

TCT AP 2013  
Seoul, Corea April 18, 2013

# CoreValve is „Enough“!

(Core Valve is Better?)



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# Eberhard Grube, MD

Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

## Physician Name

## Company/Relationship

Eberhard Grube, MD

Medtronic, CoreValve: C, SB, AB, OF  
Sadra Medical: E, C, SB, AB  
Direct Flow: C, SB, AB  
Mitralign: AB, SB, E  
Boston Scientific: C, SB, AB  
Biosensors: E, SB, C, AB  
Cordis: AB  
Abbott Vascular: AB  
Capella: SB, C, AB  
Valtech: E, SB,  
Claret: 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'

# TAVI Arrives

## *Current Generation Devices*

***>75,000 patients treated thru 2013  
in >650 interventional centers  
around the globe!***



Edwards Lifesciences



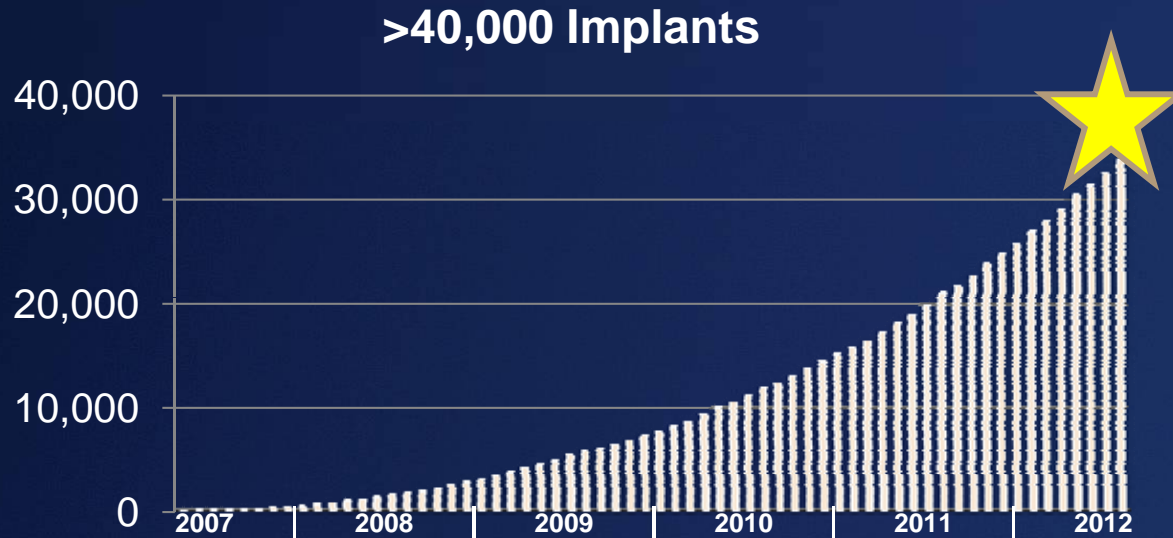
Medtronic CoreValve

# Anatomic “Footprint” of Edwards Sapien valve vs. MDT CoreValve



# CoreValve Global Growth

## Cumulative Implant Growth

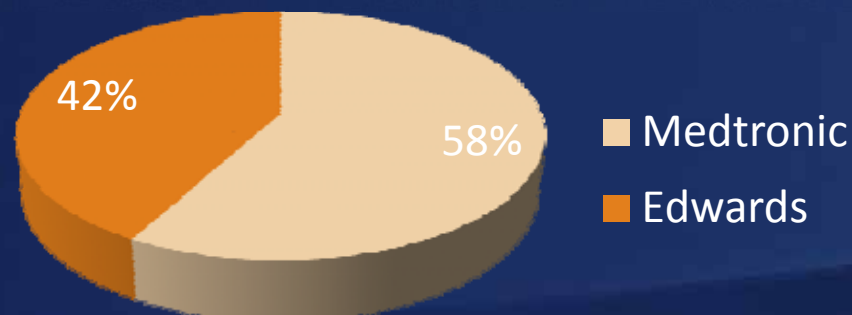


## New Market Expansion

(past 24 months)



## Addressable Market Share



MDT CoreValve share of TF OUS Market

# Advantages of BE Edwards Sapien

- Short frame design – less interference with peri-valve anatomy (conduction system, CAs)
- Precise positioning in the sub-annular zone (but requires RV pacing for deployment)
- Deflectable delivery system to negotiate arch anatomy and vessel tortuosity
- Circular frame/valve deployment in annular zone
- Full thickness bovine pericardium – good durability (?)
- Access site versatility (TF, TA, TAo)

# Advantages of SE MDT CoreValve

- More valve sizes to accommodate full range of annular dimensions (esp. large sizes)
- Slow controlled valve deployment without need for rapid RV pacing
- Partial repositioning features during deployment
- Less trauma to annulus and aorta – reduced risk of rupture
- Circular frame/valve in supra-annular zone (better for small annulus and small V-in-V)
- Access site versatility (TF, SC, TAO)
- LMA distance from annulus less important

# Areas of Consideration

- Patient Selection

- Procedure

- Post Procedure

- Future



# Aortic Size Considerations

CoreValve Able to Treat > 27-29 mm; at least ~20% more patients

Annulus Diameter in mm

16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31

Edwards  
SAPIEN XT



\* EW 20 mm Valve not yet CE marked

16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31

Medtronic  
CoreValve



Medtronic and Edwards Product IFU's

# Vessel Size Considerations

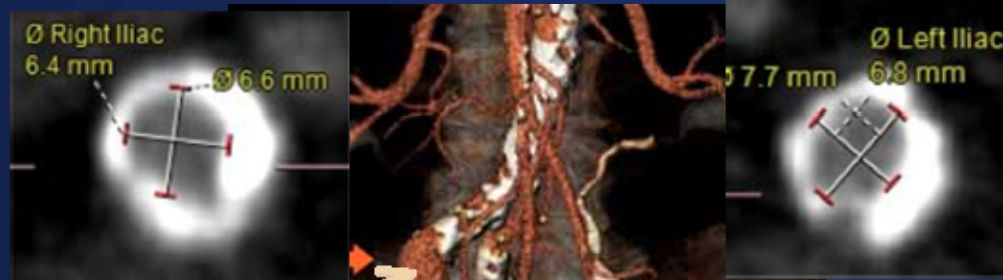
CoreValve is able to Treat Patients with Small and Challenging Vasculature  $\geq 6\text{mm}$

Low Delivery Profile: 18Fr delivery system for all valve/annulus sizes

18

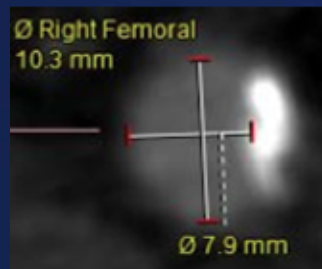
Annulus Size (mm)

