Lessons learned from the PARTNER trial

Philippe Généreux, MD

Director, Angiographic Core Laboratory

Columbia University Medical Center and the Cardiovascular Research Foundation, New York, NY

Assistant Professor of Medicine, Interventional Cardiologist,

Director, Transcatheter Aortic Valve Implantation program

Hôpital du Sacré-Coeur de Montréal, Québec, Canada

TCTAP, April 2014, Seoul, Korea

Disclosure Statement of Financial Interest

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	Company
• None	

Agenda…in 8 minutes!

- *Update*
  - PARTNER cohort 1B 3 years
  - PARTNER cohort 1A 3 years
  - PARTNER cohort 2B 1 year
  - Continued Access Registries
- *Latest publications from PARTNER*
  - Vascular Complications, Bleeding Complications, A. Fib, new PPM, new LBBB, Sex Gender, Diabetics,…and PVL
- *PARTNER 2A update*

PARTNER trial 1

TAVR

PARTNER 1B (TF)	PARTNER 1A (TF & TA)	PARTNER 1 Continued Access (TF & TA)
Inoperable & High Risk Registries	High Risk RCT	Inoperable & High Risk Registries
358 patients	*699 patients*	*2071 patients*

3128 patients

EDWARD SAPIEN DEVICE

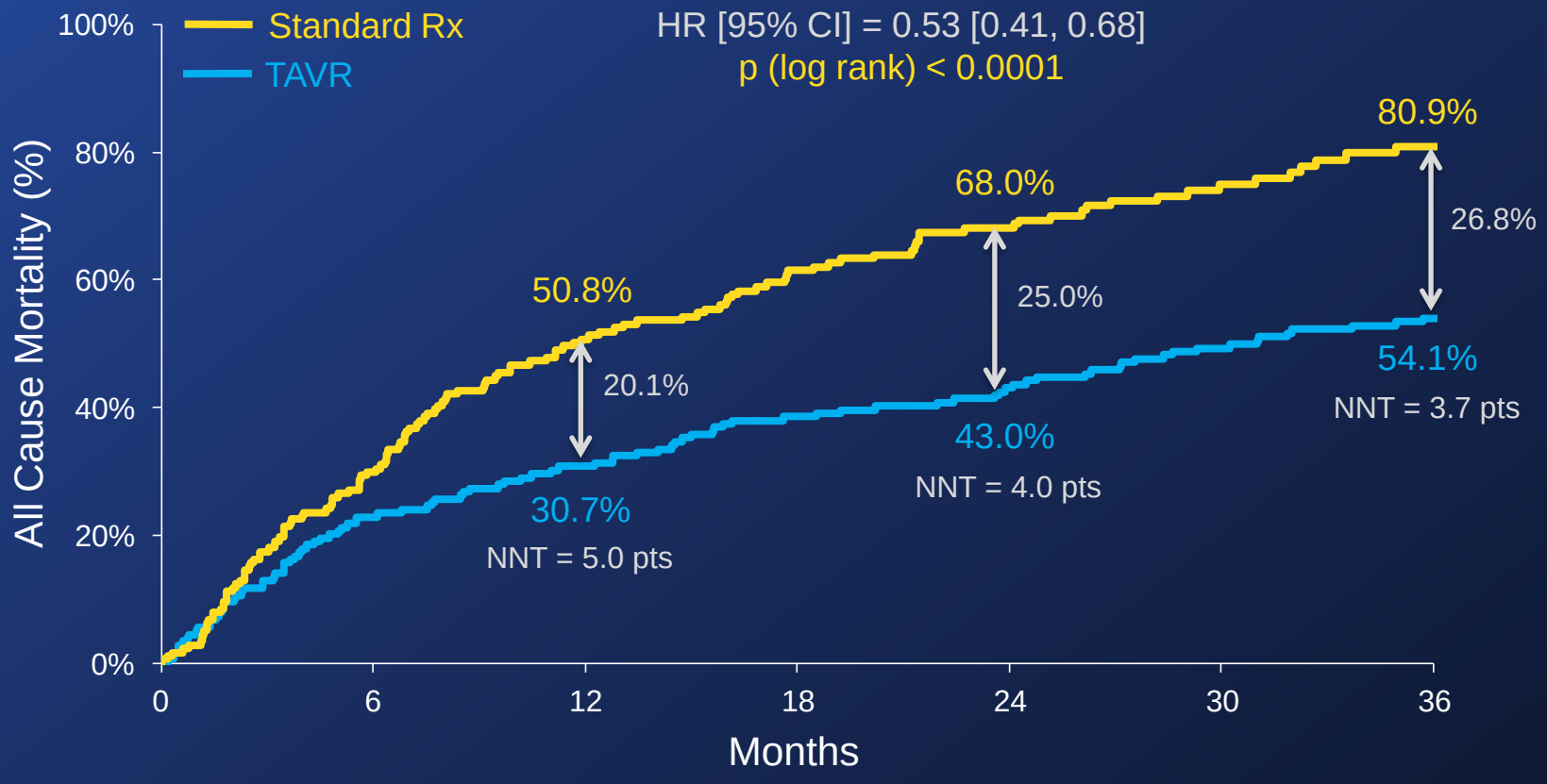
Three-Year Outcomes of Transcatheter Aortic Valve Replacement (TAVR) in "Inoperable" Patients With Severe Aortic Stenosis: The PARTNER Trial

