

Current Status of TAVR: Review of Recent Studies

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Disclosure Statement of Financial Interest

Susheel Kodali, MD

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

Affiliation/Financial Relationship

- Grant/Research Support
- Steering Committee
- SAB (Equity)

Company

- Edwards Lifesciences
- Edwards Lifesciences, Claret Medical, Meril
- Thubrikar Aortic Valve, Inc

Introduction

- 5 year results from PARTNER 1
- 2 year results from CoreValve US Pivotal
- 30 day results from SAPIEN 3 trial for both high and intermediate risk patients
- 1 year results from NOTION
- 30 day results from CoreValve Evolut

Five-Year Outcomes after Randomization to Transcatheter or Surgical Aortic Valve Replacement: Final Results of The PARTNER 1 Trial

Michael J. Mack, MD

on behalf of The PARTNER Trial Investigators

ACC 2015 | San Diego | March 15, 2015



PARTNER Study Design



Symptomatic Severe Aortic Stenosis

ASSESSMENT: High-Risk AVR Candidate
3,105 Total Patients Screened

N = 699

High Risk

Total = 1,057 patients

2 Parallel Trials:
Individually Powered

Inoperable

N = 358

ASSESSMENT:

Transfemoral

Yes

No

Transfemoral (TF)

Transapical (TA)

ASSESSMENT:

Transfemoral

Access

Yes

No

1:1 Randomization

Not In Study

N = 244

N = 248

N = 104

N = 103

TF TAVR

VS

SAVR

TA TAVR

VS

SAVR

N = 179

TF TAVR

VS

N = 179

Standard
Therapy

Primary Endpoint: All-Cause Mortality at 1 yr
(Non-inferiority)

Primary Endpoint: All-Cause Mortality
Over Length of Trial (Superiority)
Co-Primary Endpoint: Composite of All-Cause Mortality
and Repeat Hospitalization (Superiority)

Enrollment completed in 2009

Study Devices

Transfemoral

Transapical



Edwards SAPIEN THV
23 and 26 mm valves



RetroFlex 1
22 and 24 F sheaths



Ascendra
24 and 26 F sheaths

Study Devices

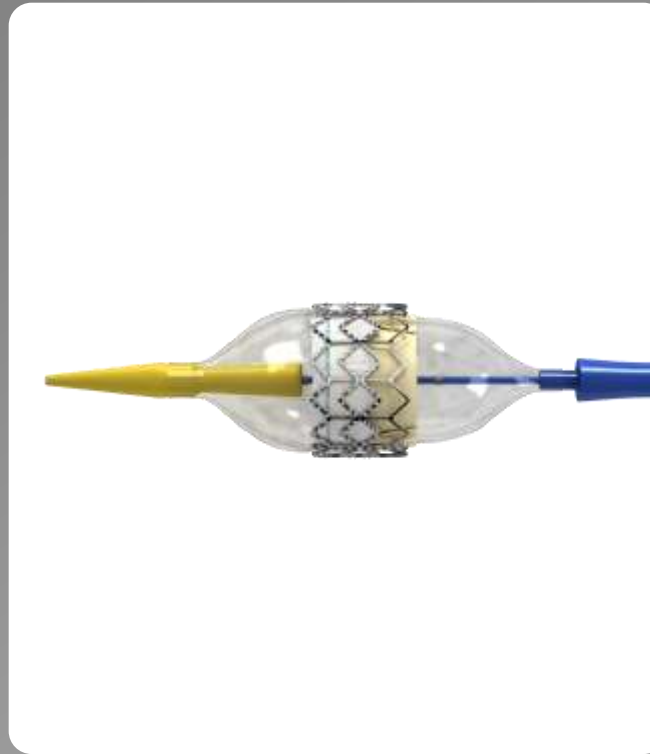


Transfemoral

Transapical



Edwards SAPIEN THV
23 and 26 mm valves



RetroFlex 3
22 and 24 F sheaths



Ascendra
24 and 26 F sheaths

Baseline Patient Characteristics

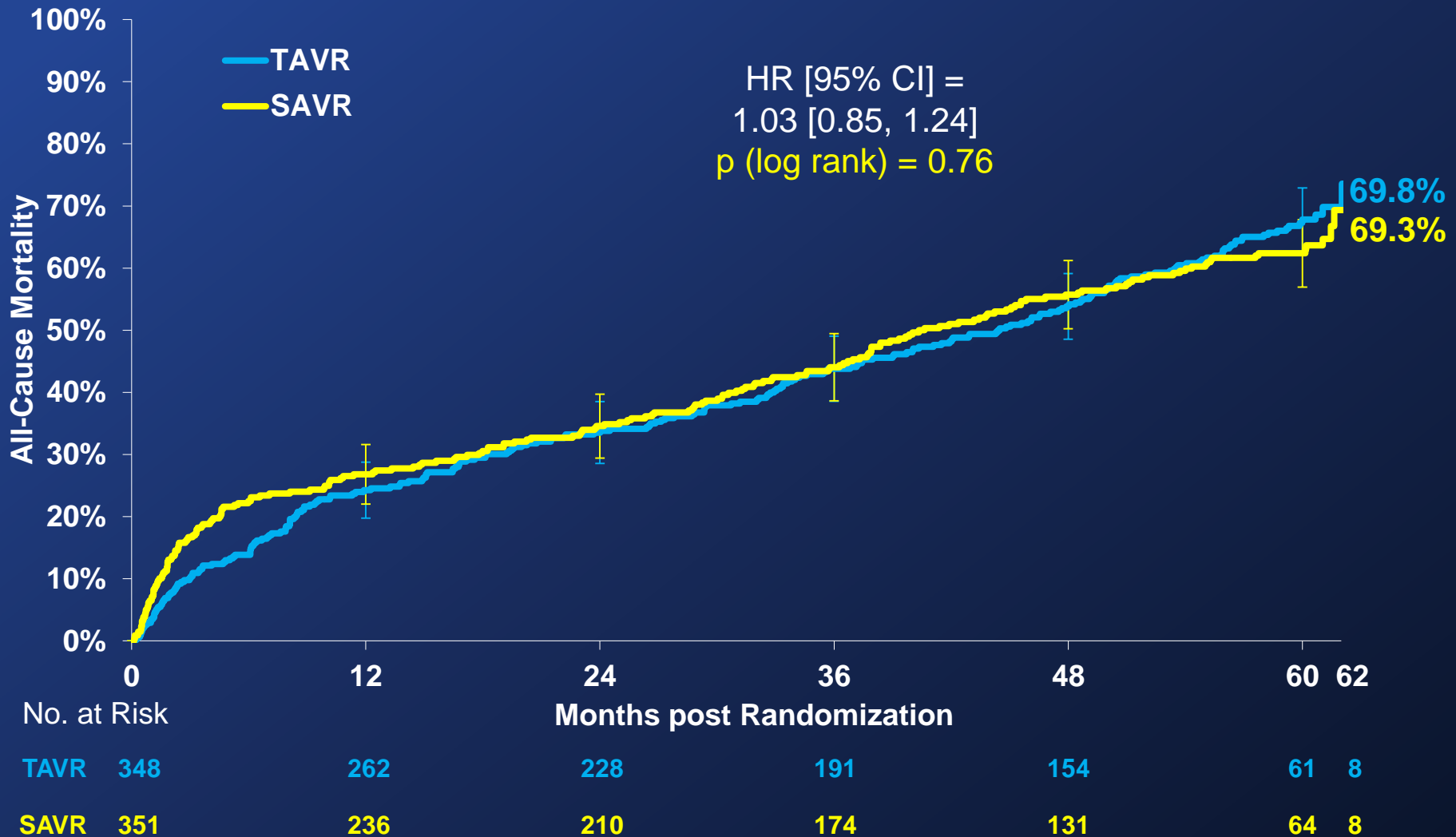
Demographics



Characteristic	TAVR (n=348)		SAVR (n=351)	
	n		n	
Age – years (Mean ± SD)	348	83.6 ± 6.8	349	84.5 ± 6.4
Male	201	57.8%	198	56.7%
NYHA Class III or IV	328	94.3%	328	94.0%
Previous CABG	148	42.5%	152	43.6%
Cerebrovascular disease	96	29.4%	87	26.8%
Peripheral vascular disease	149	43.2%	142	41.6%
STS Score (Mean ± SD)	347	11.8 ± 3.3	349	11.7 ± 3.5

All-Cause Mortality (ITT)