29















< OD 18Fr  
6.93 mm

Tortuosity,  
Calcium,  
Marginal CSA



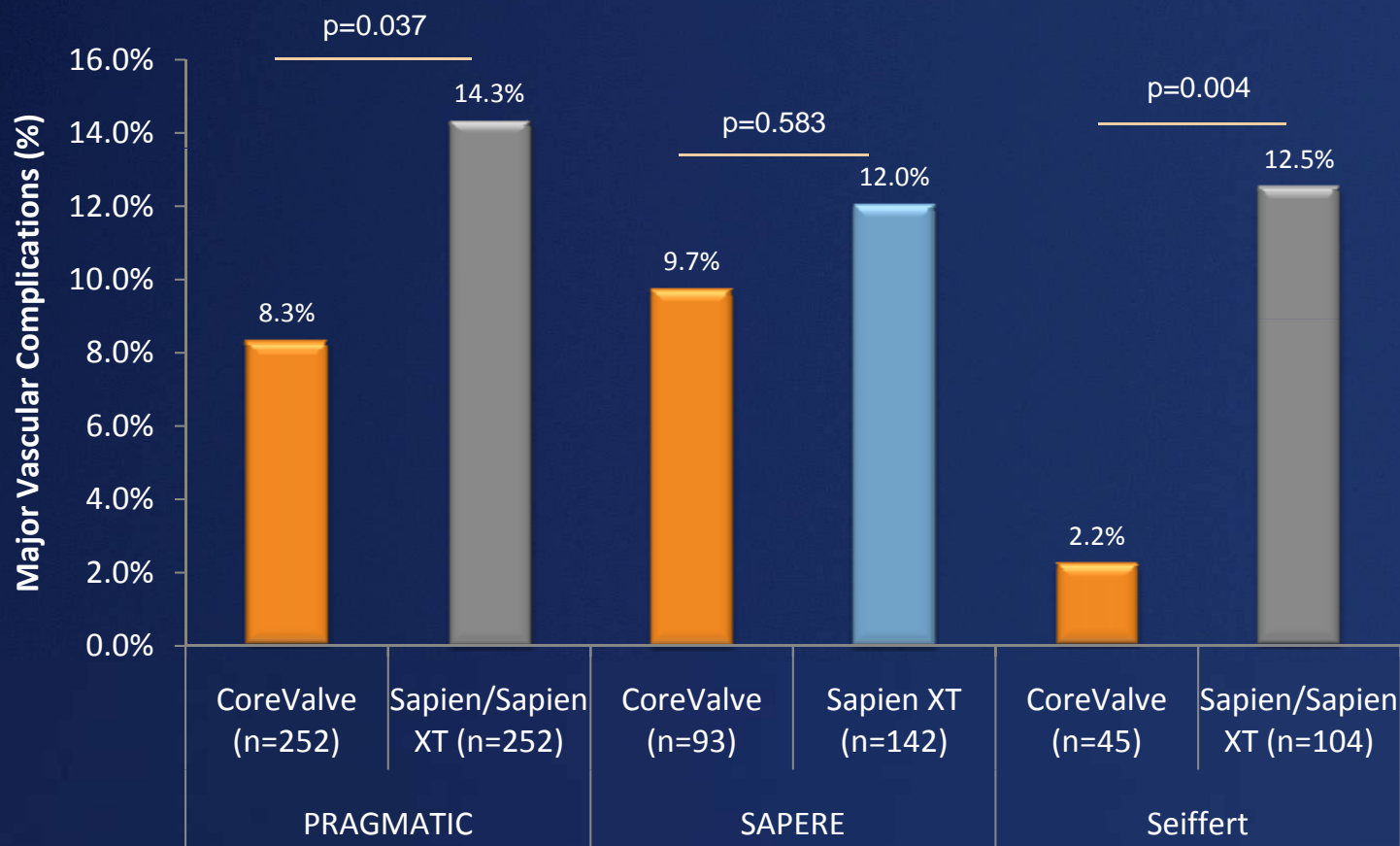
# Maximum Sheath Size

CoreValve® and CoreValve Evolut	23mm (18-20mm)	26mm (20-23mm)	29mm (23-27mm)	31mm (26-29mm)
AccuTrak® with Cook Sheath	 21.8FR	 21.8FR	 21.8FR	 21.8FR
Sapien XT™	23mm (18-22mm)	26mm (21-25mm)	29mm (24-28mm)	Not Available
w/NovaFlex and Sheath:	 21.7FR	 22.5FR		
w/ EDW e-Sheath ( <u>U</u> nexpanded and While <u>E</u> xpanded):	20.1FR  26.7FR* 	21.6FR  26.7FR* 	24.0FR  29.7FR* 	

- The E-Sheath starts as small as 16F, but expands to maximum diameter of 29.7F as the valve passes through the delivery system<sup>1</sup>.

# Direct Comparisons of CoreValve and Edwards

- 3 studies have directly compared TF-TAVI outcomes between CoreValve and Edwards valves<sup>1,2,3</sup>.
  - PRAGMATIC<sup>1</sup> performed propensity score matching due to differences in baseline characteristics. Seiffert<sup>2</sup> and Buchanan<sup>3</sup> represent real world cohorts.



1. Chieffo, abstract TCT-859 presented at TCT 2012  
2. Seiffert, et al., Cath Card Int 2012; epub Nov 21, 2011

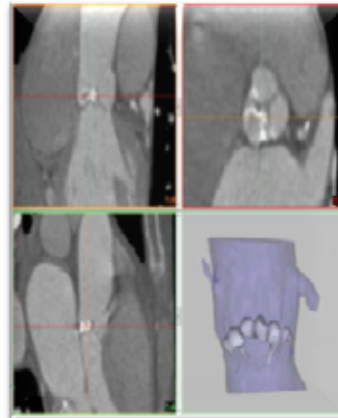
3. Buchanan et al., Poster Abstract TCT-843, Presented at TCT 2012

# Potential for Expanded Indications

Failed  
Bioprosthesis



Pure  
Aortic  
Insufficiency



Bicuspid  
Valve





# TAVI in Failed Surgical Bioprosthetic Valve

## Transcatheter Aortic-Valve Implantation for the Treatment of Degenerative Bioprosthetic Surgical Valves: Results from the Global Valve-in-Valve Registry

*Danny Dvir, John Webb, Stephen Brecker, Sabine Bleiziffer, David Hildick-Smith, Antonio Colombo, Fleur Descoutures, Nell E Moat, Luca Testa, Christian Hengstenberg, Raffi Bekerdjian, Thierry Lefevre, Victor Guetta, Henrik Nissen, José-María Hernández, David Roy, Federico De Marco, Rui Teles, Amit Segev, Andreas Baumbach, Nicolas Dumontell, Claudia Florina, Dan Ioanes, Michael Gotzmann, Massimo Napodano, Didier Tchetché, Gian P Ussia, Marc W Merx, Mohamed Abdel-Wahab, Jean-Claude Laborde, Ran Kornowski*