Samir R. Kapadia, MD
On behalf of The PARTNER Trial Investigators

TCT 2012 | Miami, FL | October 24, 2012

All Cause Mortality (ITT); n = 358

Crossover Patients Censored at Crossover

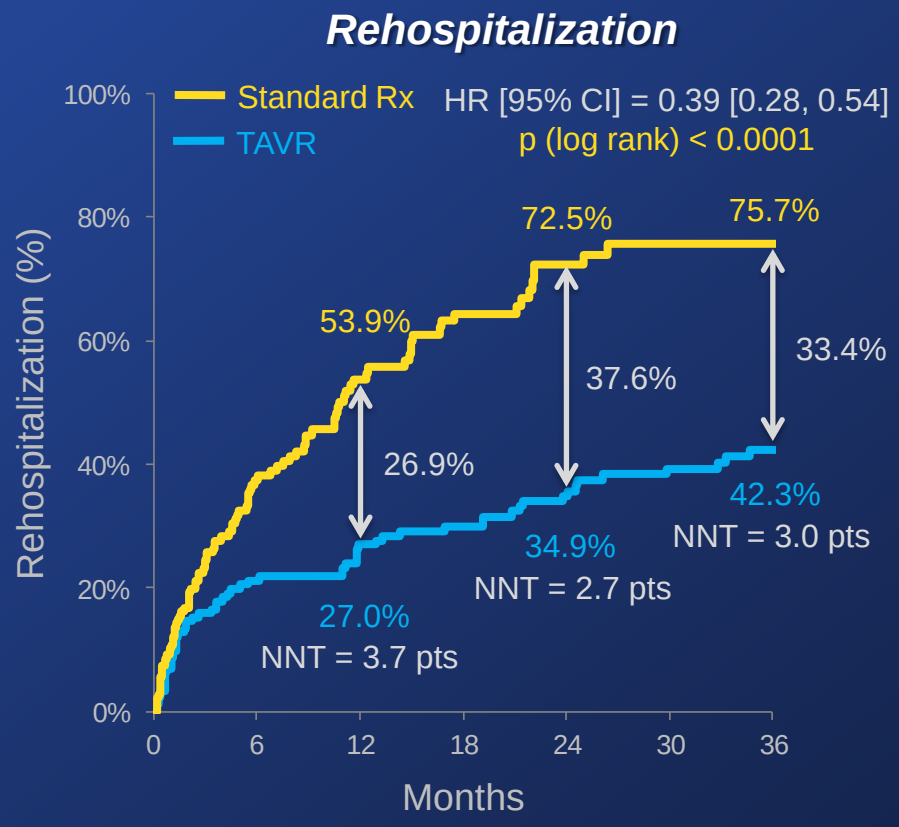


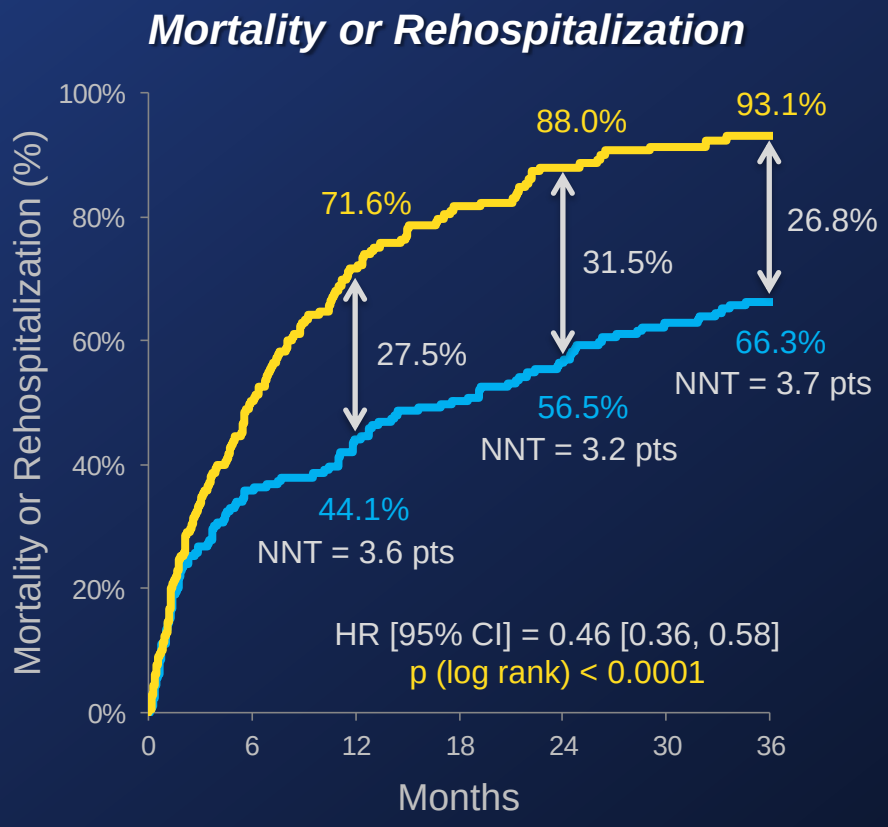
Numbers at Risk

Standard Rx	**179**	**121**	**85**	**62**	**46**	**27**	**17**
TAVR	**179**	**138**	**124**	**110**	**101**	**88**	**70**

Repeat Hospitalization (ITT)

THE PARTNER TRIAL





Days Alive Out of Hospital Median [IQR] **TAVR 944 [233-1096]** **Standard Rx 368 [147-1096]** **p <.0001**

Numbers at Risk

Standard Rx	179	86	49	30	19	11	7	179	86	49	30	19	11	7
TAVR	179	115	100	89	77	64	49	179	115	100	89	77	64	49

