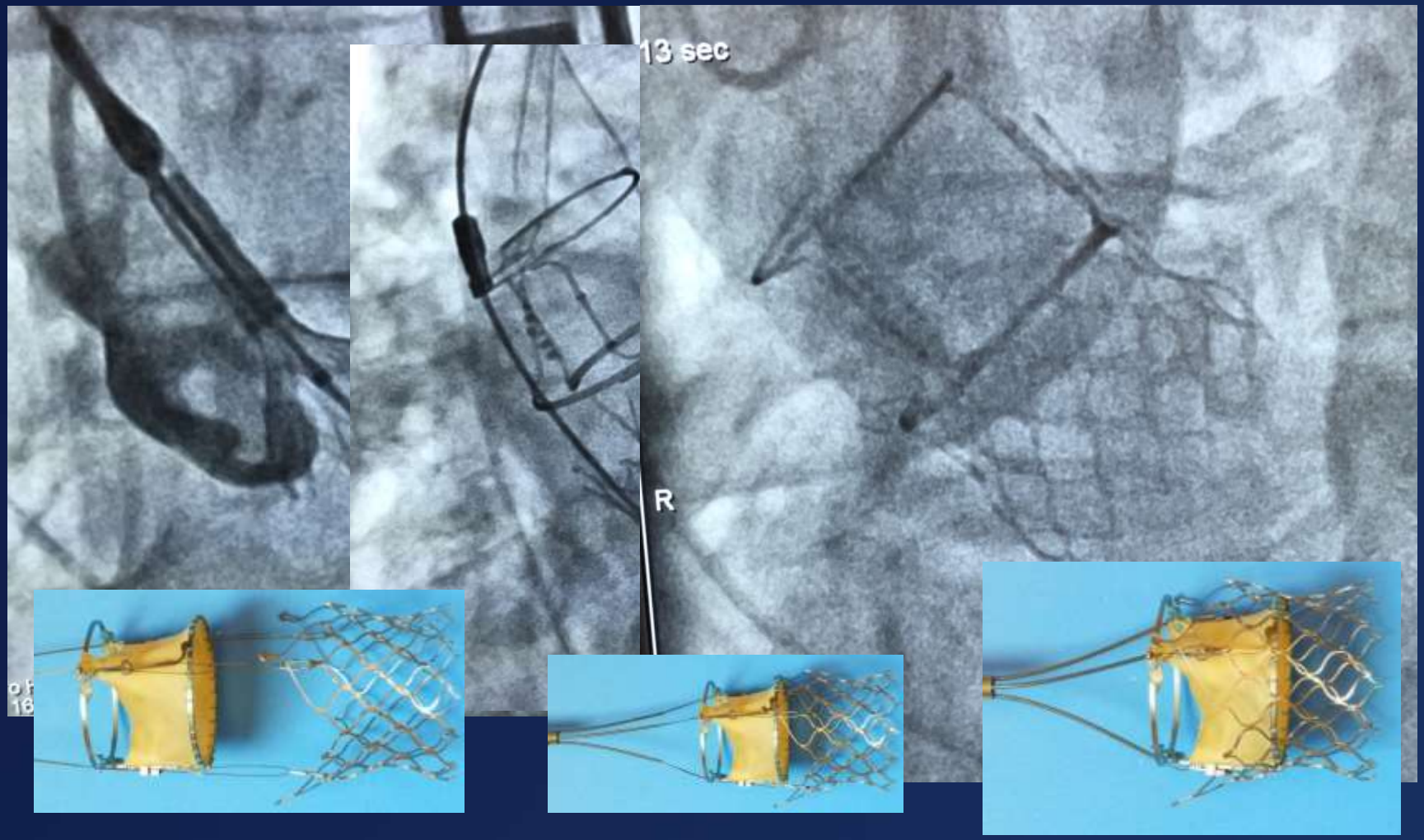
Frame Module

Valve Module



Frame and Valve Module Docking and Locking

First Successful 12 French Valve Medical TAVR Modular Implant

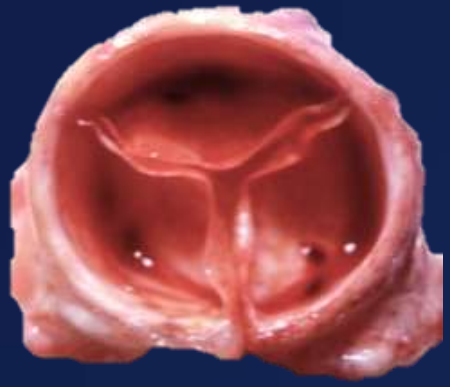


August 4, 2016, Instituto Dante Pazzanese São Paulo

Grube E, Abizaid A, Leon MBL

Xeltis

Endogenous Tissue Restoration (ERT)



Valve after bioabsorption

- Synthetic matrix made of biobsorbable polymers
- Polymer leaflets mounted on nitinol self-expanding frame
- Regrowth of endogenous tissue coincident with bioabsorption of polymer implant

Take Home Messages

- Many problems have been solved but pacemaker rates are still too high with some valves

- We need
  - more data in low surgical risk patients
  - data in younger patients
  - long term results
  - valves designed for patients with aortic insufficiency

- Based on the available data, TAVI may become the therapy of choice for most patients with aortic valve disease

Thank you for Your kind Attention!