TCT 2011 danny.dvir@gmail.com



## Valve in Valve Procedures 30-day outcome

Median Duration of hospital stay- 8 days

CoreValve  
Edwards-SAPIEN

### All cause mortality

7.5%

12.7%

P=0.24

### CV mortality

5.8%

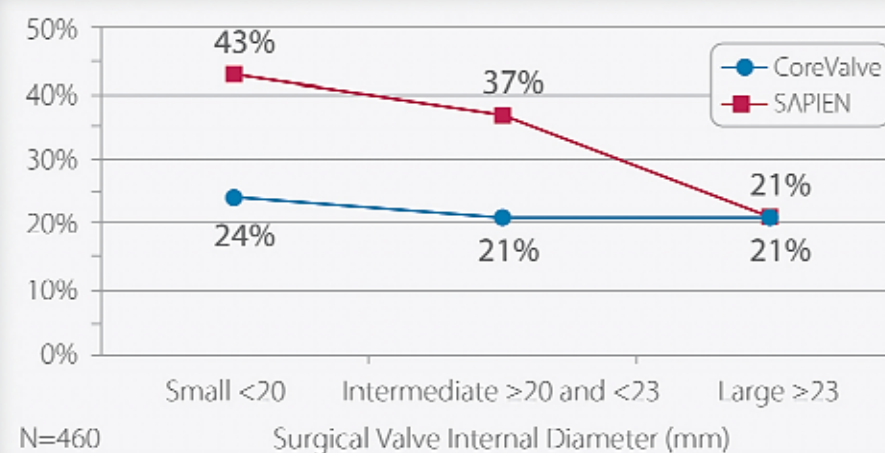
11.3%

P=0.18

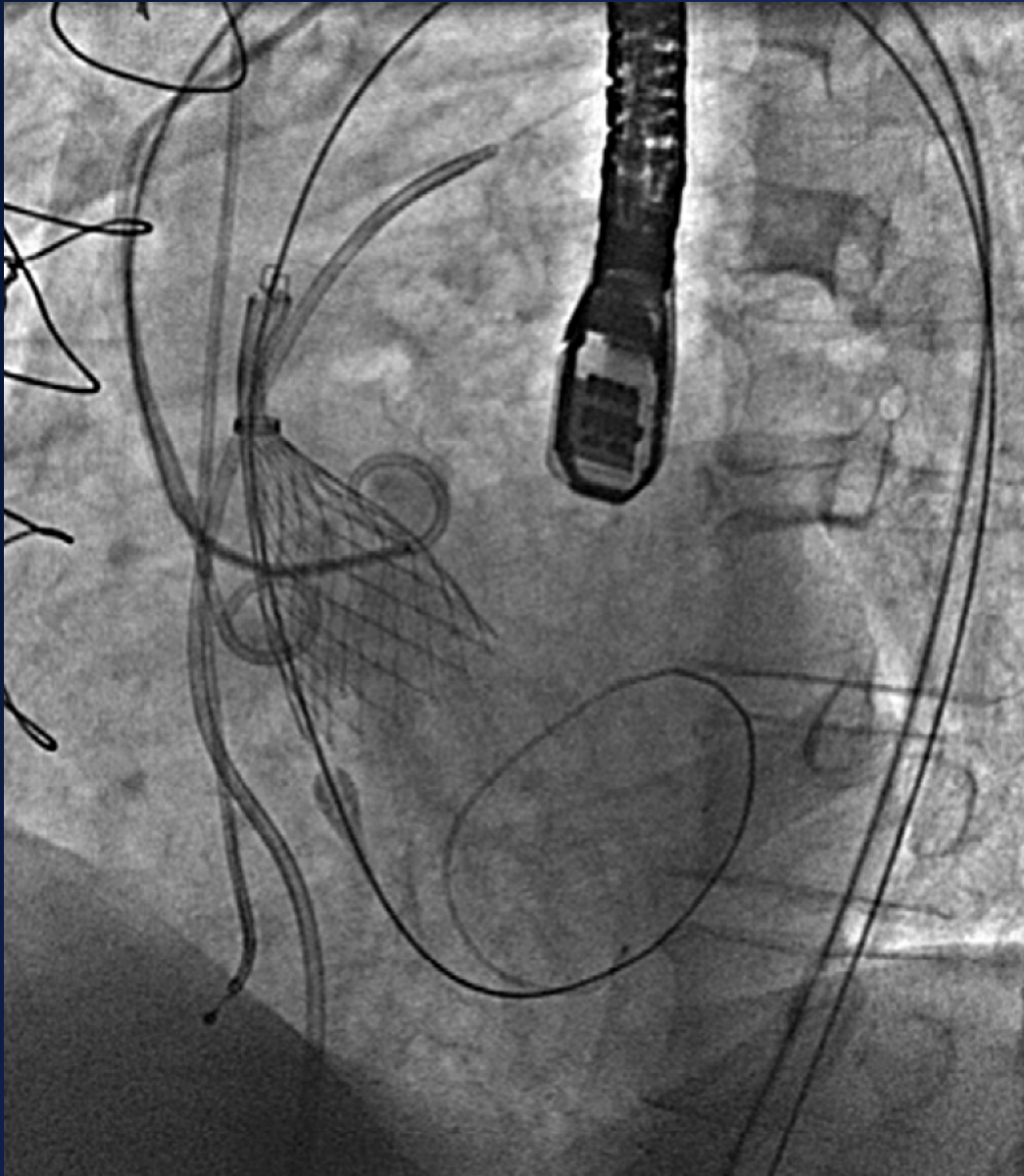
TCT 2011



## Rate of Post-Procedural Gradients >20 mmHg (%)<sup>2</sup>



# TAVI for Pure Severe Native AR



- 43 patients from 14 centers
- TAVI with CoreValve prosthesis
- Procedural success 97.7%
- 8 patients (18.6%) second valve
- AR  $\leq$  I in 79.1%
- Only in 2 patients AR  $\geq$  III
- Pacemaker in 16.3%
- 30 day-stroke rate 4.7%
- 30 day-mortality rate 9.3%
- Prosthesis deployment
  - Rapid pacing
  - “Two pigtail”-technique



# Implantation in Bicuspid Native Valve

## CARDIOVASCULAR FLASHLIGHT

doi:10.1093/eurheartj/ehr316  
Online publish-ahead-of-print 6 September 2011

### Transcatheter implantation of an aortic valve prosthesis in a female patient with severe bicuspid aortic stenosis

Janusz Kochman, Zenon Huczek, Łukasz Koltowski\*, and Marcin Michalak

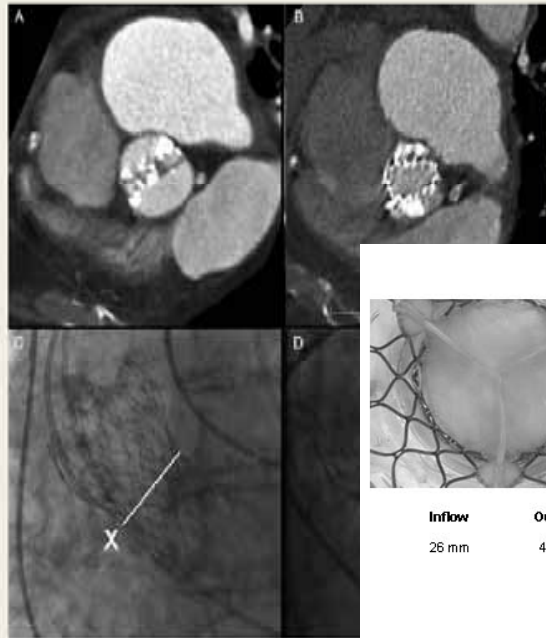
1st Department of Cardiology, Medical University of Warsaw, Warsaw, Poland

\*Corresponding author. lukasz@koltowski.com

A successful implantation of transcatheter aortic valve was performed in a high risk 85-year-old female with severe symptomatic stenosis of a bicuspid aortic valve (BAV) [Panel A] and tight lesions in left anterior descending (LAD) and circumflex artery (LCx). Until recently, BAV remained a contraindication to transcatheter aortic valve replacement (TAVR). Due to EuroSCORE of 43.6%, the Heart Team excluded the patient from surgical aortic valve repair. Four weeks after successful LAD and LCx stent angioplasty, a CoreValve<sup>TM</sup> 29 mm (Medtronic) was implanted through the right femoral artery. Follow-up echocardiography showed significant improvements in peak gradient from 81 mm Hg to 34 mm Hg, mean gradient from 44 mm Hg to 16 mm Hg, valve area from 0.5 cm<sup>2</sup> to 1.3 cm<sup>2</sup>, left ventricle ejection fraction from 29% to 50% and systolic pulmonary artery pressure from 65 mm Hg to 39 mm Hg. In spite of these, the CT angiography (Panel B) and the angiographic image (Panel C, D) showed uneven expansion of the valve. Controversy remains, whether post-dilatation would help to achieve a more 'friendly' image and, most importantly, larger valve area potentially could constitute a threat of aortic annular disruption, especially in loci with high pressure.

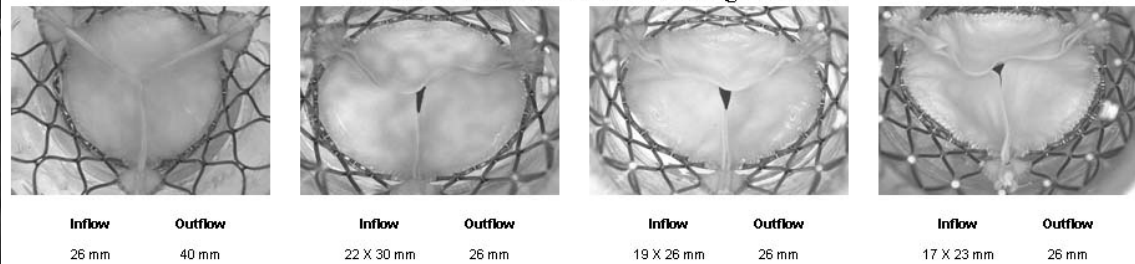
This case exemplifies how crucial it is to establish guidelines for TVAR technique in patients with BAV. This case contributes to discussion on the use of appropriate approach for safe and efficient TVAR in BAS as an indication.

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2011. For permissions please email

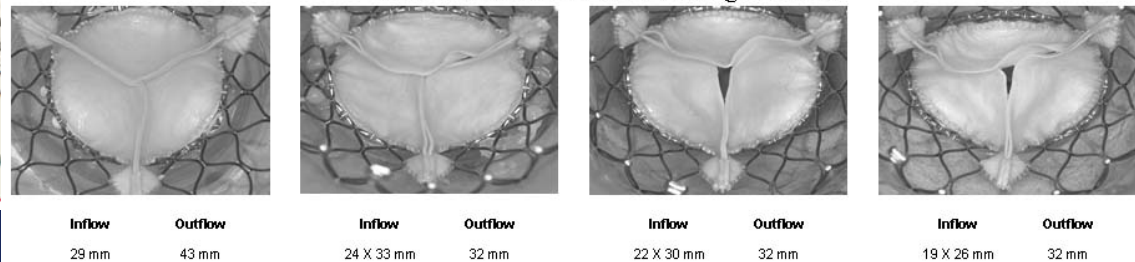


CoreValve system with conformable Nitinol frame and supra-annular valve function adapts to extreme elliptical deployments