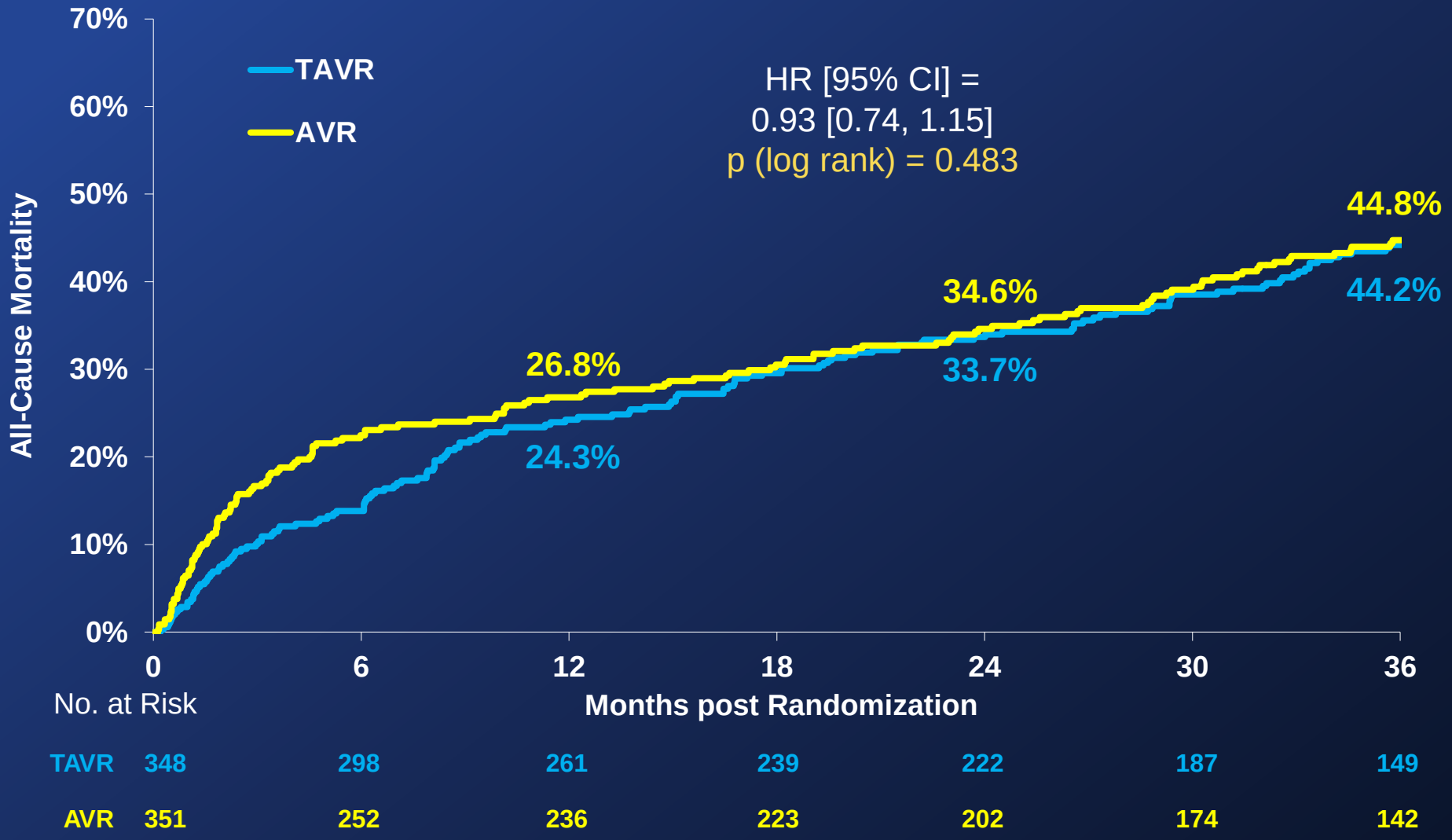
Three-Year Outcomes after Transcatheter or Surgical Aortic Valve Replacement in High-Risk Patients with Severe Aortic Stenosis