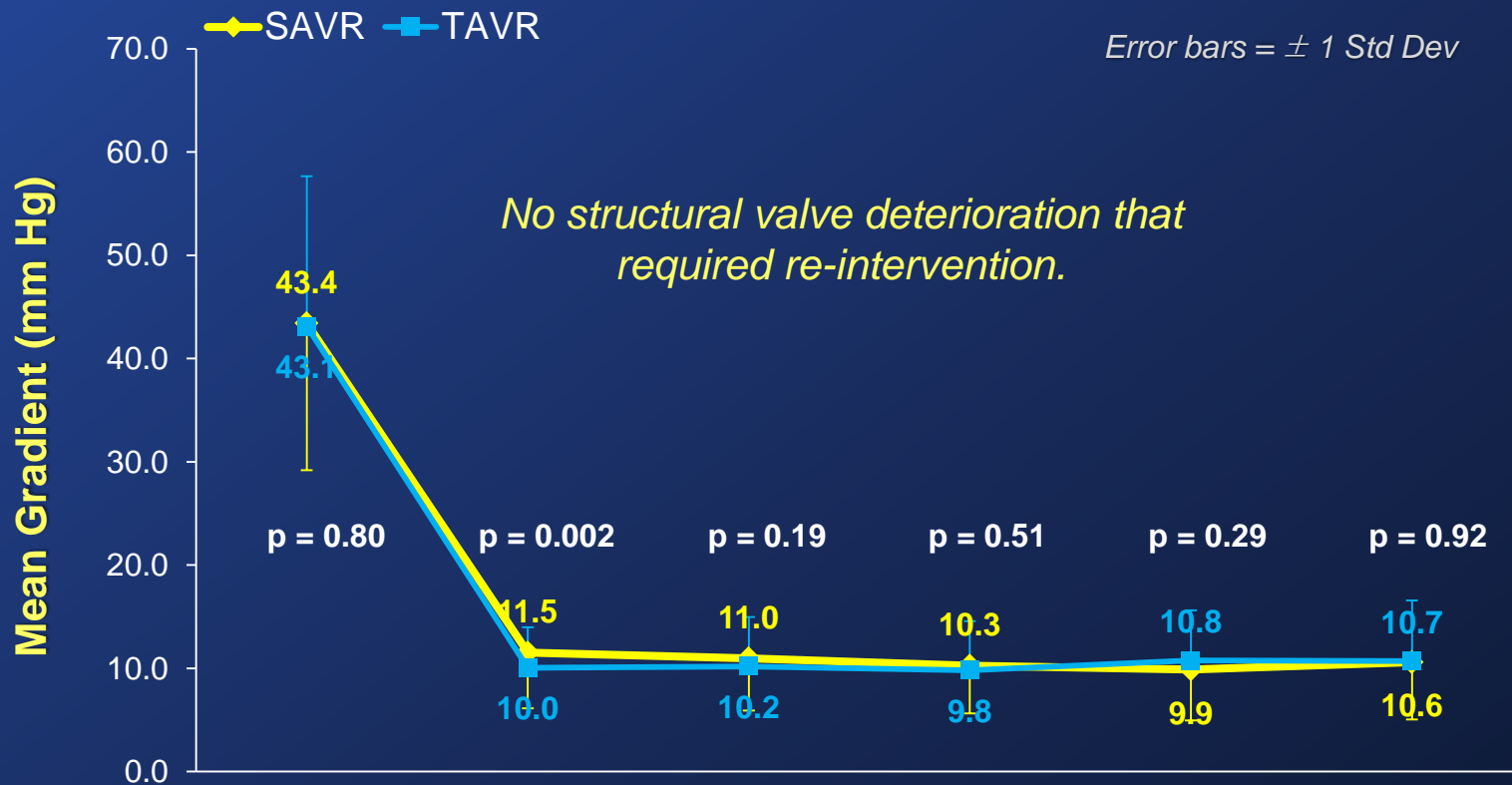
Pooled Approaches



All-Cause Mortality (ITT) Landmark Analysis



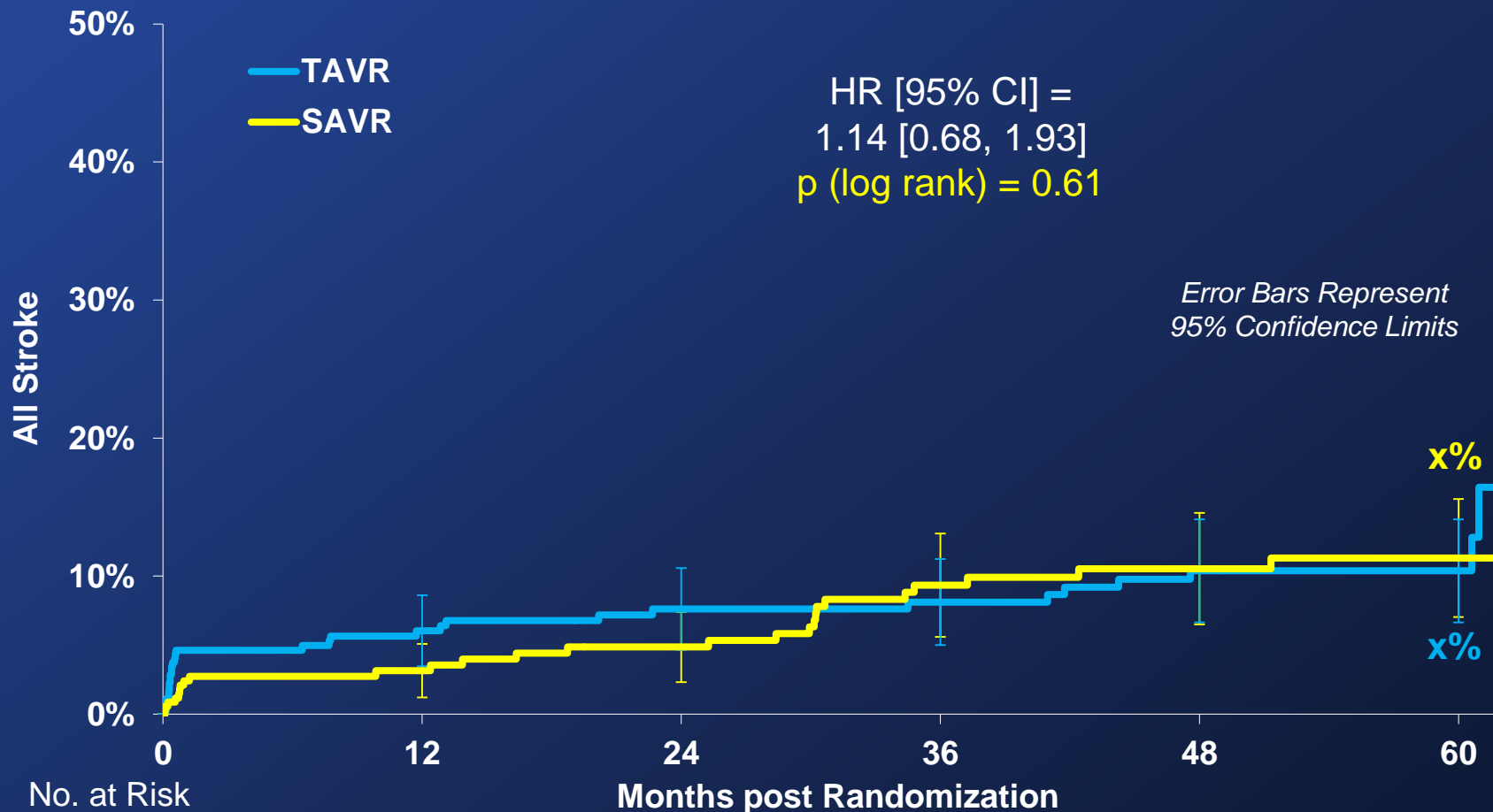
Aortic Valve Mean Gradient



	Baseline	1 Year	2 Year	3 Year	4 Year	5 Year
TAVR	310	219	156	106	79	56
SAVR	299	158	123	86	61	48

Strokes - All (ITT)

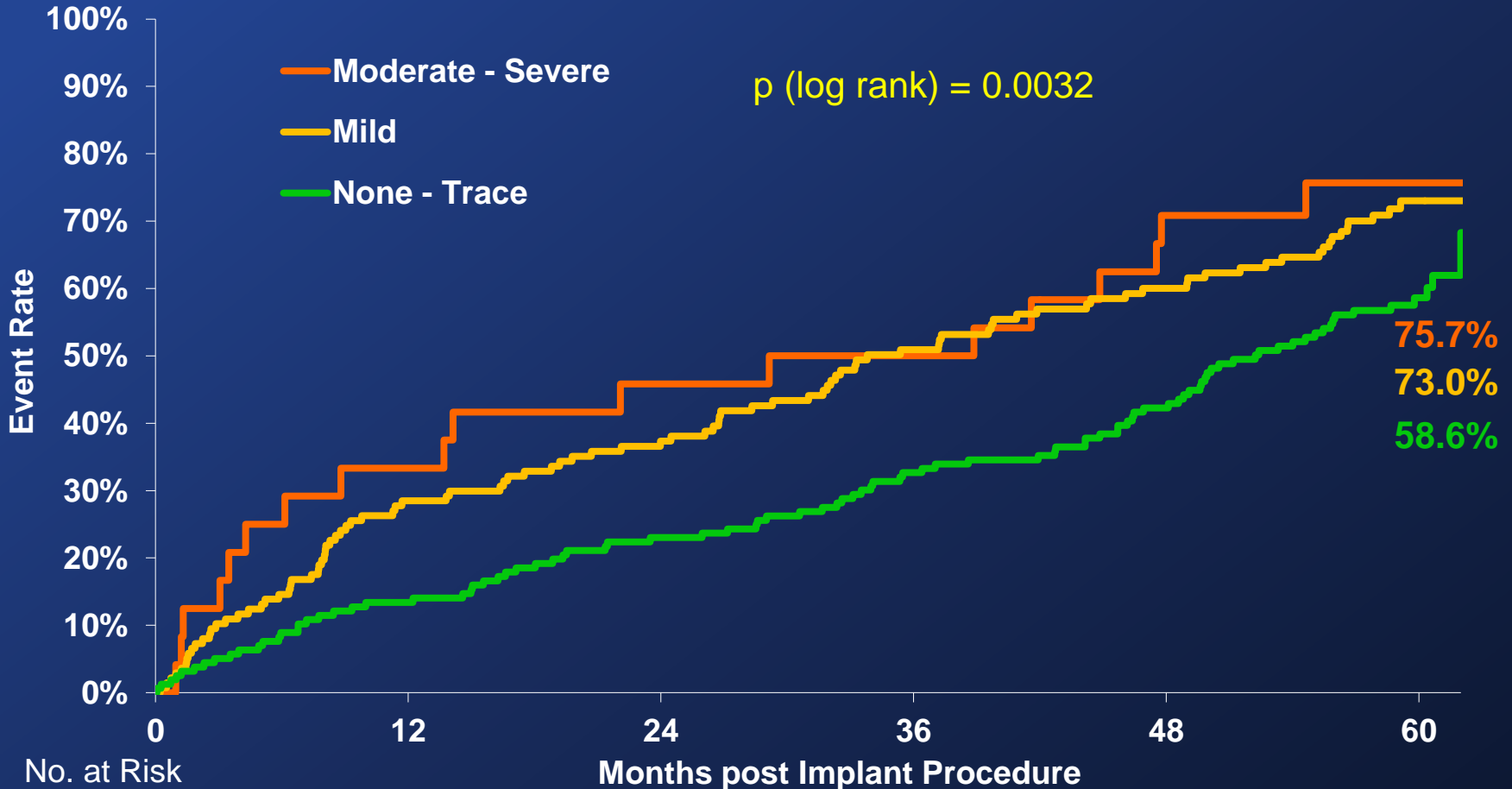
All Patients



No. at Risk

	0	12	24	36	48	60
TAVR	348	251	217	181	144	57
SAVR	351	230	205	169	128	64

Mortality and Post Procedural PVL TAVR Patients



M-S	24	16	13	12	7	2
Mild	137	98	84	65	52	11
N-T	158	135	120	105	88	34

CoreValve US Pivotal Trial

A Randomized Comparison of Self-expanding Transcatheter and Surgical Aortic Valve Replacement in Patients with Severe Aortic Stenosis Deemed at Increased Risk for Surgery
2-Year Outcomes

Michael J Reardon, MD, FACC

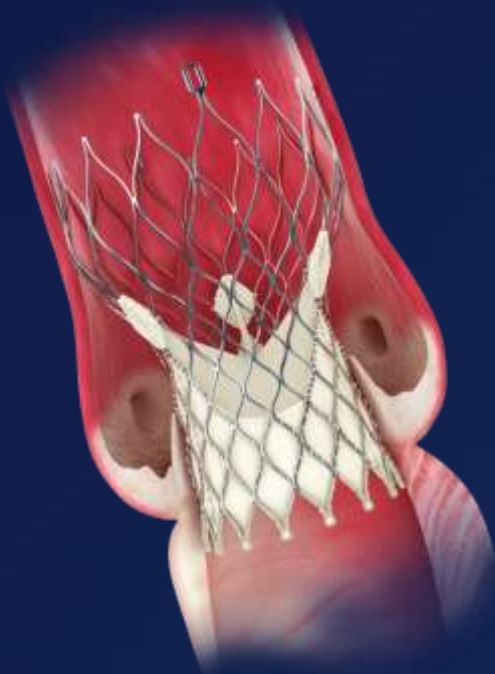
On Behalf of the CoreValve US Investigators