### 26mm CoreValve Test Configurations



### 29mm CoreValve Test Configurations





# Areas of Consideration

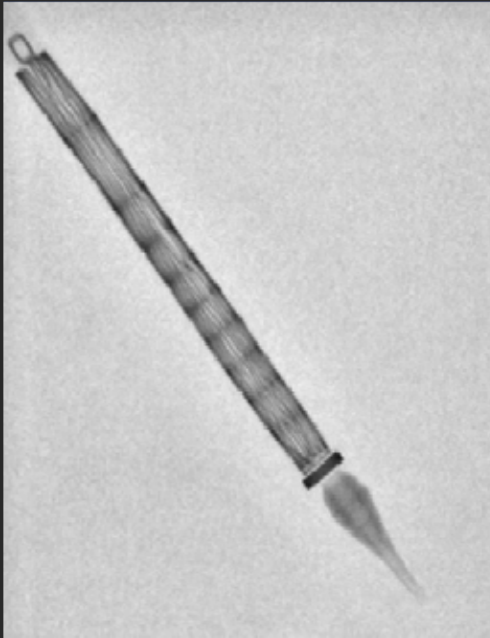
- Patient Selection

- Procedure

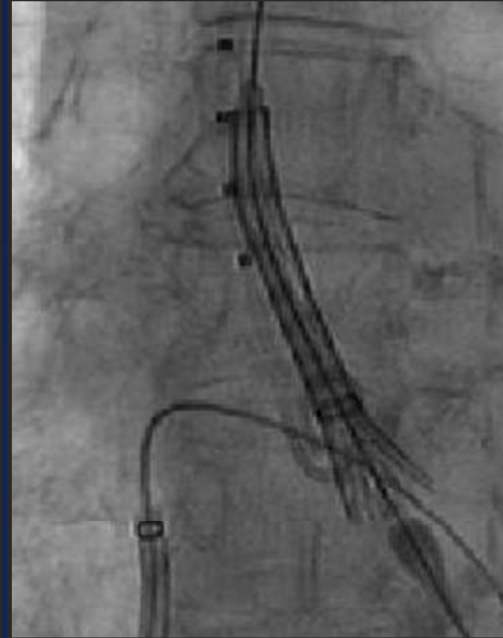
- Post Procedure

- Future

# Ease of Implant



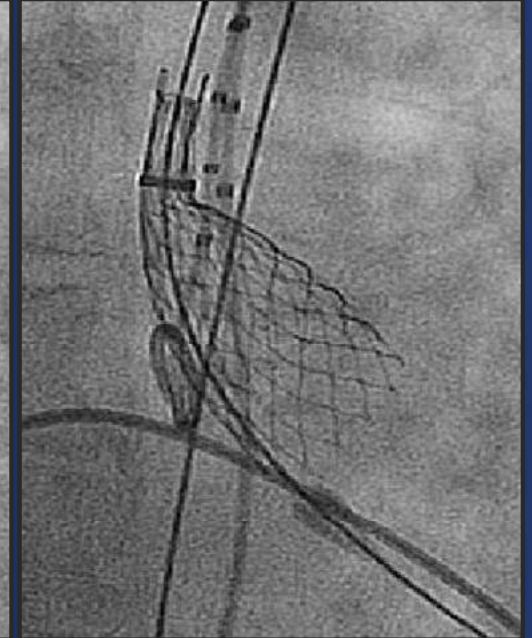
**18Fr delivery**



**Partial repositioning with gradual Release**



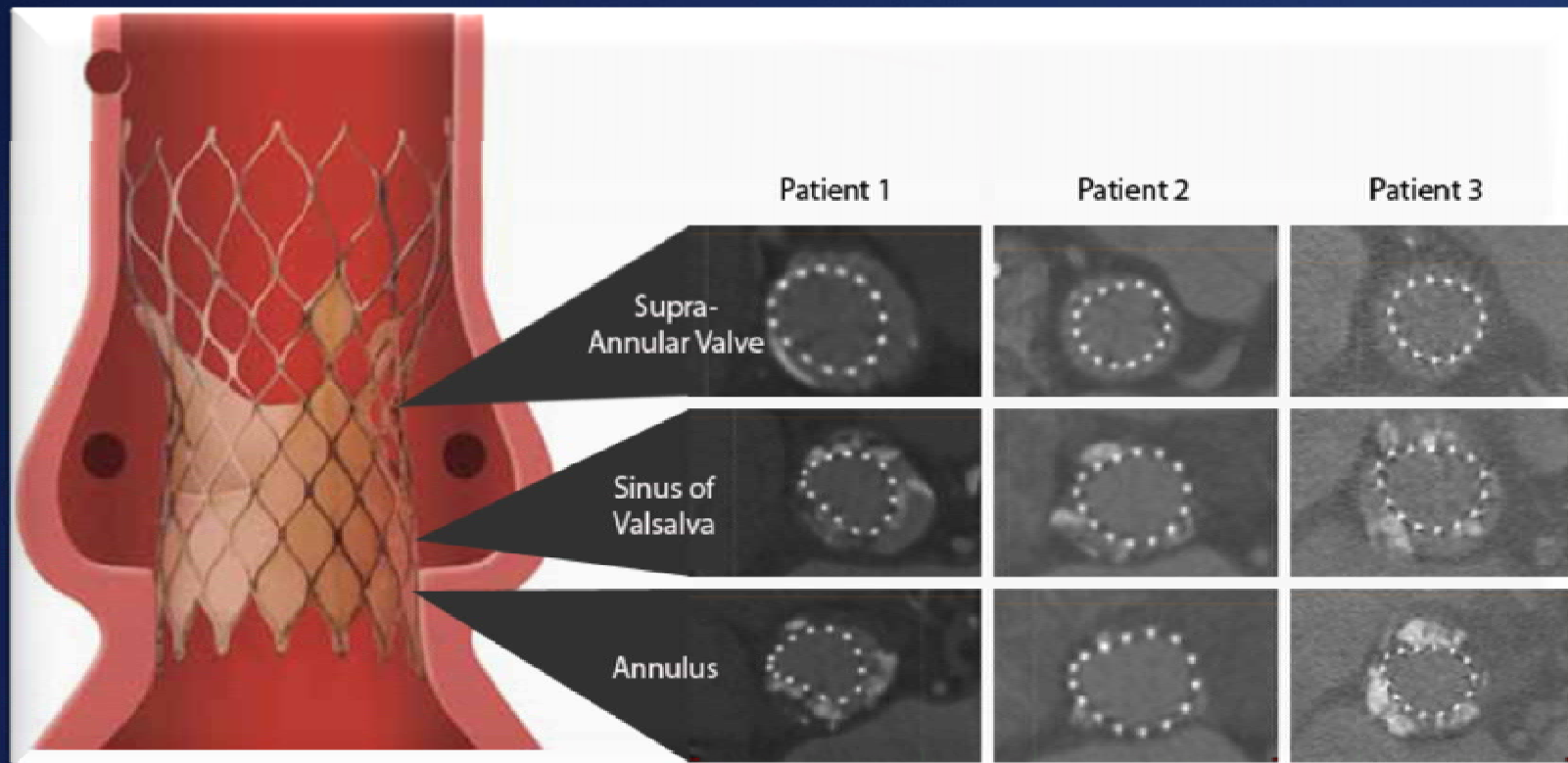
**Slow, controlled valve deployment without need for rapid ventricular pacing**



**Conformable at annulus with supra-annular function**

# Frame Design Flexibility

- Valve in supra-annular zone (better for elliptical annulus, and V-in-V)
- Less trauma to annulus and aorta – reduced risk of annular rupture