Vinod H. Thourani, MD
on behalf of The PARTNER Trial Investigators

ACC 2013 | San Francisco | March 11, 2013

THE PARTNER TRIAL

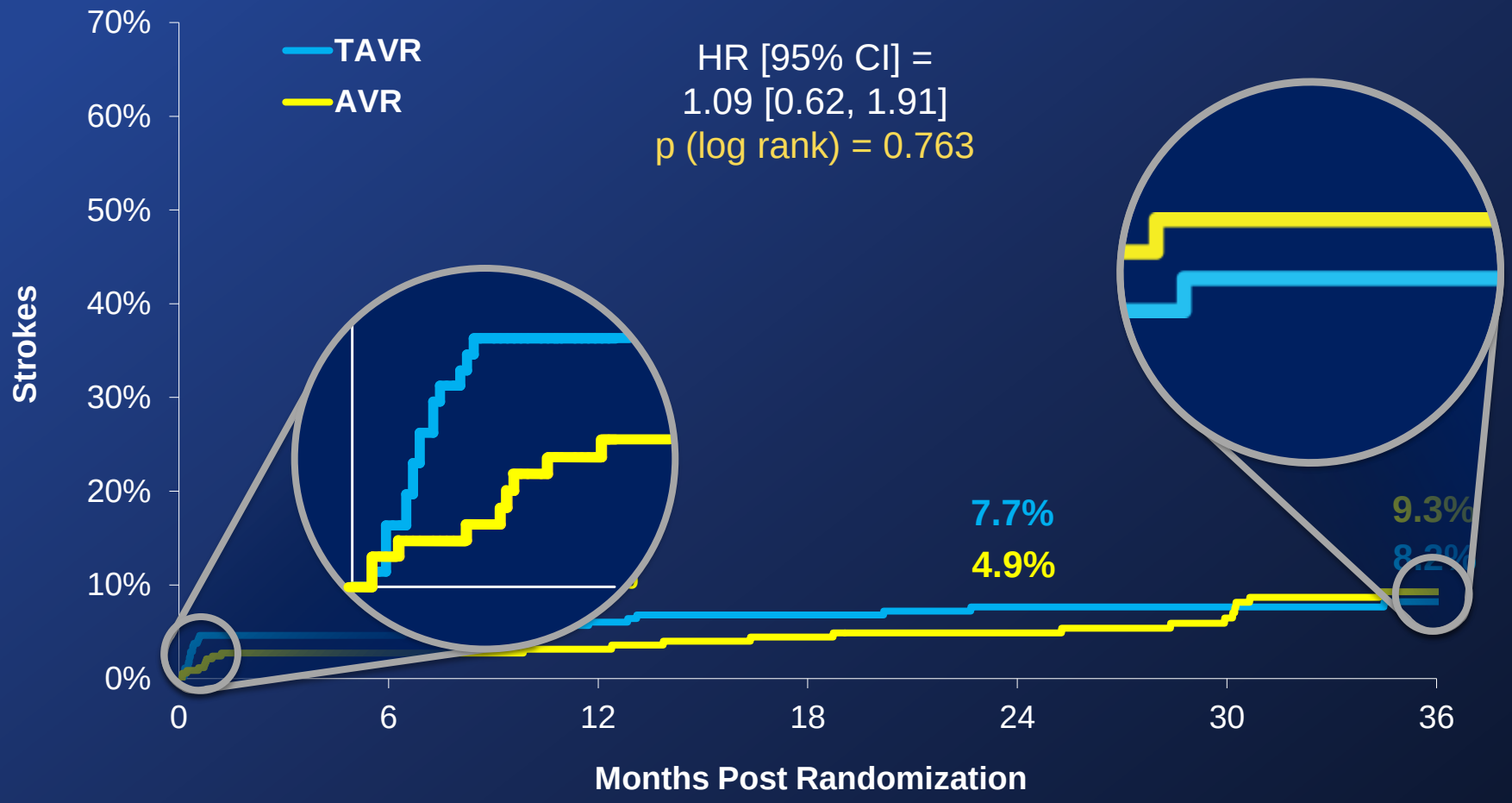
All-Cause Mortality (ITT); N = 699



No. at Risk

TAVR	348	298	261	239	222	187	149
AVR	351	252	236	223	202	174	142

Strokes (ITT)



No. at Risk

TAVR	348	287	250	228	211	176	139
AVR	351	246	230	217	197	169	139

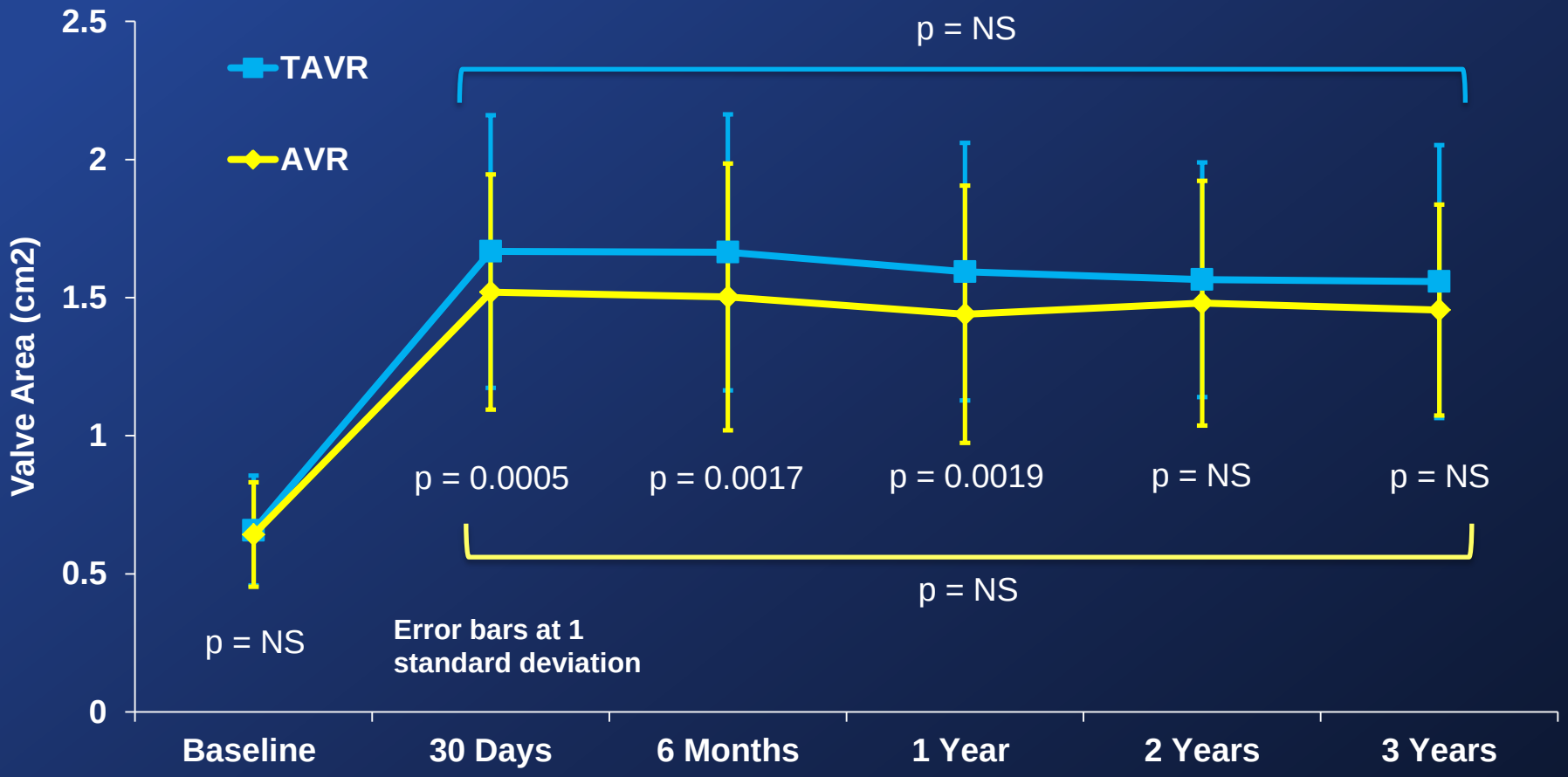
Clinical Outcomes at 1, 2, and 3 Years (ITT)
All Patients (N=699)