Pivotal Trial Design



* Randomization stratified by intended access site

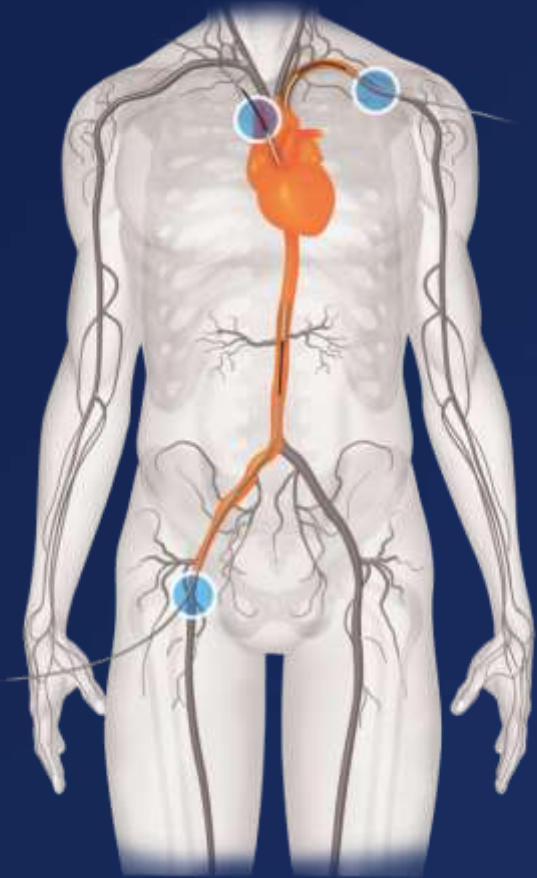
Study Device and Access Routes



4 Valve Sizes (23, 26, 29, 31 mm)
(18-29 mm Annular Range)

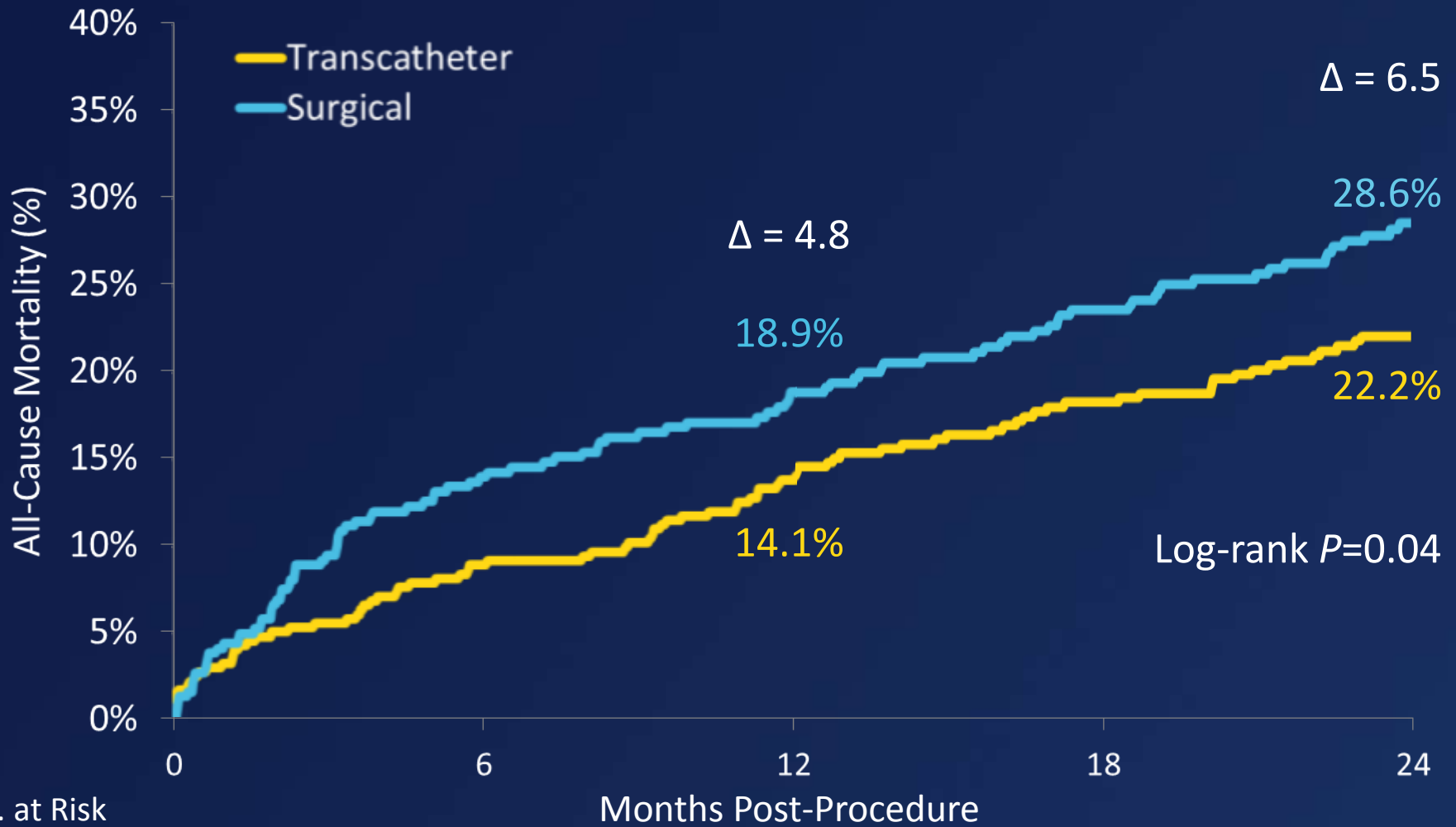


18F Delivery System



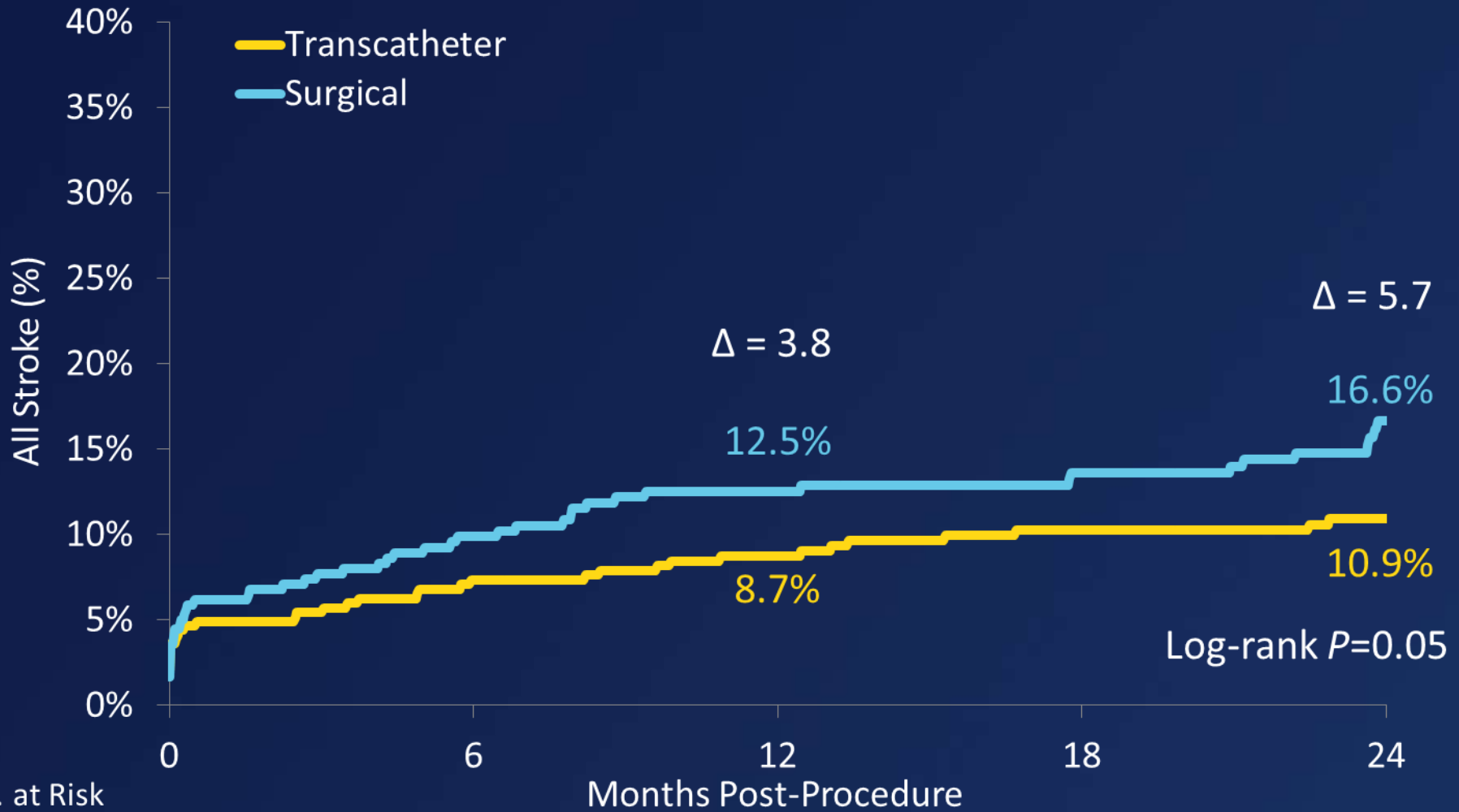
Transfemoral
Subclavian
Direct Aortic

All-Cause Mortality



No. at Risk	0	6	12	18	24
Transcatheter	391	378	354	334	219
Surgical	359	343	304	282	191

All Stroke

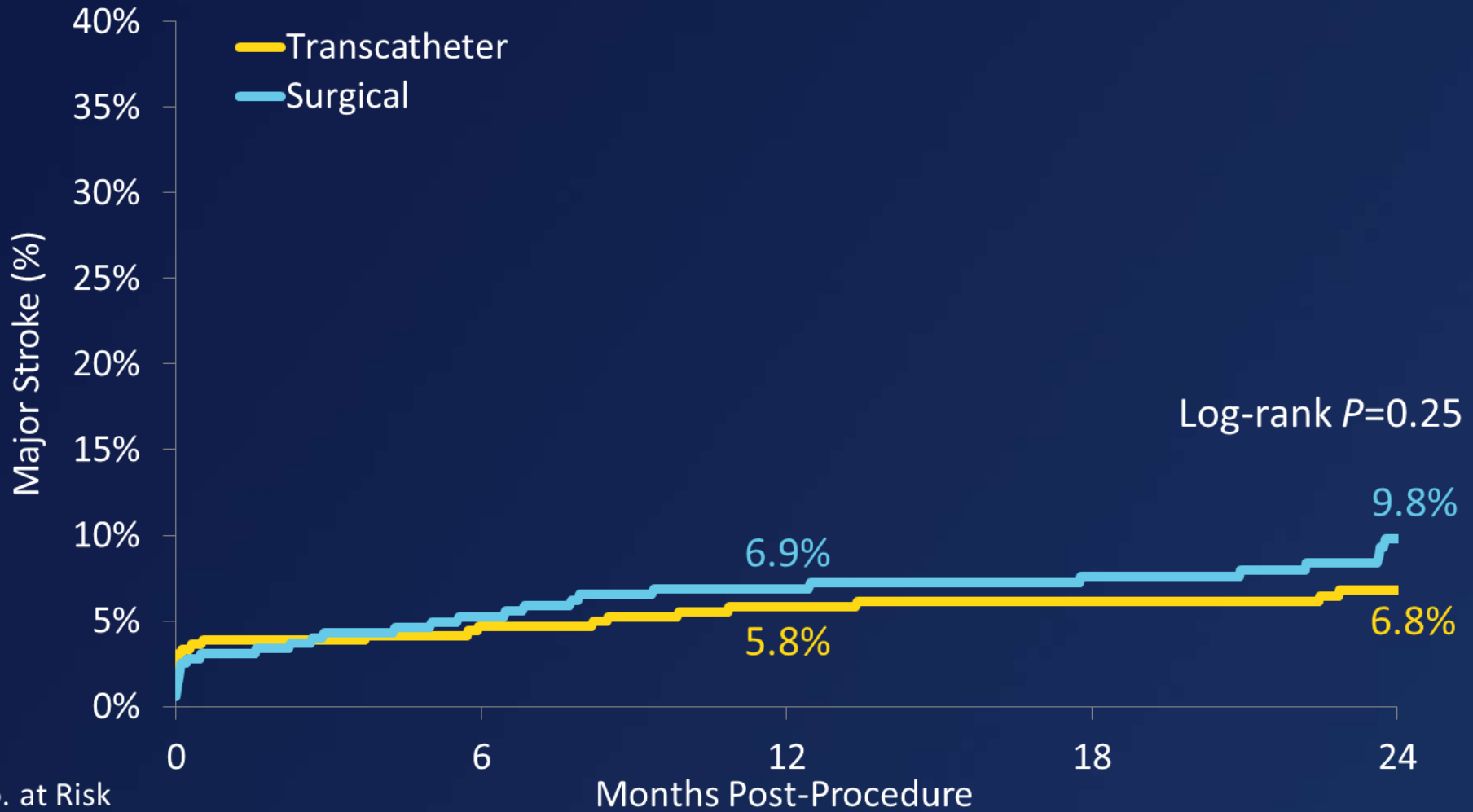


No. at Risk

Months Post-Procedure

Transcatheter	391	364	335	318	205
Surgical	359	324	281	256	169

Major Stroke



No. at Risk

Transcatheter	391	368	345	326	214
Surgical	359	335	296	271	184

Other Clinical Endpoints

Events*	1 Month			1 Year			2 Years		
	TAVR	SAVR	<i>P</i>	TAVR	SAVR	<i>P</i>	TAVR	SAVR	<i>P</i>
Vascular complications (major)	6.2	1.7	0.002	6.4	2.0	0.003	7.1	2.0	0.001
Pacemaker implant	20.0	7.1	<0.001	22.5	11.6	<0.001	25.8	12.8	<0.001
Bleeding (life threatening or disabling)	13.6	35.1	<0.001	16.5	38.4	<0.001	18.1	39.6	<0.001
New onset or worsening atrial fibrillation	11.7	31.0	<0.001	16.4	33.2	<0.001	19.5	34.9	<0.001
Acute kidney injury	6.2	15.1	<0.001	6.2	15.1	<0.001	6.2	15.1	<0.001

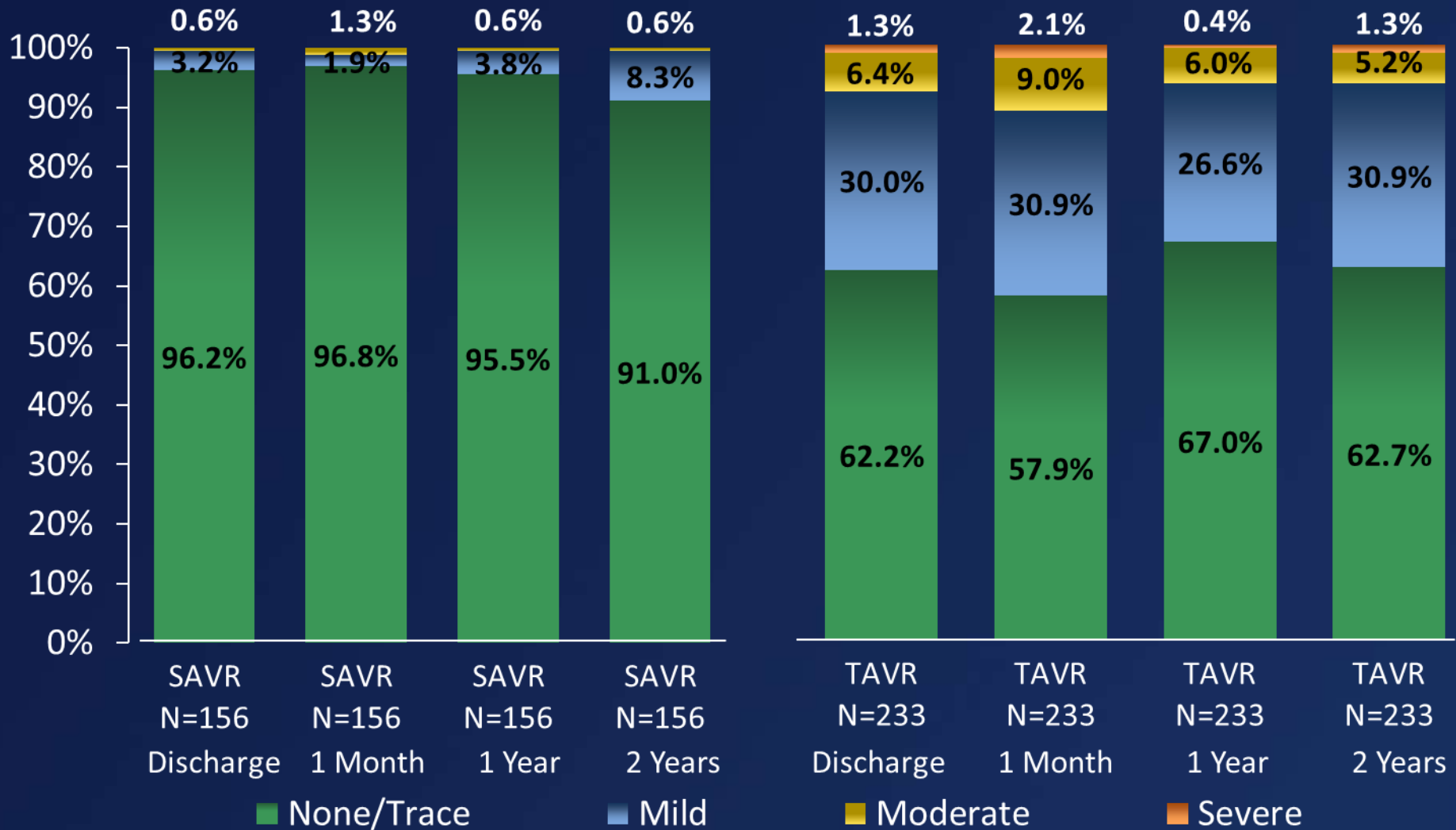
* Percentages reported are Kaplan-Meier estimates and log-rank *P* values

Echocardiographic Findings

TAVR had significantly better valve performance over SAVR at all follow-up visits ($P < 0.001$)