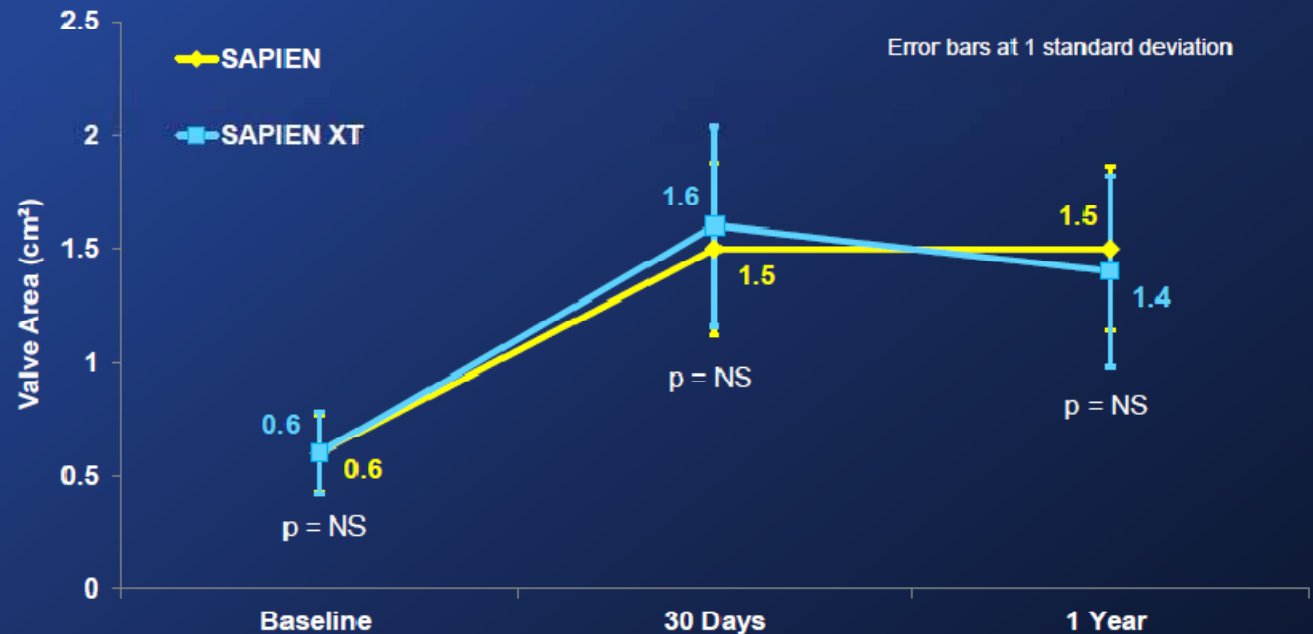
# CoreValve Supra Annular Valve Location May Produce Higher EOA

A Randomized Evaluation of the SAPIEN XT Transcatheter Valve System in Patients with Aortic Stenosis Who Are Not Candidates for Surgery: PARTNER II, Inoperable Cohort

Martin B. Leon, MD  
on behalf of The PARTNER Trial Investigators

ACC 2013 | San Francisco | March 10, 2013

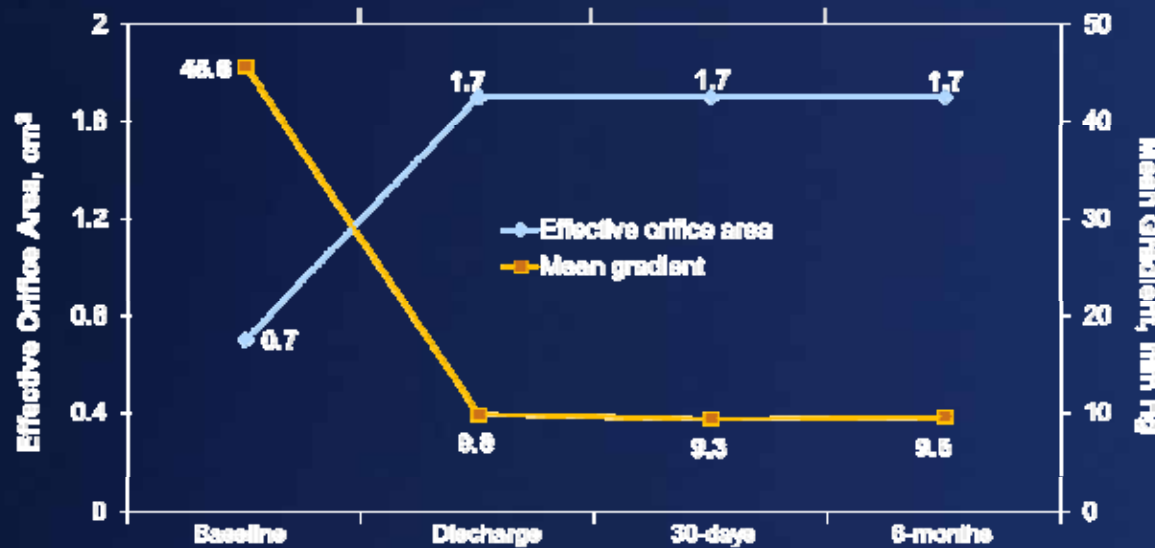
## Echocardiographic Findings: Aortic Valve Area (AT, Valve Implanted)