	1 Year			2 Years			3 Years		
Outcome	***AVR (N = 351)***	***TAVR (N = 348)***	***p-value***	***AVR (N = 351)***	***TAVR (N = 348)***	***p-value***	***AVR (N = 351)***	***TAVR (N = 348)***	***p-value***
Major Vasc. Comp. – no. (%)	13 (3.8)	42 (12.1)	<0.001	13 (3.8)	43 (12.5)	<0.001	13 (3.8)	43 (12.5)	<0.001
Major Bleeding – no. (%)	88 (26.7)	52 (15.7)	<0.001	95 (29.5)	61 (19.3)	0.003	99 (31.5)	64 (20.8)	0.003
New PM – no. (%)	16 (5.0)	21 (6.4)	0.44	19 (6.3)	24 (7.6)	0.54	20 (6.8)	25 (8.1)	0.56
Endocarditis – no. (%)	3 (1.0)	2 (0.6)	0.63	3 (1.0)	4 (1.5)	0.62	6 (2.6)	4 (1.5)	0.37
SVD§ Requiring AVR	0	0		0	0		0	0	
MI – no. (%)	2 (0.6)	0	0.16	4 (1.5)	0	0.05	6 (2.7)	2 (1.1)	0.23
Acute Kidney Inj.* – no. (%)	20 (6.5)	18 (5.4)	0.57	22 (7.3)	20 (6.2)	0.59	23 (7.9)	22 (7.2)	0.76

§ SVD = Structural Valve Deterioration

* Renal replacement therapy

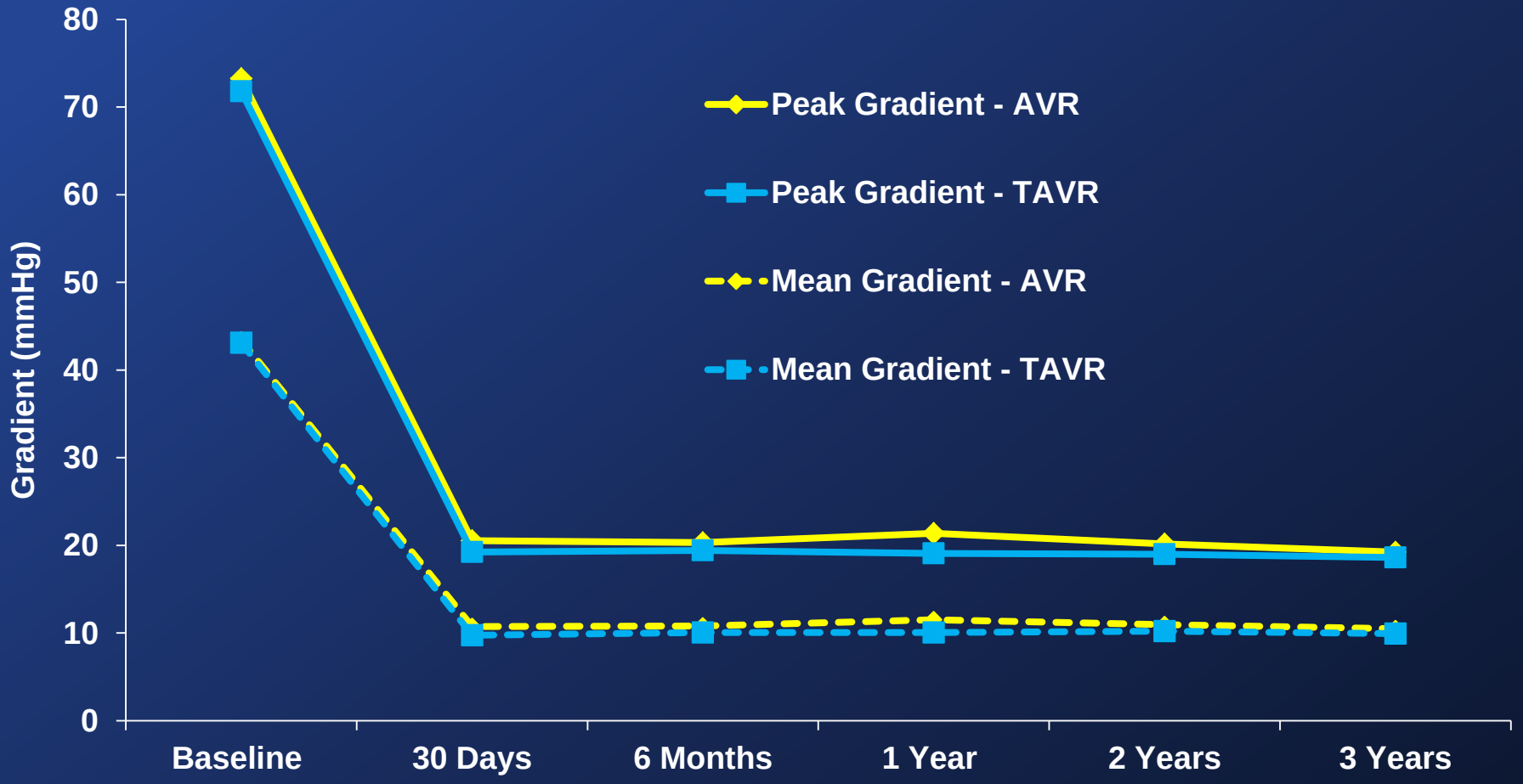
Echocardiographic Findings (AT)
Aortic Valve Area