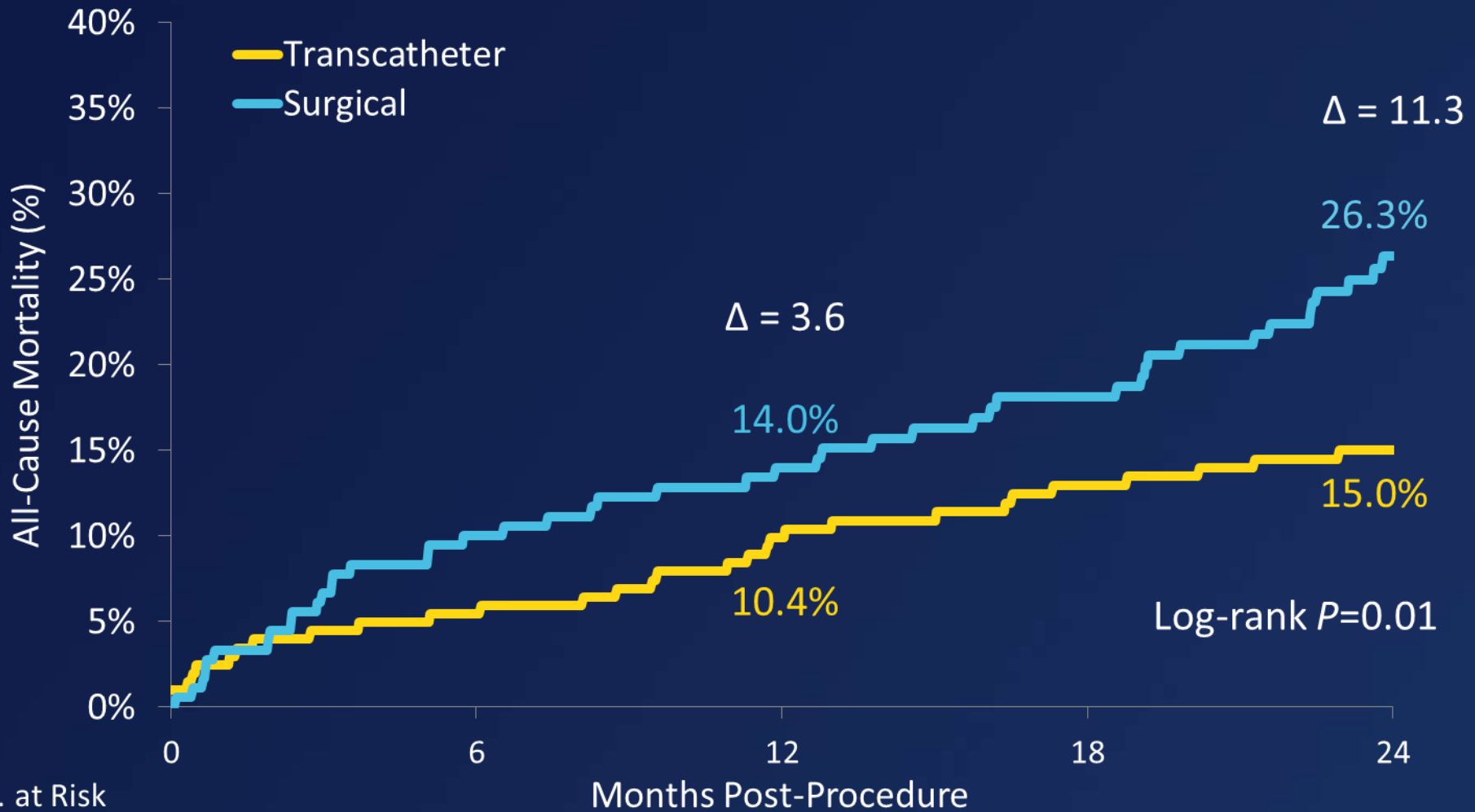


Paravalvular Regurgitation (Paired)



There was significantly lower PVL with SAVR over TAVR at each time point ($P < 0.001$)

All-Cause Mortality STS $\leq 7\%$



No. at Risk

Months Post-Procedure

Transcatheter	202	197	191	182	128
Surgical	181	174	161	151	93

Clinical and Echocardiographic Outcomes at 30 Days with the SAPIEN 3 TAVR System in Inoperable, High-Risk and Intermediate-Risk AS Patients

Susheel Kodali, MD

on behalf of The PARTNER Trial Investigators

ACC 2015 | San Diego | March 15, 2015



THE
PARTNER II
TRIAL

Evolution of the Edwards Balloon-Expandable Transcatheter Valves



Cribier-Edwards

2002



SAPIEN

2006



SAPIEN XT

2009



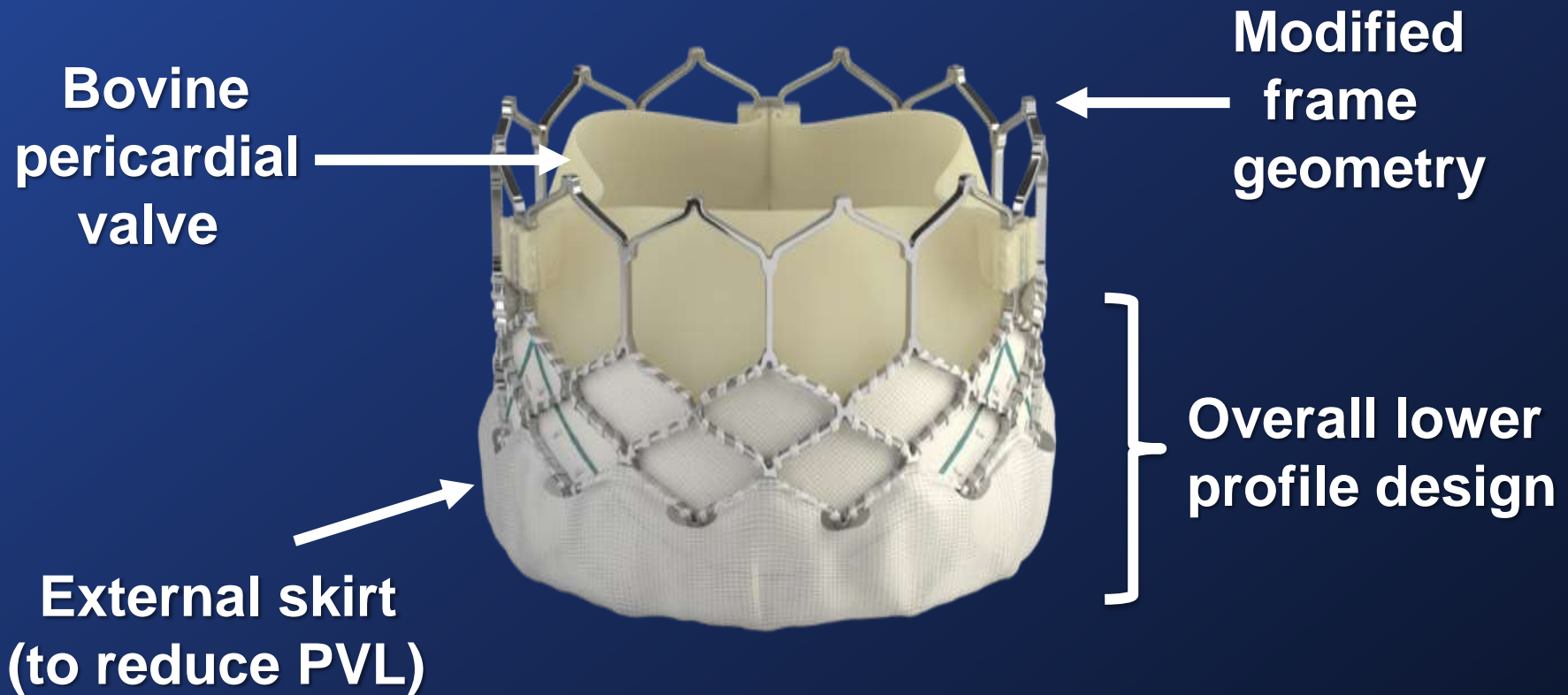
SAPIEN 3

2013



SAPIEN 3 Transcatheter Heart Valve

Distinguishing Features

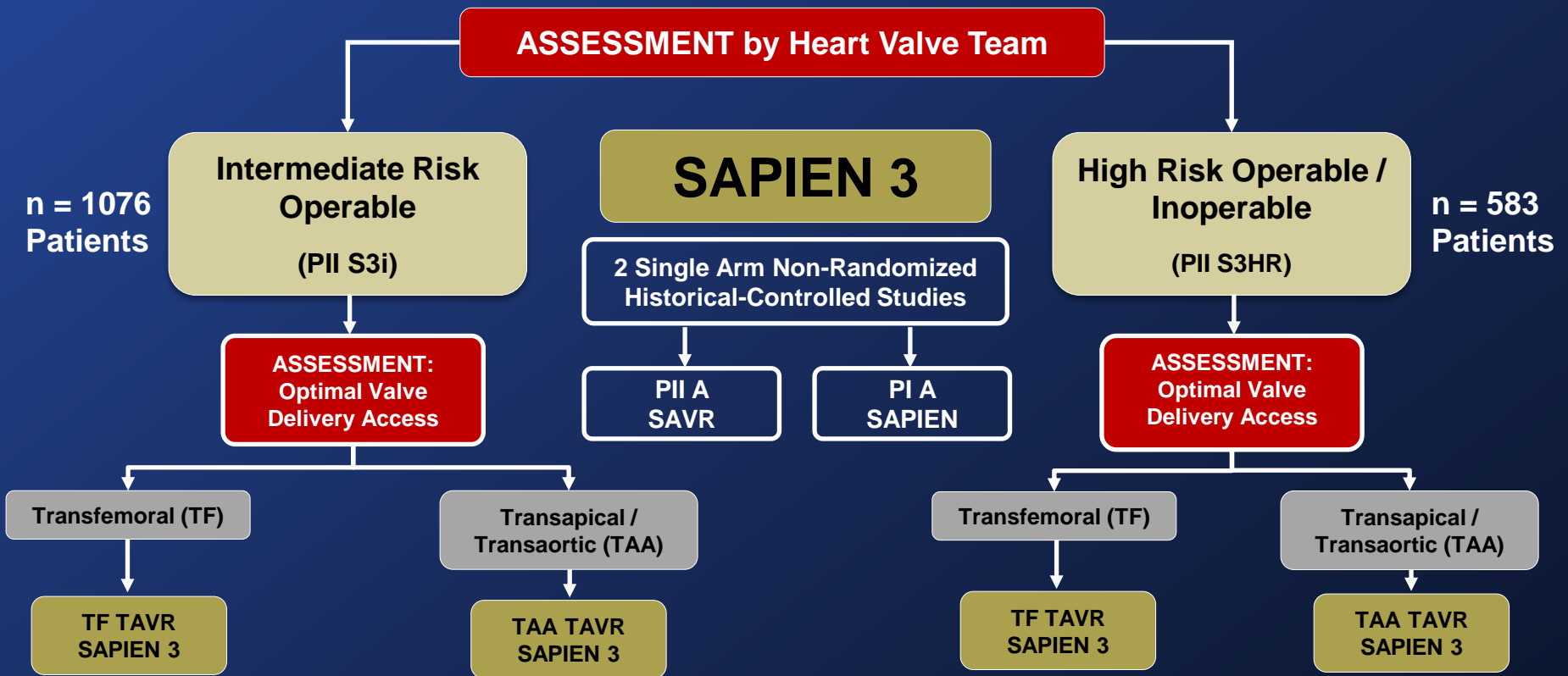


The PARTNER II S3 Trial

Study Design



Symptomatic Severe Aortic Stenosis



Baseline Patient Characteristics

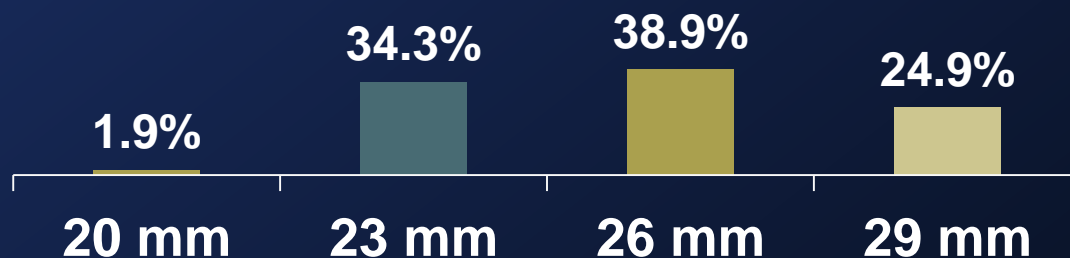
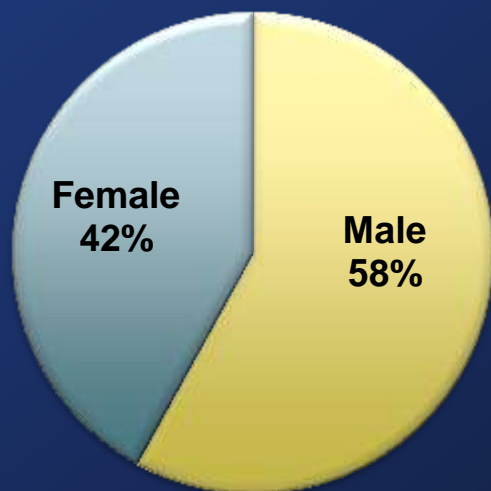
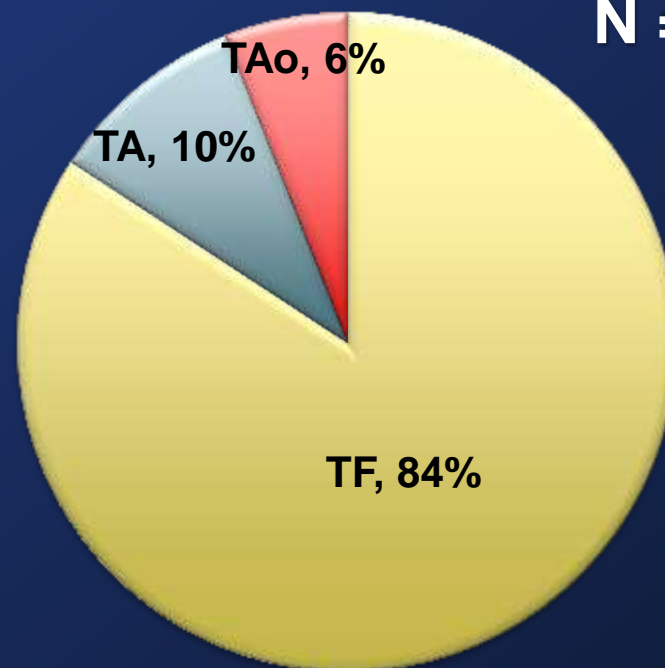
S3HR Patients