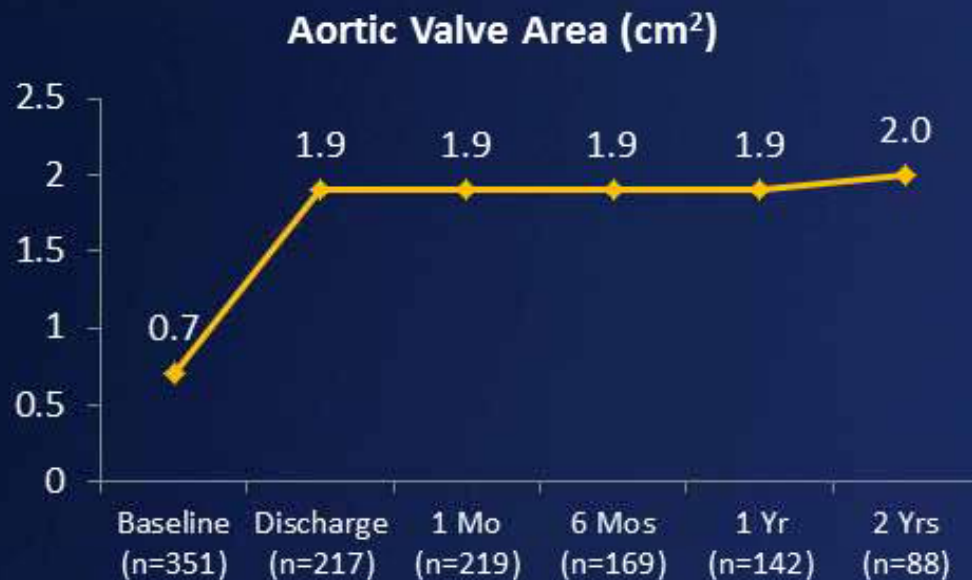
No. of Echos

SAPIEN	229	215	112
SAPIEN XT	256	233	117

# CoreValve Hemodynamic Results

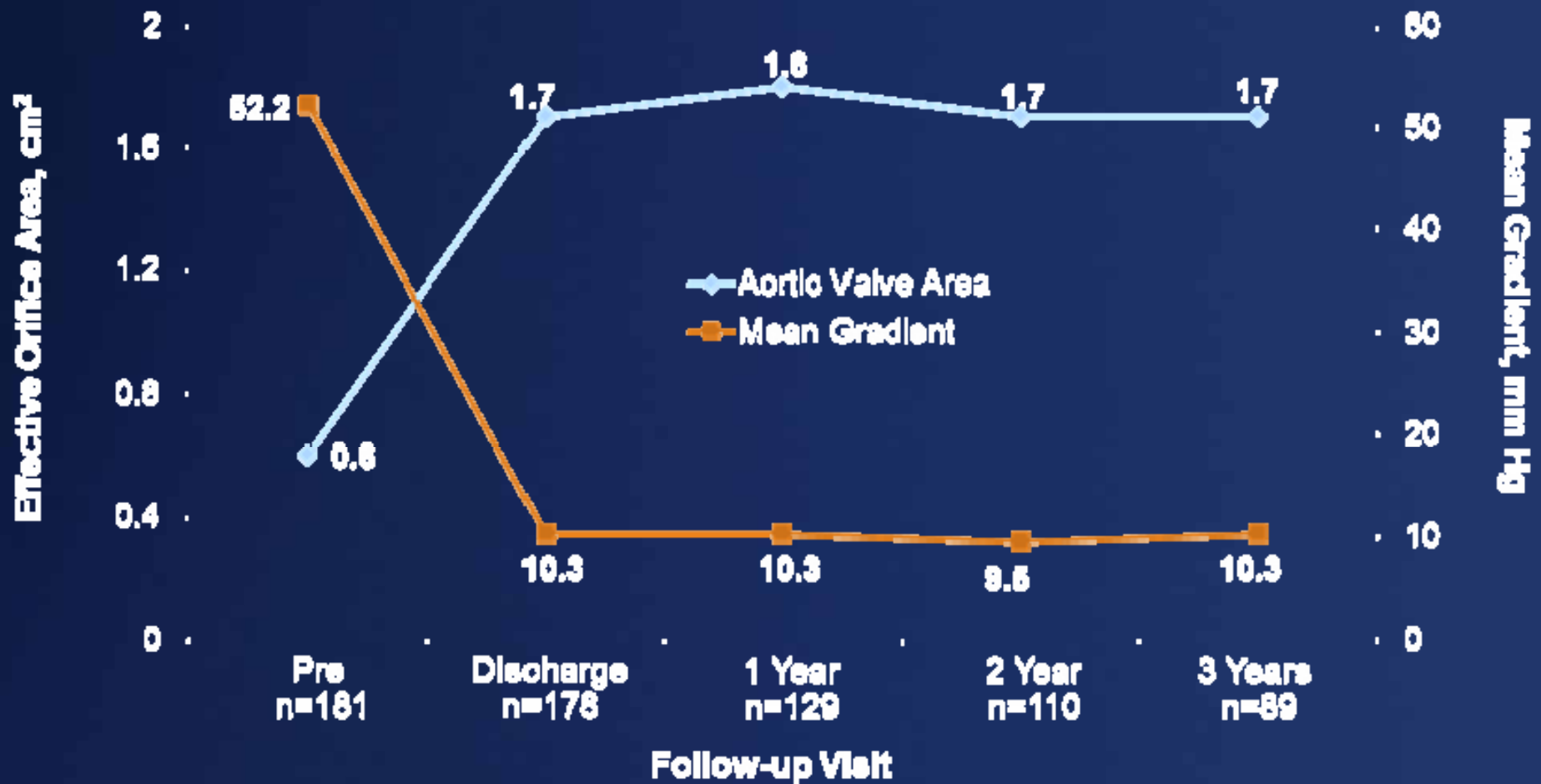


ADVANCE  
Registry



ANZ Registry  
Results @ 2 Years

# CoreValve Results Sustained to Three Years





# Opportunity for Further Procedural Simplification

## Feasibility of Transcatheter Aortic Valve Implantation Without Balloon Pre-Dilation

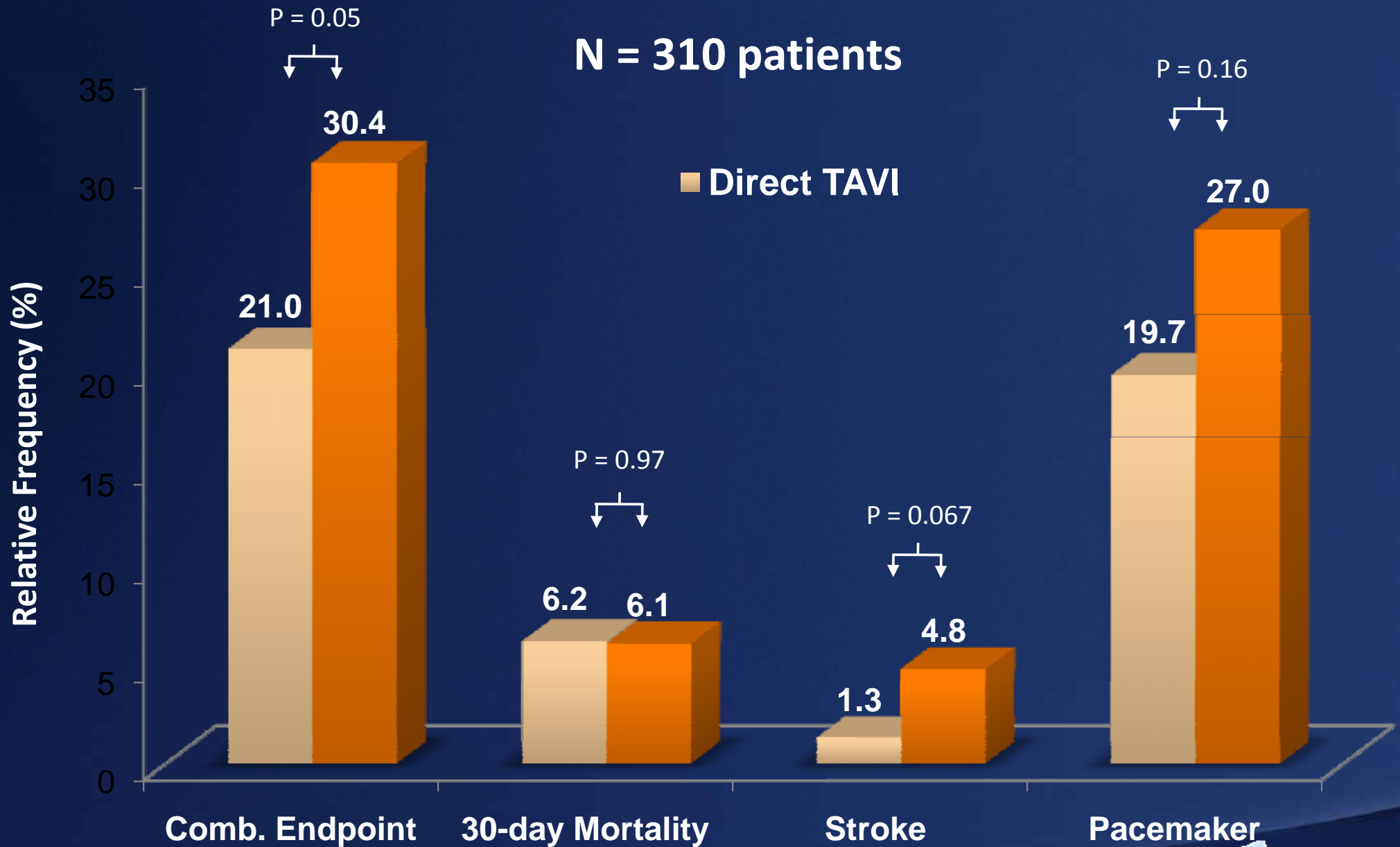
### A Pilot Study

Eberhard Grube, MD,\* Christoph Naber, MD,† Alexandre Abizaid, MD,‡  
Eduardo Sousa, MD,‡ Oscar Mendiz, MD,§ Pedro Lemos, MD,|| Roberto Kalil Filho, MD,||  
Jose Mangione, MD,¶ Lutz Buellesfeld, MD#

*Bonn and Essen, Germany; Sao Paulo, Brazil; Buenos Aires, Argentina; and Bern, Switzerland*

- Pilot study of **60 consecutive patients** undergoing CoreValve implantations at 13 international centers from 2009 to 2010.
- Procedural success was **96.7%** (58 of 60 patients).
- A **new pacemaker** was implanted in **11.7%** (7 of 60) of the patients w/out balloon pre-dilation, as compared to 27.8% in a historical control group (n=126)
- **The stroke rate was 5%** in patients without balloon pre-dilation as compared to 11.9% in the historical control group.
- Indicates that TAVI w/out balloon pre-dilation seems to be feasible and should be investigated further in a larger Trial.

# Direct TAVI: Bonn-Heidelberg Cohort





# Areas of Consideration

- Patient Selection

- Procedure

- Post Procedure

- Future

# Post Procedure Considerations

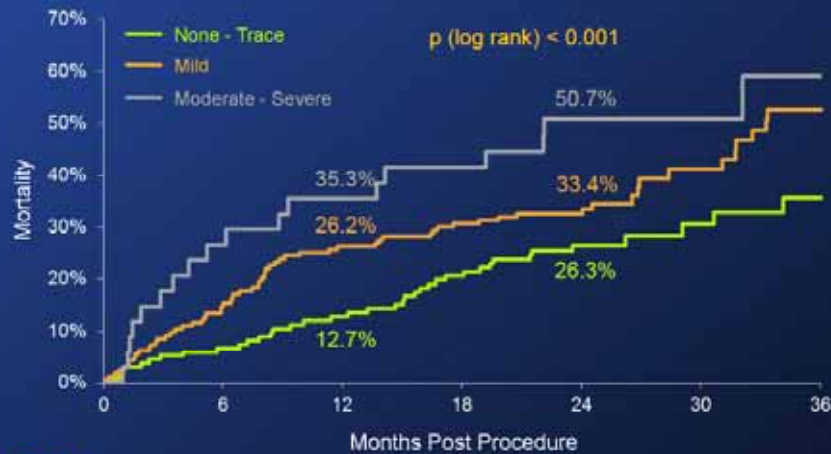
- Positive Survival Results Across Trials for Both Devices
- ParaValvular Leak Remains a Concern for Both Devices
- Longer Term Performance of the Valves and Associated Complications Needs Further Assessment