No. of Echos

TAVR	304	271	223	211	150	88
AVR	294	226	163	154	121	70

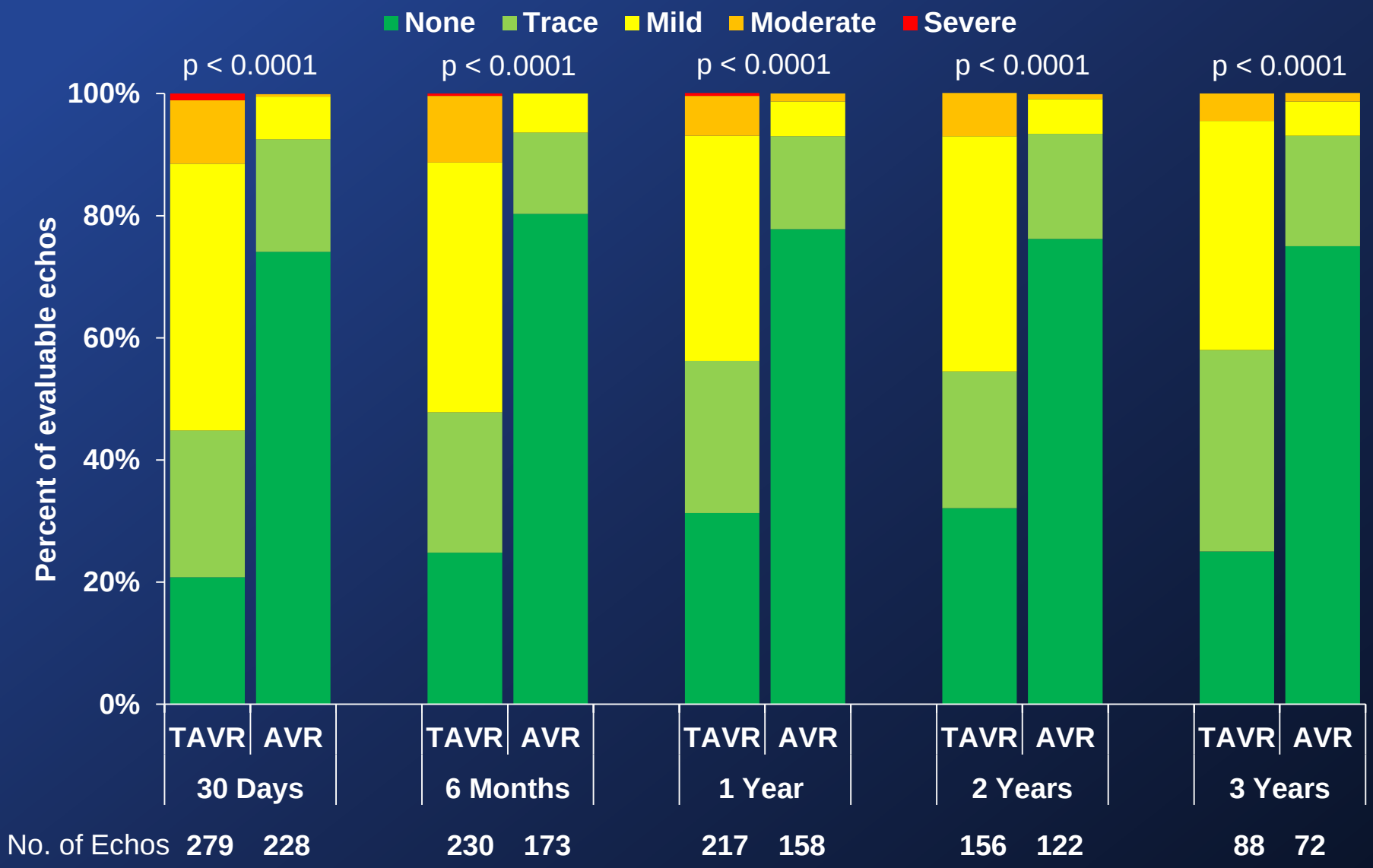
Echocardiographic Findings (AT)
Mean & Peak Gradients