Average STS =
8.6%
(Median 8.4%)

Average Age =
82.8yrs

N = 583



Baseline Patient Characteristics

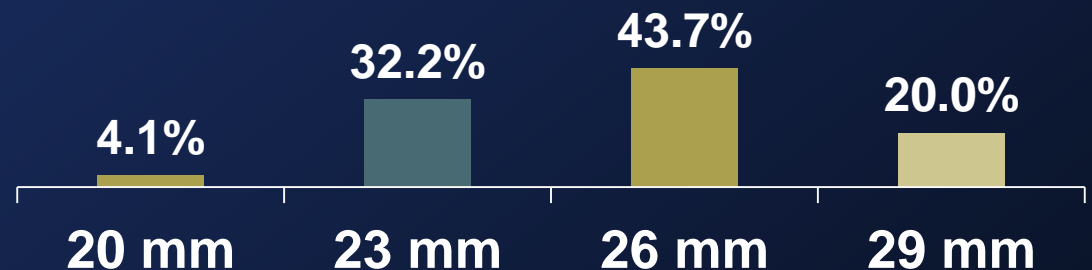
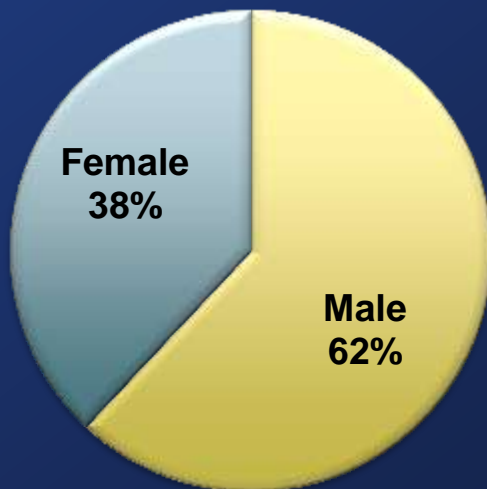
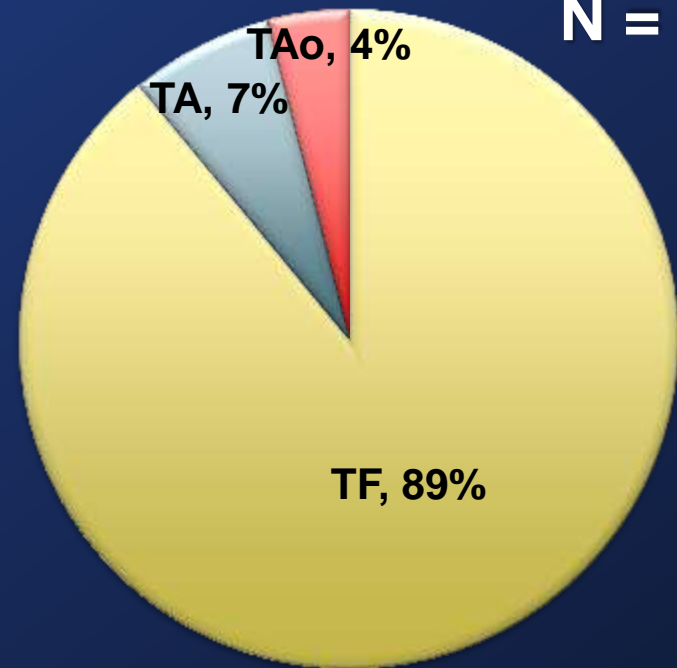
S3i Patients



Average STS =
5.3%
(Median 5.2%)

Average Age =
81.9yrs

N = 1076

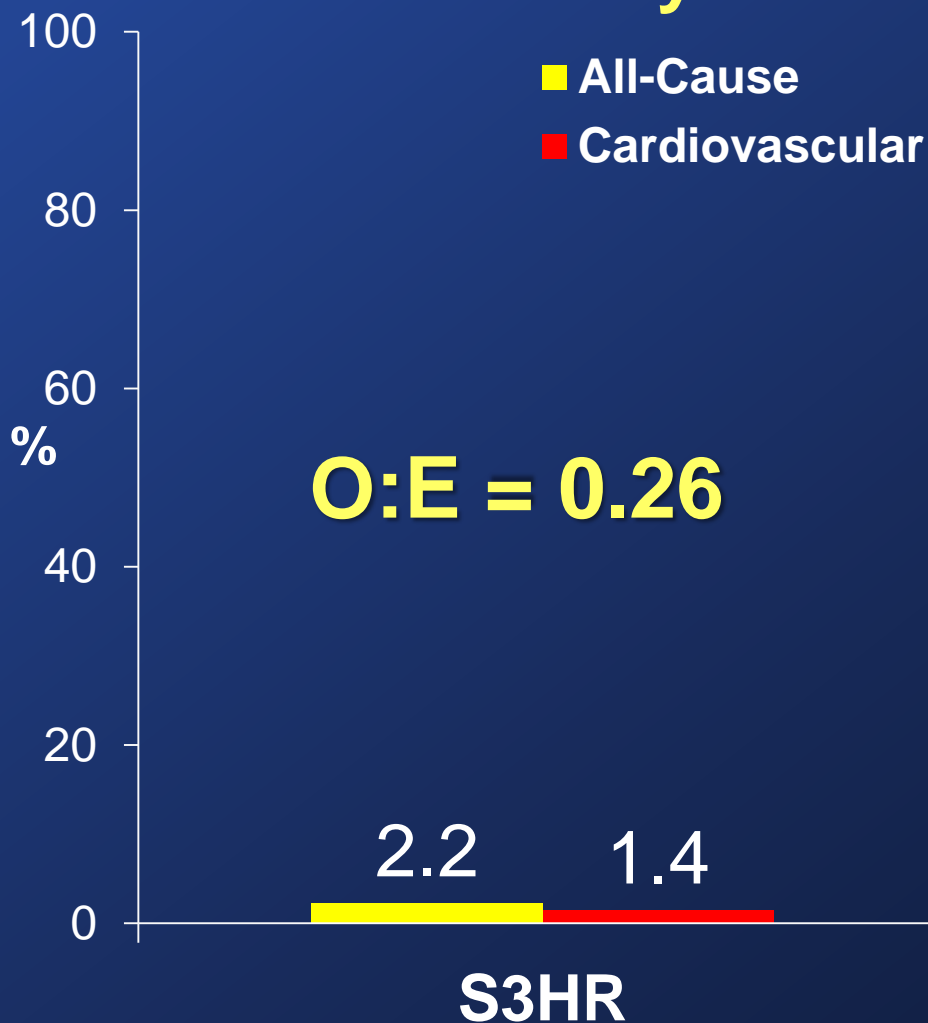


Mortality and Stroke (S3HR)

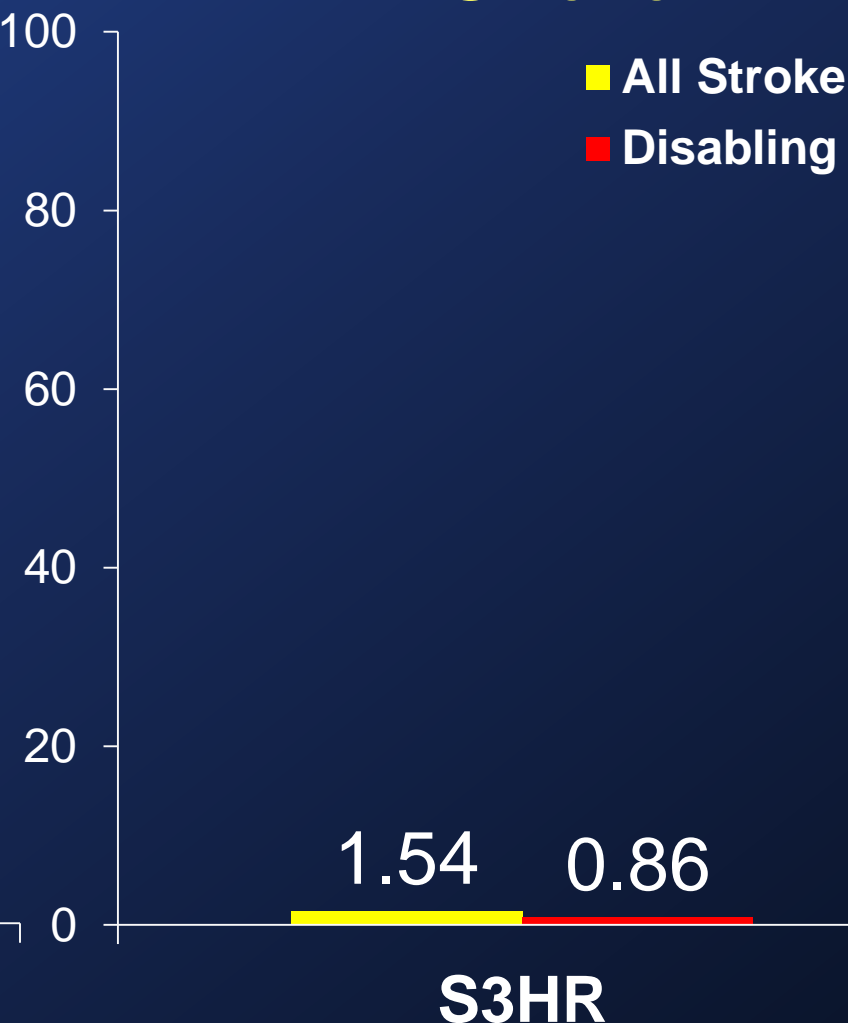
At 30 Days (As Treated Patients)



Mortality



Stroke

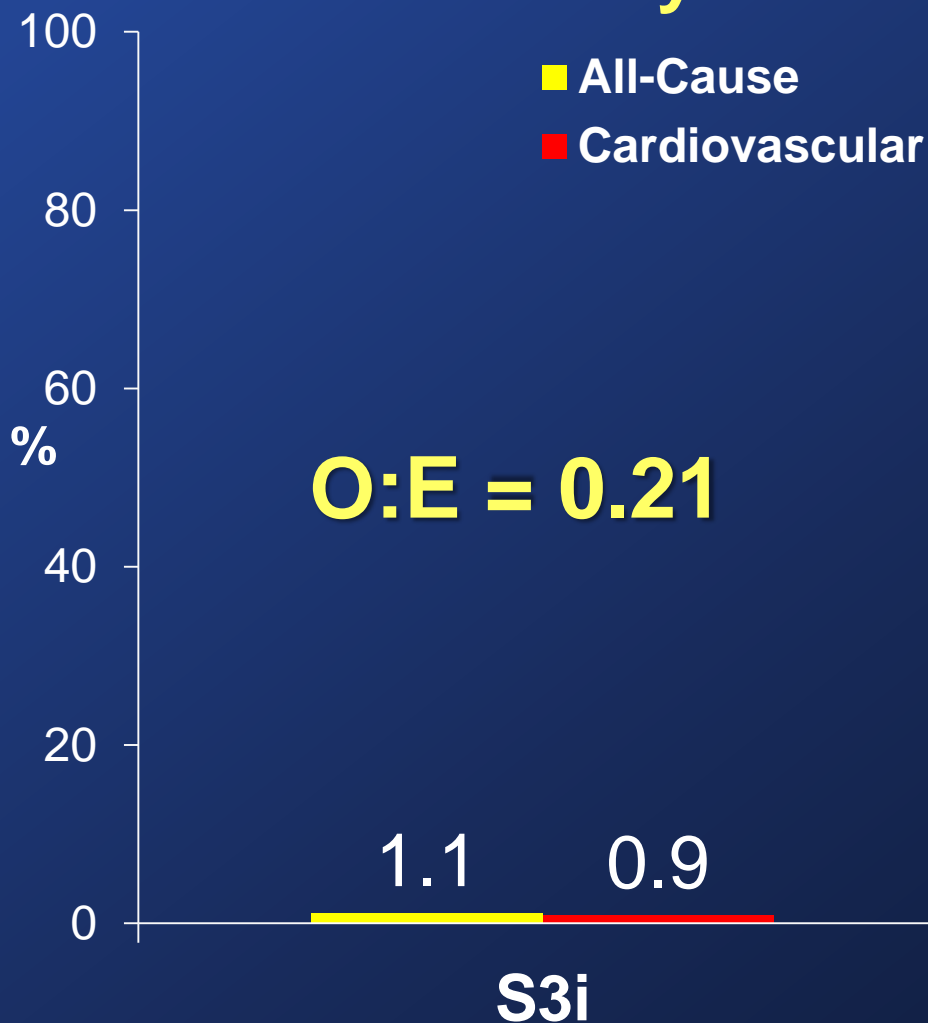


Mortality and Stroke (S3i)