# Paravalvular Leak is Associated with Mortality

## PARTNER

## ADVANCE

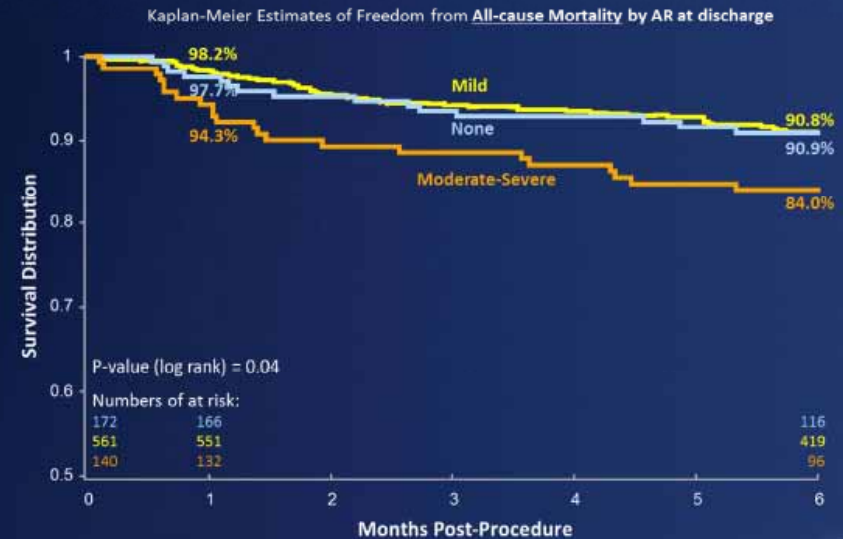
**Total AR and Mortality  
TAVR Patients (AT)**



**Numbers at Risk**

	0	6	12	18	24	30	36
None-Tr	135	125	115	101	88	31	11
Mild	165	139	121	111	71	33	16
Mod-Sev	34	25	22	19	15	6	2

**CoreValve ADVANCE | Survival by AR**

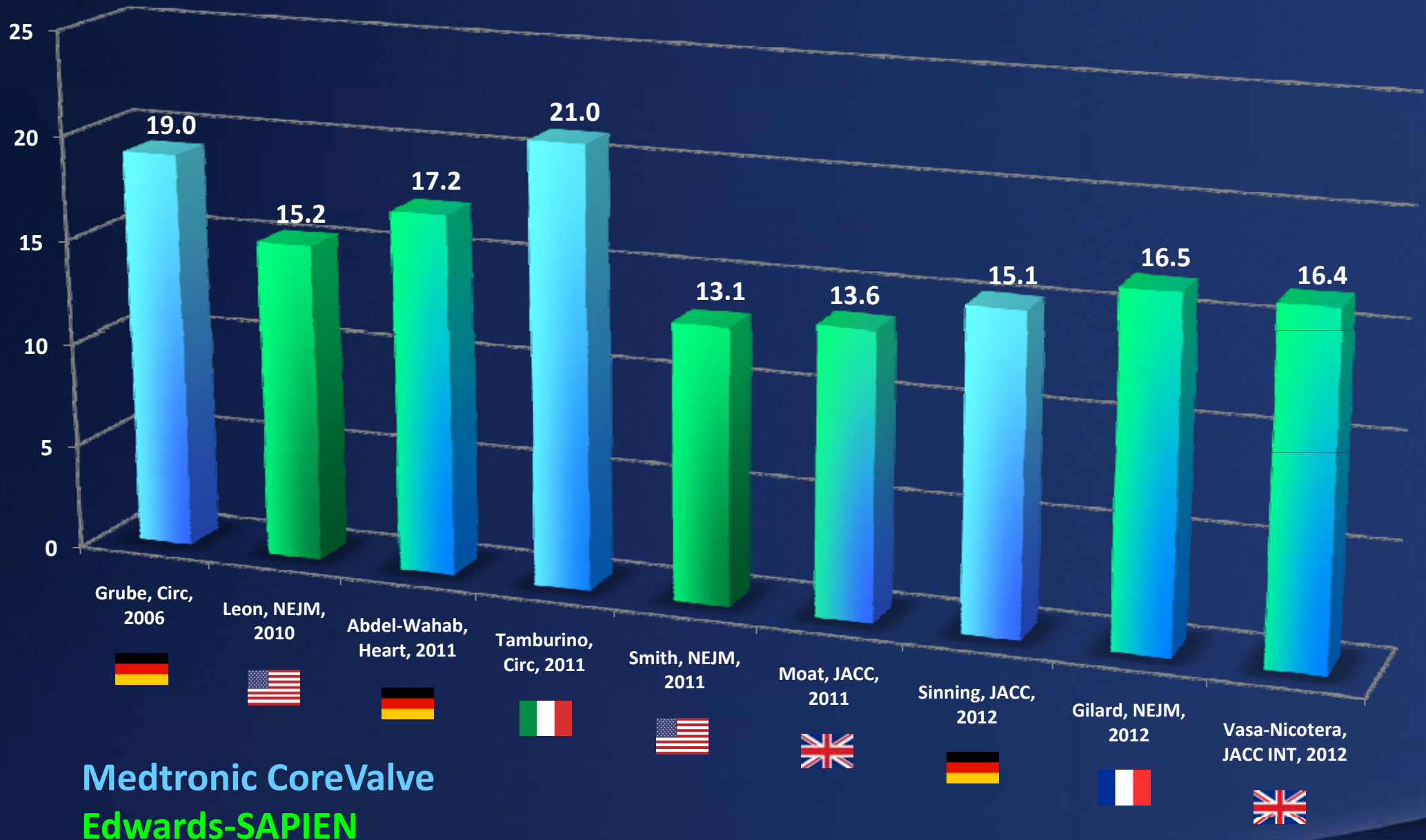


**Numbers at risk:**

	0	1	6
Mild	172	166	116
None	561	551	419
Moderate-Severe	140	132	96

COREVALVE  
ADVANCE STUDY

# Moderate/severe paravalvular AR



Medtronic CoreValve  
Edwards-SAPIEN

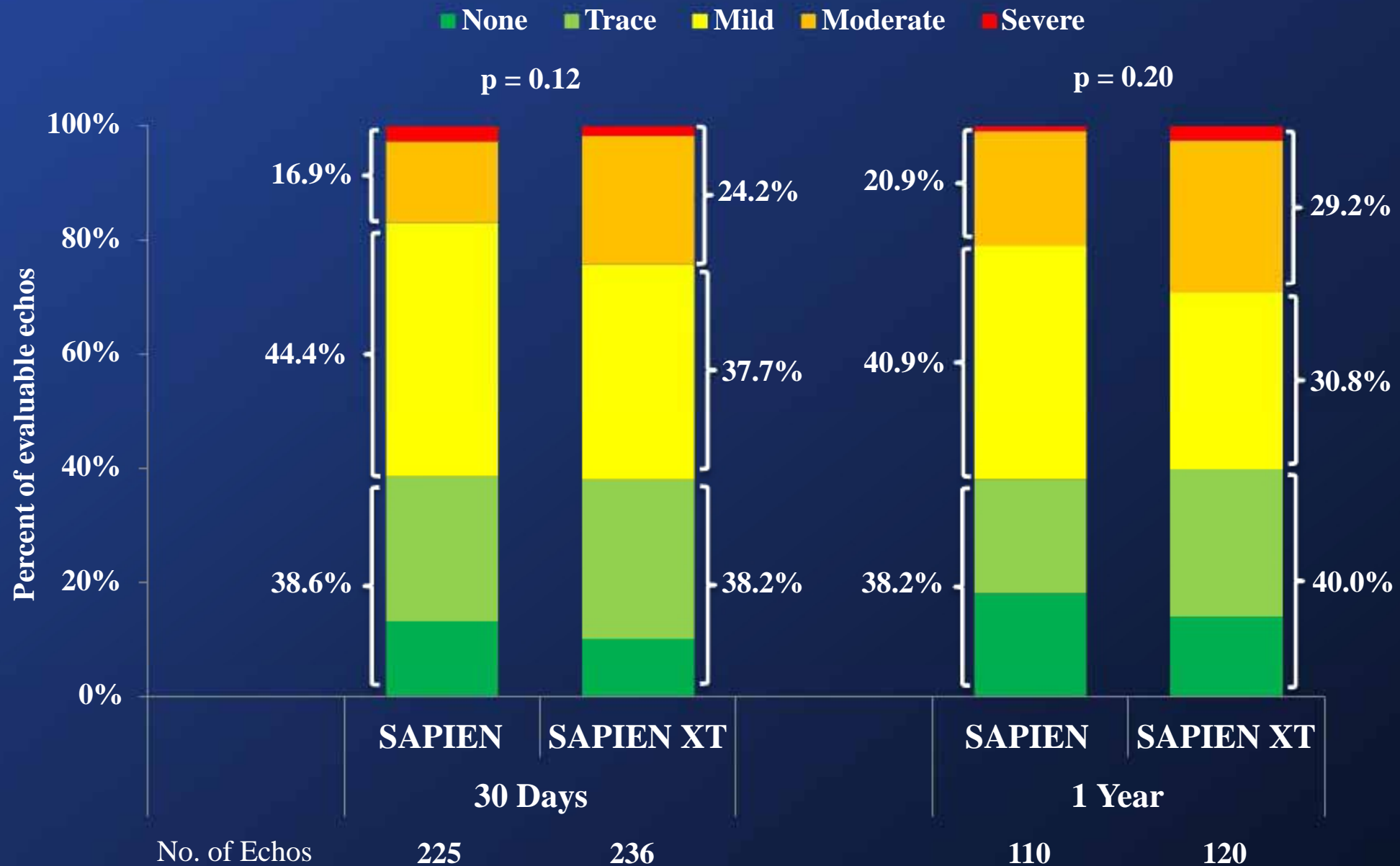
# AR Similar in Matched Patient Populations