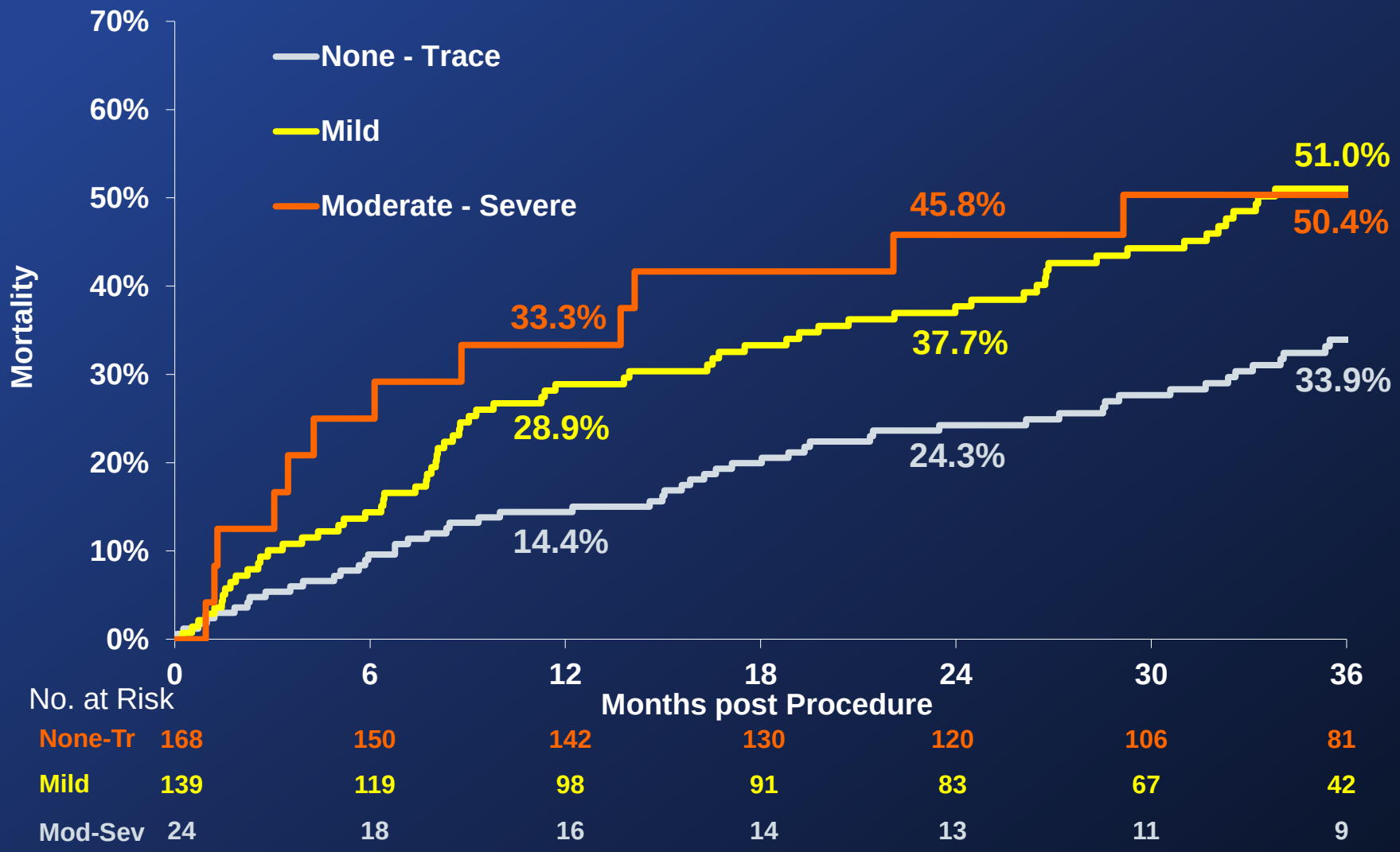
No. of Echos

	Baseline	30 Days	6 Months	1 Year	2 Years	3 Years
TAVR	310	277	233	219	155	88
AVR	299	230	169	158	123	72

Paravalvular Aortic Regurgitation (AT)



Impact of Mild PVL on Mortality (AT)
TAVR Patients



No. at Risk

None-Tr	168	150	142	130	120	106	81
Mild	139	119	98	91	83	67	42
Mod-Sev	24	18	16	14	13	11	9

Implications

- 3-year results from the high-risk operable PARTNER cohort indicate…
  - TAVR should be ***considered an alternative to surgery with similar mortality and similar other major clinical outcomes***
  - Peri-procedural stroke concerns after TAVR have diminished with longer term follow-up
  - TAVR valve hemodynamics have remained stable, although peri-procedural regurgitation (even mild) has emerged as a predictor of late mortality
- Future efforts should be directed towards reducing TAVR procedure-related complications, including strokes, vascular events, and paravalvular regurgitation

New Data from the PARTNER Non-Randomized Continued Access Registry:

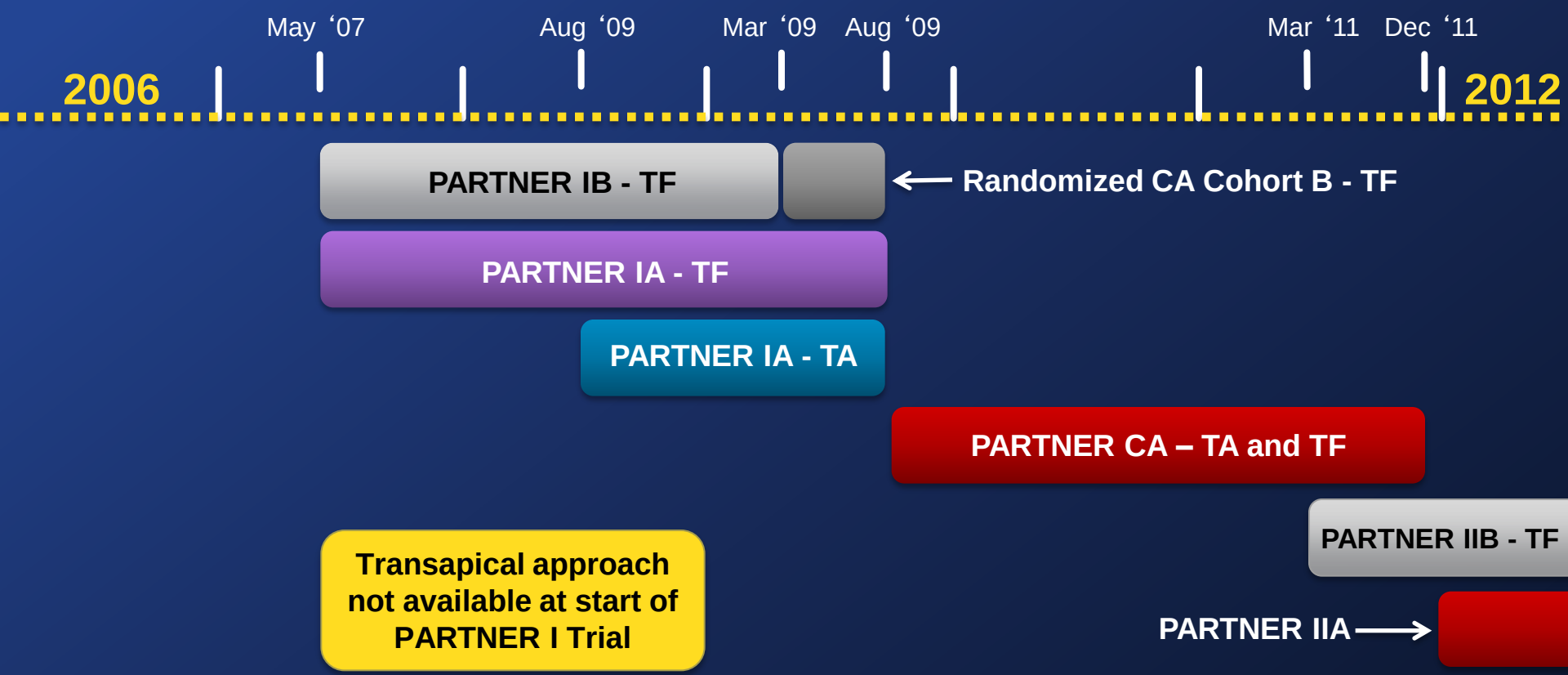
Outcomes After Transfemoral Transcatheter Aortic Valve Replacement