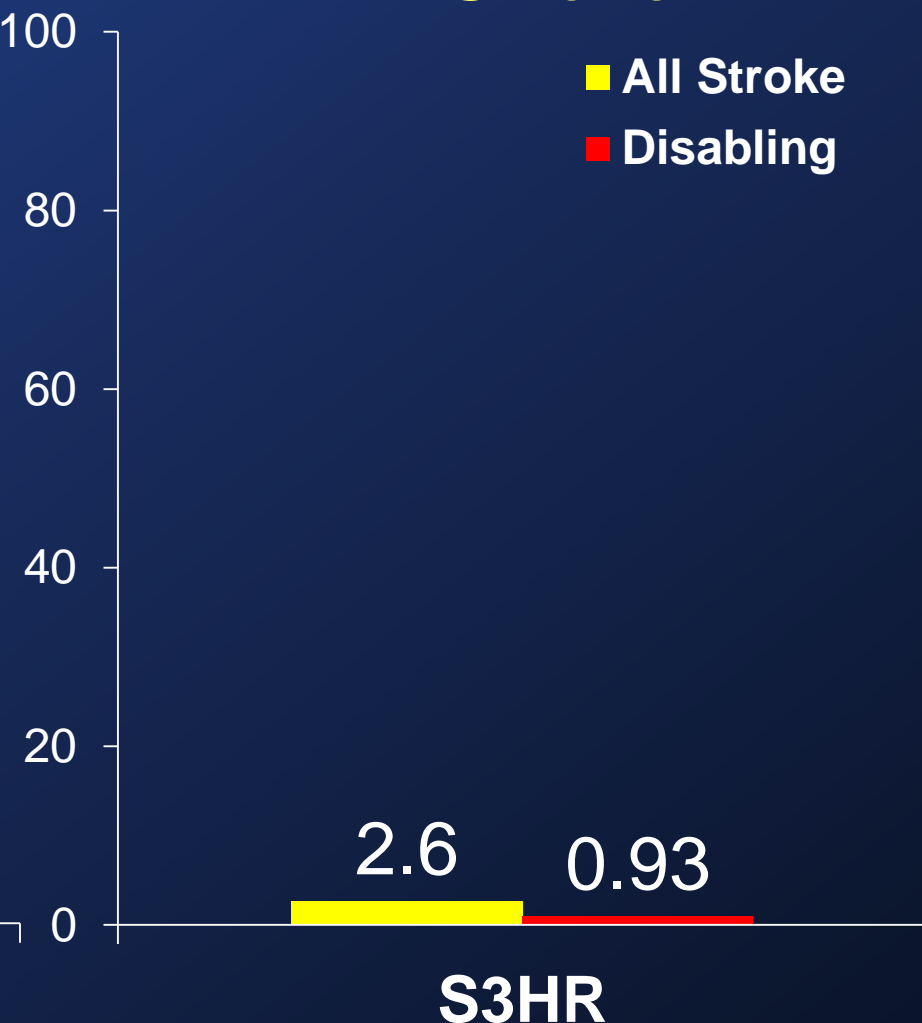
At 30 Days (As Treated Patients)



Mortality



Stroke

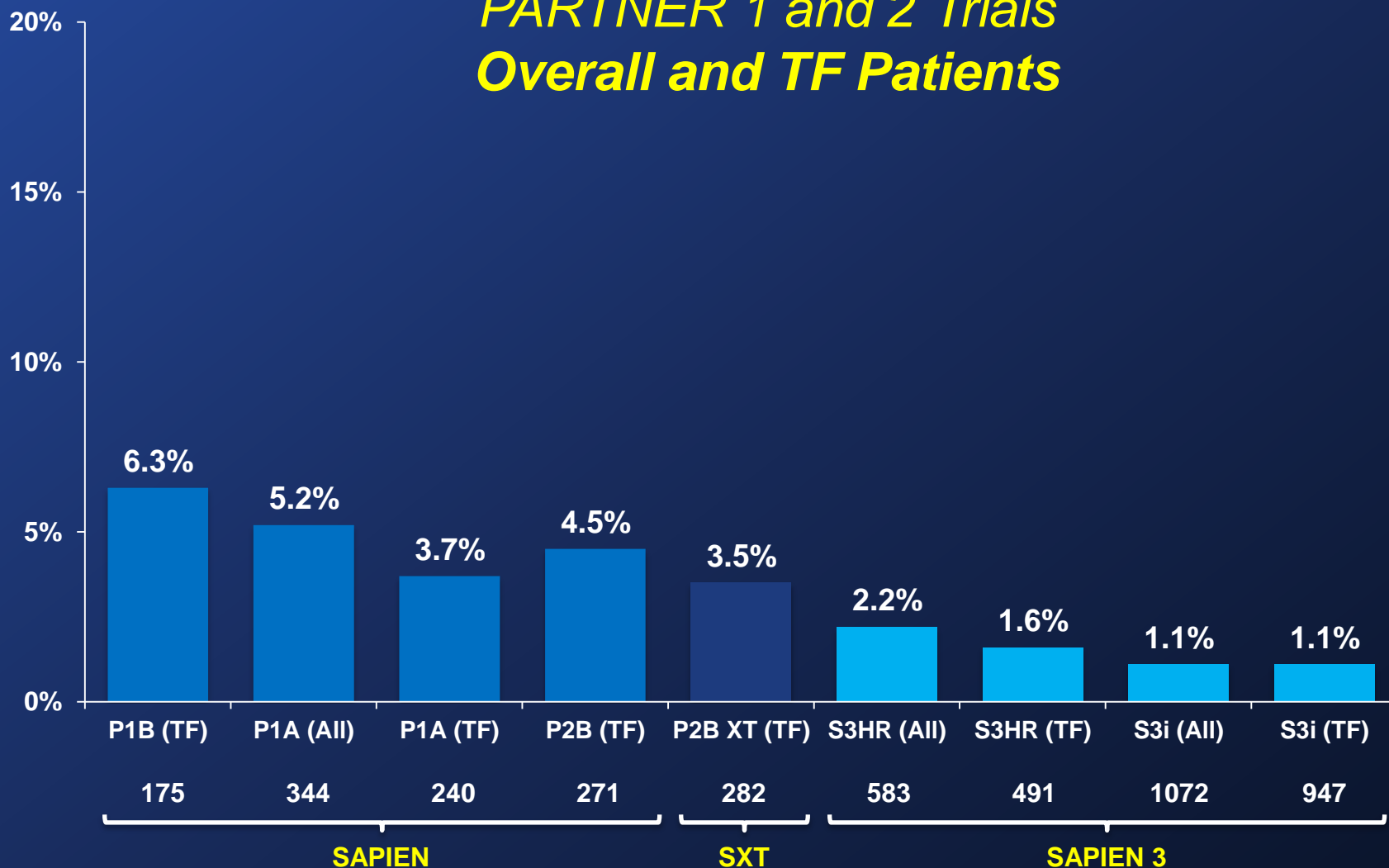


All-Cause Mortality at 30 Days

Edwards SAPIEN Valves (As Treated Patients)



*PARTNER 1 and 2 Trials
Overall and TF Patients*



Strokes

At 30 Days (As Treated Patients)



Events (%)	S3HR	S3HR	S3HR	S3i	S3i	S3i
	All (n=583)	TF (n=491)	TA/TAo (n=92)	All (n=1076)	TF (n=951)	TA/TAo (n=125)
All	1.54	1.63	1.09	2.60	2.42	4.00
Disabling*	0.86	1.02	0	0.93	0.84	1.60
Non-Disabling	0.69	0.61	1.09	1.67	1.58	2.40
TIA	0.69	0.61	1.09	0.37	0.42	0

*CEC adjudicated or Modified Rankin Score ≥ 2 at 30 days

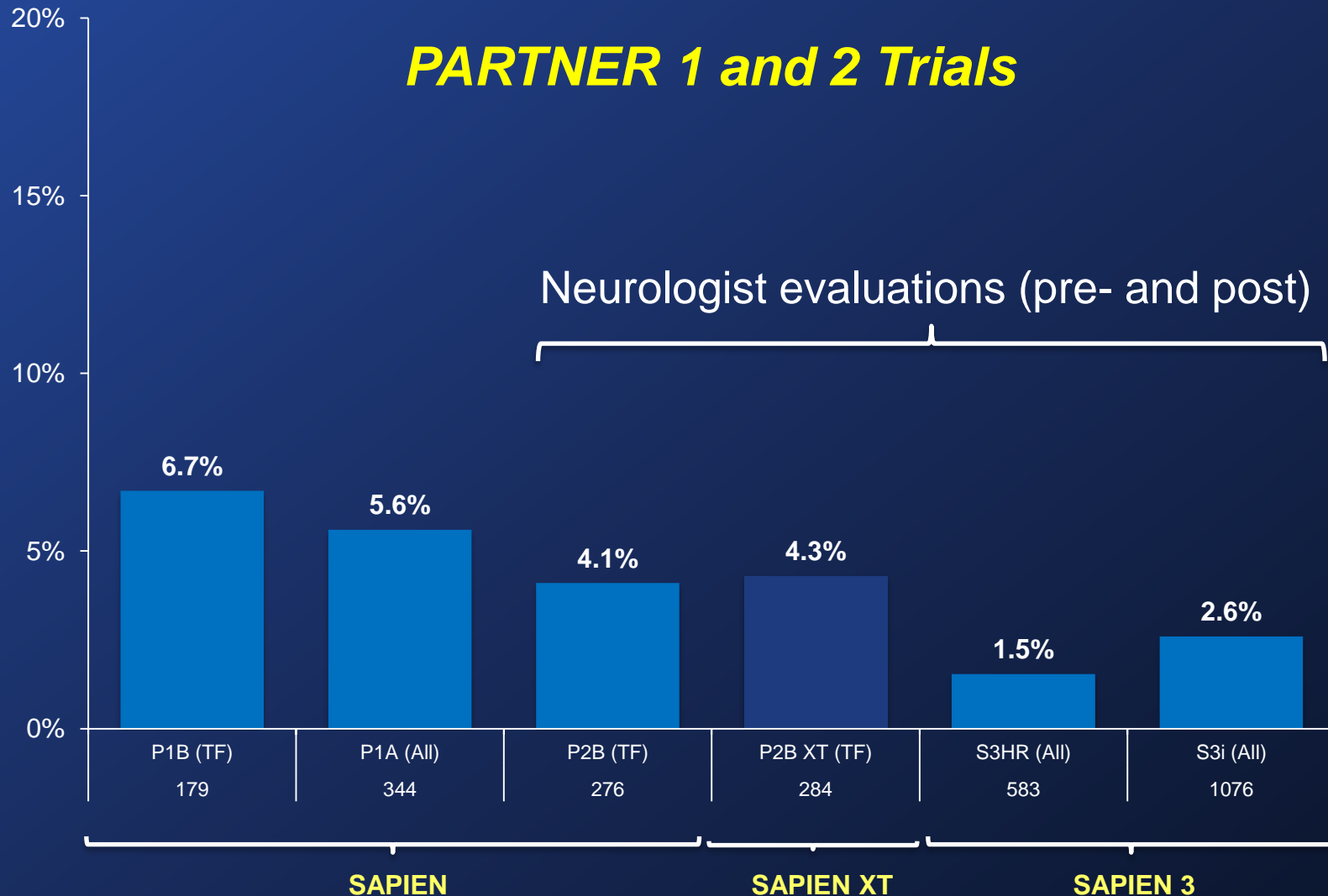
For comparison, the surgical stroke rate at 30 days is **3.5%**
in a STS PROM $> 8\%$ group reported by Thourani et al.

Strokes (All) at 30 Days

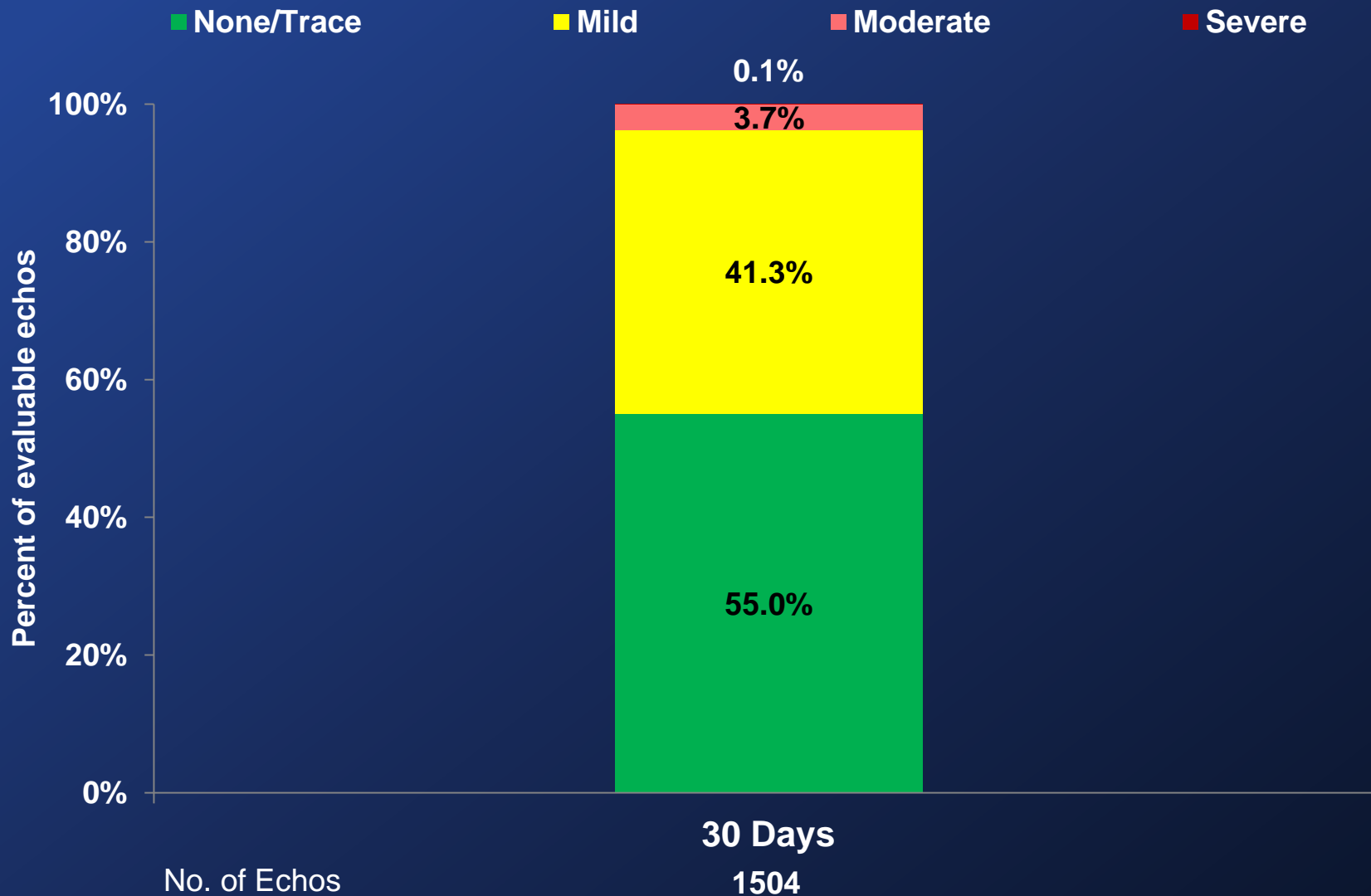
Edwards SAPIEN Valves



PARTNER 1 and 2 Trials



Paravalvular Leak: S3HR & S3i (Valve Implant Patients)