- Difficult to compare AR rates across studies due to differences in relevant patient characteristics
- In a propensity matched patient data set (PRAGMATIC) comparing CoreValve and SAPIEN XT:
  - No differences in combined safety and efficacy endpoints
  - No differences in AR
  - No differences in 30-day or 1-year mortality

	CV	SAPIEN	p
<b>30-Day Outcomes</b>			
All-Cause Mortality	8.8	6.4	NS
CV Mortality	6.9	6.4	NS
<b>1-Year Outcomes</b>			
Mod/Severe AR	6.2	2.8	NS
All-Cause Mortality	16.2	12.3	NS
CV Mortality	8.3	7.4	NS

San Raffaele, Milan; Clinique Pasteur,, Toulouse; Erasmus Med Center, Rotterdam; Hôpital Rangueil, Toulouse

# Paravalvular Aortic Regurgitation (Valve Implant)



# Late embolization

	Total Number of Reported Late Embolized Valves	Number of Required Open Heart Surgeries	Number of Resulting Patient Deaths
Sapien or Sapien XT	11	11	3
CoreValve	0	0	0

- Late embolizations occurred anytime from 4 hours to 6 weeks after implant.
- Potential reasons for late embolizations:
  - Impingement by a mitral prosthesis<sup>1</sup>
  - Bileaflet native valve<sup>2</sup>
  - Root calcification causing inadequate anchoring<sup>3, 4</sup>
  - Stent malposition<sup>4</sup>
  - Undersized valve<sup>4</sup>
  - Possible recoil given frame material

1. Baumbach et. al., Ann Thorac Surg 2011; 92: 728-9

3. Maroto et. al., Eur J Cardiothorac Surg 2009; 36(5): 935-7

2. Schroeter et. al., Thorac Cardiovasc Surg 2011; 59(8): 503-6

4. Lida et. al., JACC Cardiovasc Imag 2012; 5(11): 1181-6

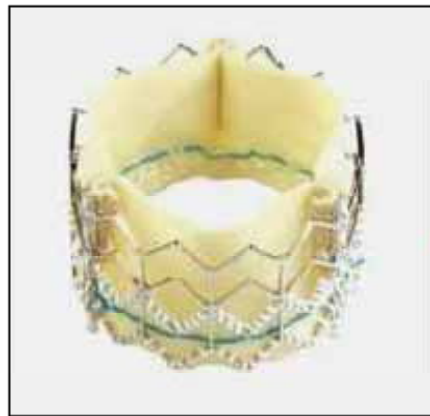


# Reasons for Increased AR, Late Migrations?



## Edwards SAPIEN XT™ Evolution

- Stainless Steel Frame
- Equine Pericardial Tissue



2004

Cribier-Edwards™ THV  
23mm

- Stainless Steel Frame
- Bovine Pericardial Tissue



2007

Edwards SAPIEN™ THV  
23 mm and 26 mm

- Cobalt-Chromium Frame
- Bovine Pericardial Tissue
- Semi-closed leaflets
- Reduced crimped profile

?



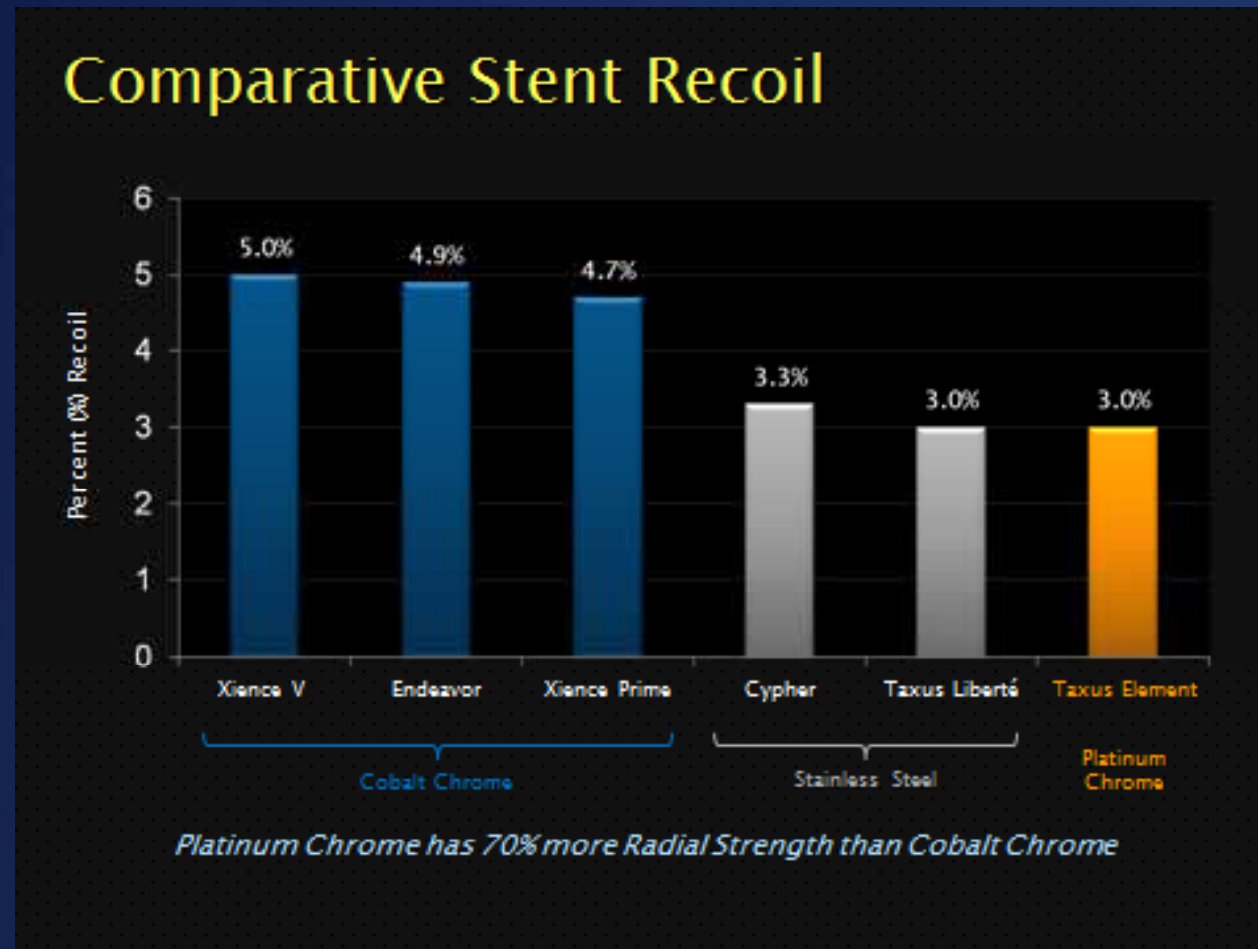
2010

Edwards SAPIEN XT™ THV  
23 mm, 26 mm, and 29mm





# Recoil in Cobalt Chrome used in Coronary Stents is Well Understood



# Areas of Consideration

- Patient Selection
- Procedure
- Post Procedure
- Future

# Platform Matters



**Dirigible**  
1894

**The End**  
1930s



**Wright  
Brothers**  
1903



**Propeller  
Plane**  
1936



**Turbo Jet**  
1939



**Fighter  
Jet**  
1950s



**Unmanned  
Ariel  
Vehicle**  
1959

# Future Platforms