ACC.15

TCT@ACC-12 | innovation in intervention

64th Annual Scientific Session & Expo

An All-comers Randomized Clinical Trial Comparing Transcatheter with Surgical Aortic Valve Replacement in Patients with Aortic Valve Stenosis

On behalf of NOTION investigators:

Hans Gustav Hørsted Thyregod, MD

Dep. of Cardiothoracic Surgery

Copenhagen University Hospital, Denmark

MARCH 14 – 16, 2015
SAN DIEGO
CALIFORNIA

Nordic Aortic Valve Intervention (NOTION) Trial

Objective: Compare TAVR vs. SAVR in patients ≥ 70 years eligible for surgery (all-comers population)

Primary outcome: Composite rate of death from any cause, stroke or myocardial infarction at 1 year (VARC II-defined)

Secondary outcomes: Safety and efficacy (NYHA), echocardiographic outcomes
(VARC II-defined)

Design: Prospective, multicenter, non-blinded, randomized trial

Enrollment period: December 2009 - April 2013

Sample Size Determination

Alternative hypothesis: TAVR is superior to SAVR regarding the composite rate of death from any cause, stroke or myocardial infarction after 1 year

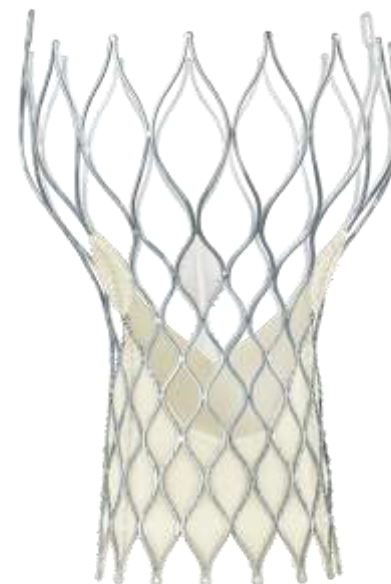
Sample Size Determination:

1:1 treatment allocation
Two-sided alpha = 0.05
Power = 80%

Expected rate_{SAVR} = 15%
Expected rate_{TAVR} = 5%

Trial Size: 280 patients

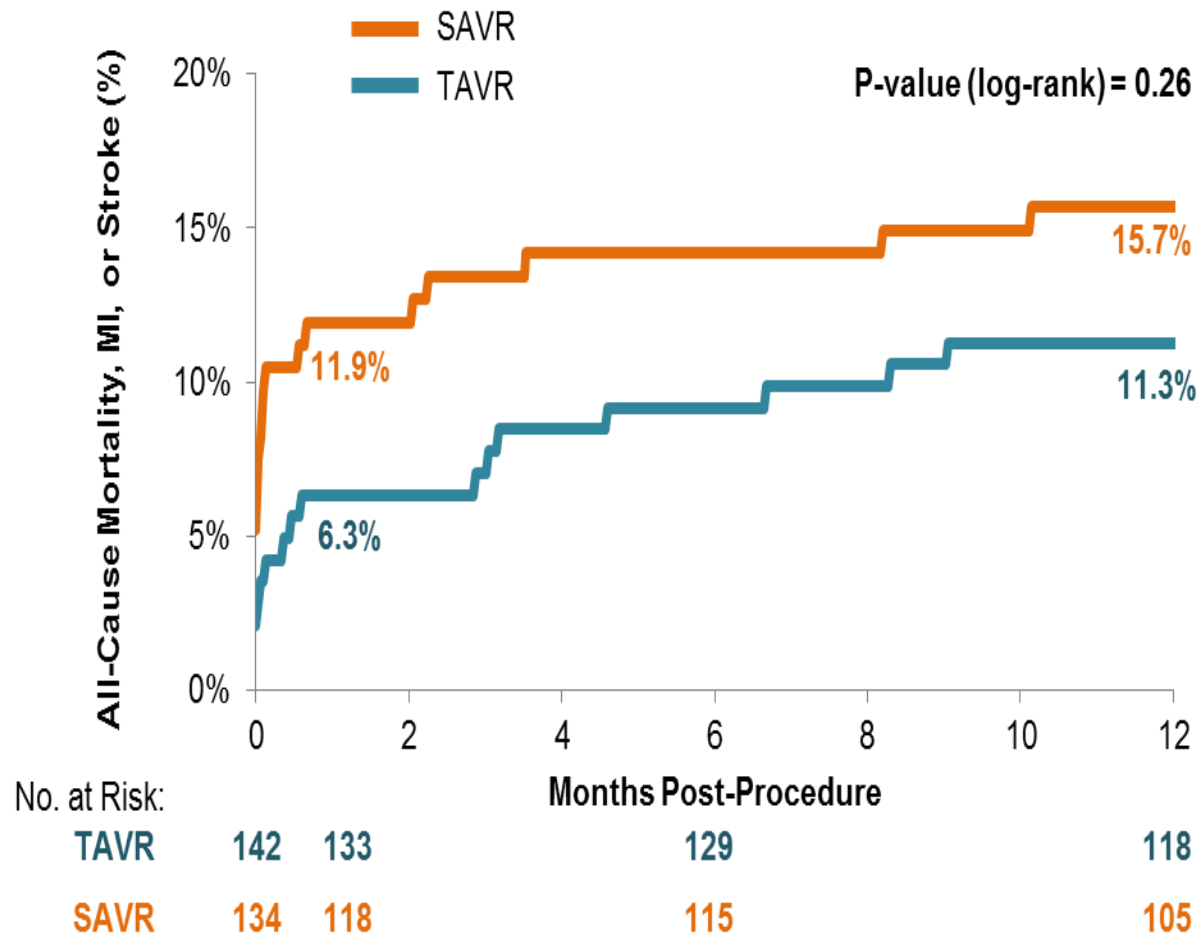
Self-expanding
bio-prosthesis
4 valve sizes
(annulus diameter
18-29 mm)



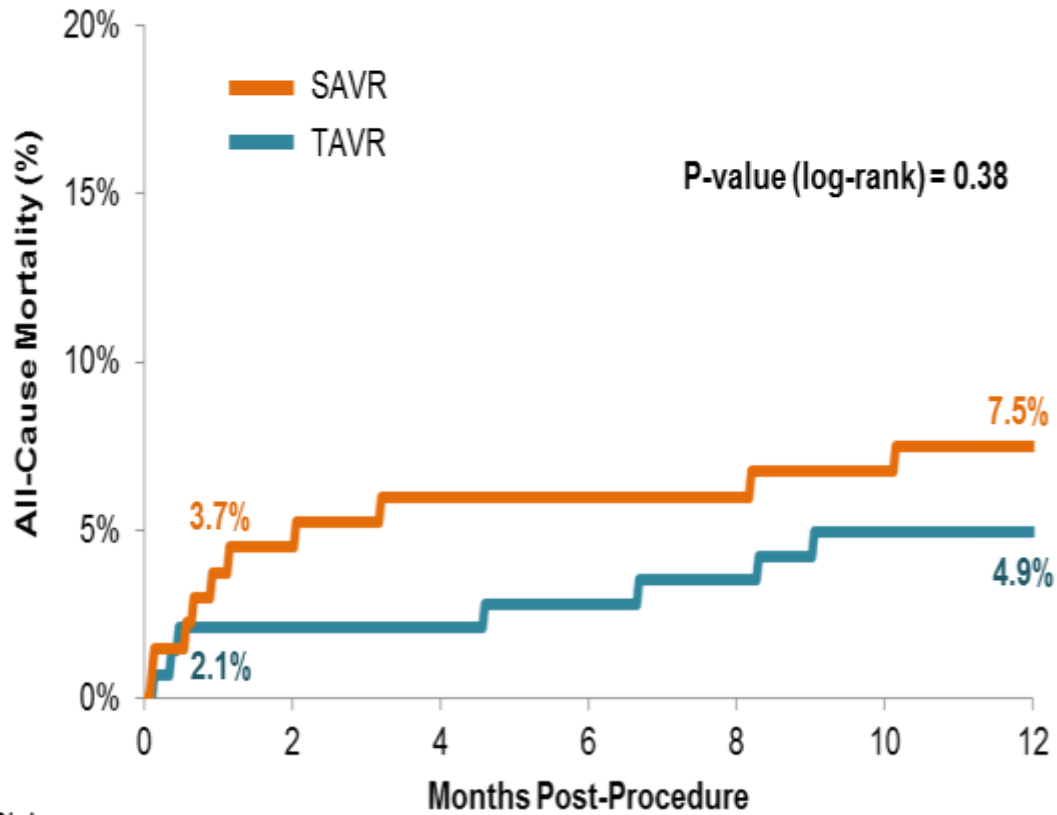
Baseline Characteristics

Characteristic, % or mean \pm SD	TAVR n=145	SAVR n=135	p-value
Age (yrs)	79.2 \pm 4.9	79.0 \pm 4.7	0.71
Male	53.8	52.6	0.84
Society of Thoracic Surgeons (STS) Score	2.9 \pm 1.6	3.1 \pm 1.7	0.30
STS Score < 4%	83.4	80.0	0.46
Logistic EuroSCORE I	8.4 \pm 4.0	8.9 \pm 5.5	0.38
NYHA class III or IV	48.6	45.5	0.61

Death from Any Cause, Stroke or Myocardial Infarction at 1 Year in As-Treated Population

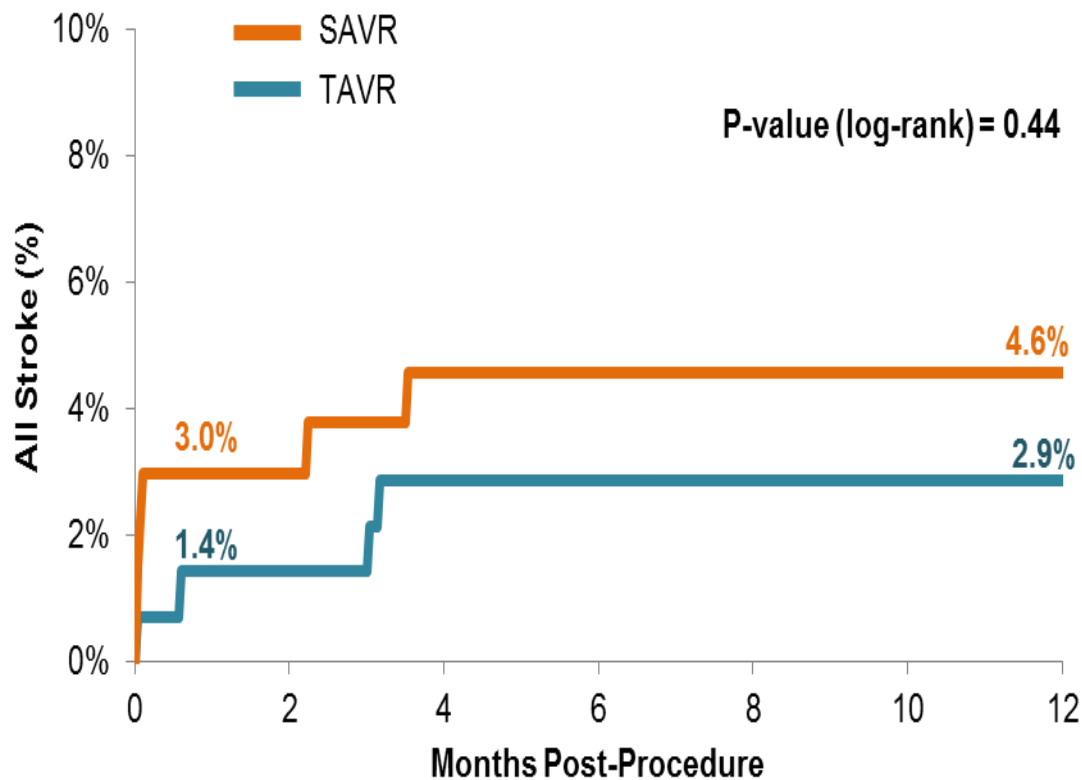


Death from Any Cause at 1 Year



No. at Risk:	0	2	4	6	8	10	12
TAVR	142	139		137			126
SAVR	134	128			125		115

All Stroke at 1 Year



No. at Risk:

TAVR	142	137	134	123
SAVR	134	124	120	110

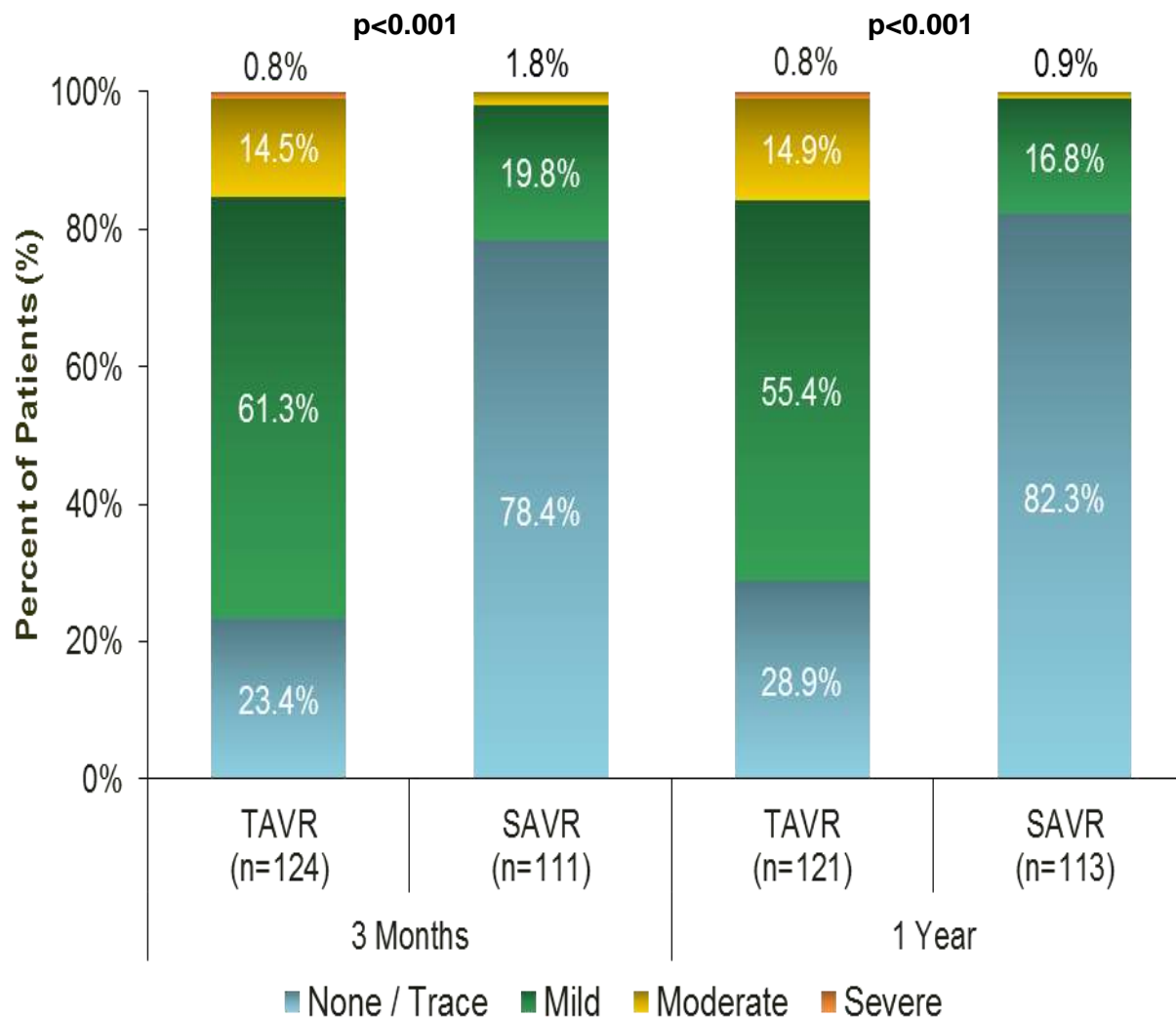
Secondary Outcomes at 30 Days

Outcome, %	TAVR n=142	SAVR n=134	p-value
Death, any cause	2.1	3.7	0.43
Death, cardiovascular	2.1	3.7	0.43
Bleeding, life-threatening+major	11.3	20.9	0.03
Cardiogenic shock	4.2	10.4	0.05
Vascular lesion, major	5.6	1.5	0.10
Acute kidney injury (stage II+III)	0.7	6.7	0.01
Stroke	1.4	3.0	0.37
TIA	1.4	0	0.17
Myocardial infarction	2.8	6.0	0.20
Atrial fibrillation	16.9	57.8	<0.001
Pacemaker	34.1	1.6	<0.001

Secondary Outcomes at 1 Year

Outcome, %	TAVR n=142	SAVR n=134	p-value
Death, any cause	4.9	7.5	0.38
Death, cardiovascular	4.3	7.5	0.25
Stroke	2.9	4.6	0.44
TIA	2.1	1.6	0.71
Myocardial infarction	3.5	6.0	0.33
Atrial fibrillation	21.2	59.4	<0.001
Pacemaker	38.0	2.4	<0.001
Aortic valve re-intervention	0.0	0.0	na

Aortic Valve Regurgitation



CoreValve Evolut System

EnVeo R w/
InLine Sheath



18 Fr
OD

[2101-295] Early Results From the CoreValve Evolut R CE Study

Ian T. Meredith, MBBS, PhD, FACC¹; Antony Walton, MBBS²; Stephen Brecker, MD³; Sanjeev...
¹MonashHEART and Monash University, Melbourne, Australia; ²Epworth Hospital, Melbourne, Australia; ³St. George's Hospital, London, United Kingdom; ⁴Royal Victoria Hospital, Belfast, United Kingdom

CoreValve Evolut R CE Study

Daniel Blackman, MD⁵; Ganesh Mandhoo, MD⁶
⁵Waikato Hospital, Hamilton, New Zealand; ⁶Leeds University, Leeds, United Kingdom

Background	Baseline Characteristics	Outcomes	Clinical Performance
<p>Study Design & Methods</p> <p>The CoreValve Evolut R CE Clinical Study evaluated the safety and clinical performance of the CoreValve Evolut R System (26 mm, 30 mm, 34 mm, 40 mm, 46 mm, 50 mm, 56 mm, 60 mm, 66 mm, 70 mm, 76 mm, 82 mm, 88 mm, 94 mm, 100 mm, 106 mm, 112 mm, 118 mm, 124 mm, 130 mm, 136 mm, 142 mm, 148 mm, 154 mm, 160 mm, 166 mm, 172 mm, 178 mm, 184 mm, 190 mm, 196 mm, 202 mm, 208 mm, 214 mm, 220 mm, 226 mm, 232 mm, 238 mm, 244 mm, 250 mm, 256 mm, 262 mm, 268 mm, 274 mm, 280 mm, 286 mm, 292 mm, 298 mm, 304 mm, 310 mm, 316 mm, 322 mm, 328 mm, 334 mm, 340 mm, 346 mm, 352 mm, 358 mm, 364 mm, 370 mm, 376 mm, 382 mm, 388 mm, 394 mm, 400 mm, 406 mm, 412 mm, 418 mm, 424 mm, 430 mm, 436 mm, 442 mm, 448 mm, 454 mm, 460 mm, 466 mm, 472 mm, 478 mm, 484 mm, 490 mm, 496 mm, 502 mm, 508 mm, 514 mm, 520 mm, 526 mm, 532 mm, 538 mm, 544 mm, 550 mm, 556 mm, 562 mm, 568 mm, 574 mm, 580 mm, 586 mm, 592 mm, 598 mm, 604 mm, 610 mm, 616 mm, 622 mm, 628 mm, 634 mm, 640 mm, 646 mm, 652 mm, 658 mm, 664 mm, 670 mm, 676 mm, 682 mm, 688 mm, 694 mm, 700 mm, 706 mm, 712 mm, 718 mm, 724 mm, 730 mm, 736 mm, 742 mm, 748 mm, 754 mm, 760 mm, 766 mm, 772 mm, 778 mm, 784 mm, 790 mm, 796 mm, 802 mm, 808 mm, 814 mm, 820 mm, 826 mm, 832 mm, 838 mm, 844 mm, 850 mm, 856 mm, 862 mm, 868 mm, 874 mm, 880 mm, 886 mm, 892 mm, 898 mm, 904 mm, 910 mm, 916 mm, 922 mm, 928 mm, 934 mm, 940 mm, 946 mm, 952 mm, 958 mm, 964 mm, 970 mm, 976 mm, 982 mm, 988 mm, 994 mm, 1000 mm).</p>	<p>Baseline Characteristics</p> <p>Age, mean ± SD, N=80: 82.8 ± 6.1</p> <p>Female, n (%): 66.7</p> <p>Body surface area (m²): 1.7 ± 0.2</p> <p>STS Predicted Risk of Mortality (%): 7.0 ± 3.7</p> <p>Logistic EuroSCORE I (%): 20.5 ± 12.5</p> <p>New York Heart Association class III or IV: 68.3</p> <p>Previous CABG: 23.3</p> <p>Any chronic lung disease: 43.3</p> <p>Diabetes: 26.3</p> <p>Previous stroke: 11.7</p> <p>Atrial fibrillation/atrial flutter: 38.7</p> <p>Frailty: 68.3</p> <p>Pre-existing permanent pacemaker: 11.7</p>	<p>Outcomes</p> <p>Successful valve positioning, if attempted (n=15)*: 100 (22/22)†</p> <p>Valve resheathing, n (%): 10</p> <p>Valve recapture, n (%): 12</p> <p>Valve size implanted:</p> <ul style="list-style-type: none"> 26 mm: 31.7 29 mm: 68.3 38.7 <p>Post TAVR balloon dilatation: 21.7</p> <p>Valve-related dysfunction requiring repeat procedure: 0.0</p>	<p>Clinical Performance</p> <p>Event, %</p> <p>Absence of procedural mortality: 100.0 (60/60)</p> <p>Correct positioning of 1 valve in proper location: 100.0 (60/60)</p> <p>Mean gradient < 20 mm Hg or peak velocity < 3m/sec: 98.3 (59/60)</p> <p>Absence of moderate or severe regurgitation: 93.3 (56/60)</p> <p>Absence of patient prosthesis mismatch*: 83.6 (46/55)</p> <p>VARC-2 device success: 78.6 (44/56)</p> <p>Effective orifice area < 2.0 cm²: 49.1</p> <p>Mean gradient > 19 mmHg: 1.9</p>
<p>30-Day Outcomes</p> <p>All-cause mortality: 0.0</p> <p>All stroke: 0.0</p> <p>Absence of moderate or severe PVL: 96.6</p> <p>Permanent pacemaker implantation: 11.7</p>	<p>Summary & Conclusions</p> <p>All attempts at repositioning of the Evolut R TAV were successful and resulted in a final implant depth of 4.25 ± 0.3 ± 4.1 mm, NCS = 5.9 ± 3.4 mm. The ability to achieve a final implant depth of 4 mm or greater in patients with moderate or severe aortic stenosis and aortic regurgitation was 100% in patients who were not on a pacemaker compared with 83.3% in patients who were on a pacemaker (P=0.001). In addition, the percentage of patients with mild or less paravalvular leak (PVL) was 93.2% at the early post-procedure time point and 96.6% at 30 days.</p> <p>The VARC-2 overall device success rate was 78.6% in patients who were not on a pacemaker and 83.6% in patients who were on a pacemaker. There were no deaths or strokes at 30 days. The Evolut R TAV system is safe and effective at treating aortic stenosis and aortic regurgitation. Device implantation was successful in all patients which required, and resulted in low rates of moderate or severe PVL and the need for permanent pacemakers.</p>		

Procedural Result Event, %

14 Fr Equivalent

Procedural mortality

Correct positioning of 1 valve in proper location

30 Day Event, %

Mean gradient < 20 mm Hg or peak velocity < 3m/sec

100.0 (60/60)

98.3 (59/60)

98.3 (59/60)

All-cause mortality

Absence of moderate or severe regurgitation

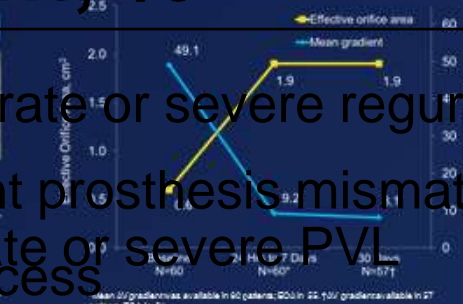
All stroke

Absence of patient prosthesis mismatch*

Absence of moderate or severe PVL

VARC-2 device success

Permanent pacemaker implantation



All attempts at repositioning of the Evolut R TAV were successful and resulted in a final implant depth of 4.25 ± 0.3 ± 4.1 mm, NCS = 5.9 ± 3.4 mm. The ability to achieve a final implant depth of 4 mm or greater in patients with moderate or severe aortic stenosis and aortic regurgitation was 100% in patients who were not on a pacemaker compared with 83.3% in patients who were on a pacemaker (P=0.001). In addition, the percentage of patients with mild or less paravalvular leak (PVL) was 93.2% at the early post-procedure time point and 96.6% at 30 days.

The VARC-2 overall device success rate was 78.6% in patients who were not on a pacemaker and 83.6% in patients who were on a pacemaker. There were no deaths or strokes at 30 days. The Evolut R TAV system is safe and effective at treating aortic stenosis and aortic regurgitation. Device implantation was successful in all patients which required, and resulted in low rates of moderate or severe PVL and the need for permanent pacemakers.

Final Thoughts

- 5 year data from PARTNER demonstrates mid-term durability of TAVR
- 2 year data from CoreValve demonstrates continued superiority of TAVR over SAVR
- The Sapien 3 data demonstrates continued improvement in outcomes in high risk and intermediate risk patients with next gen devices
- All-comers trial is challenging but current data supports movement of TAVR into lower risk patients