William F. Fearon, MD

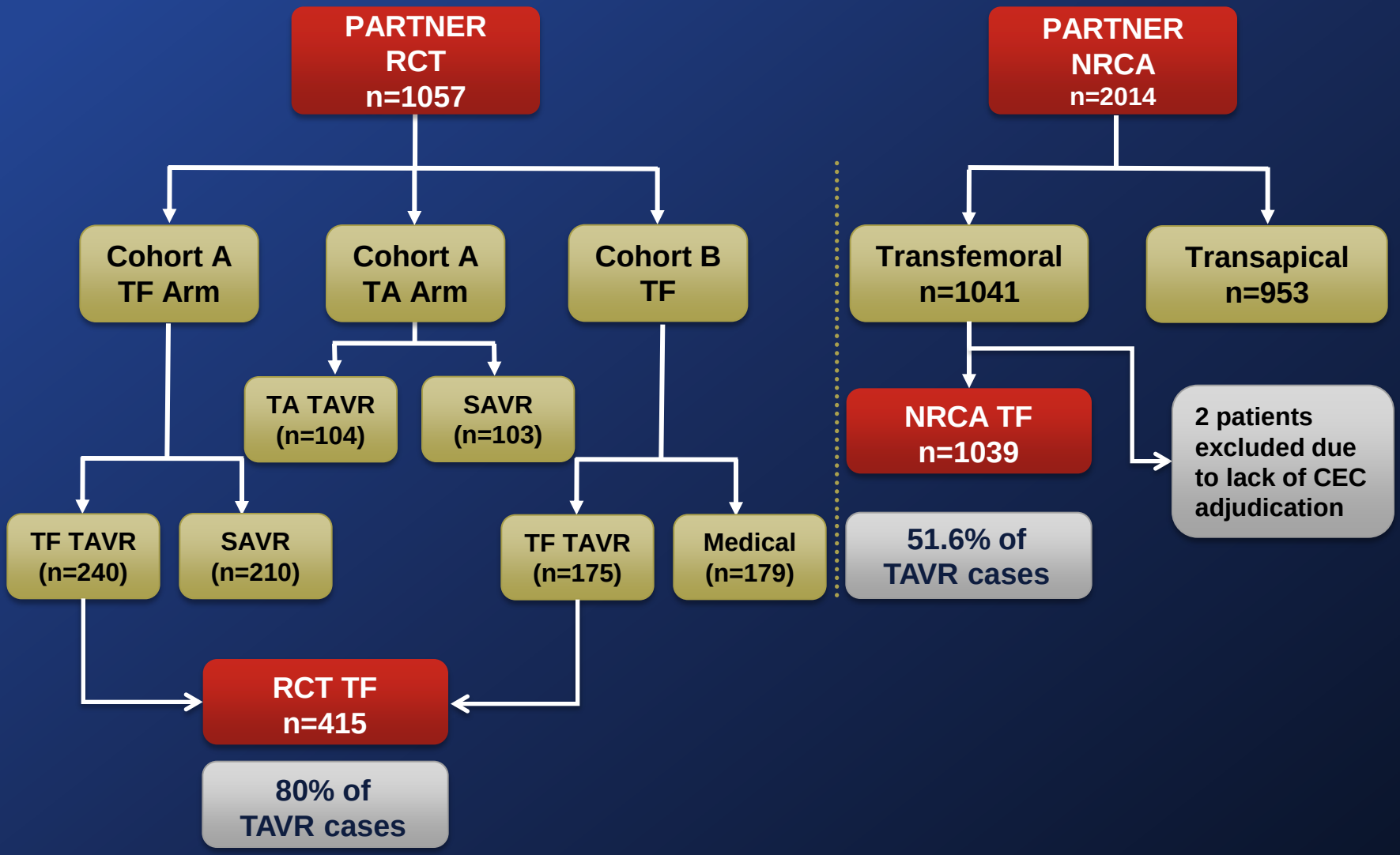
on behalf of The PARTNER Trial Investigators
and The PARTNER Publications Office

ACC 2013 | San Francisco | March 11, 2013

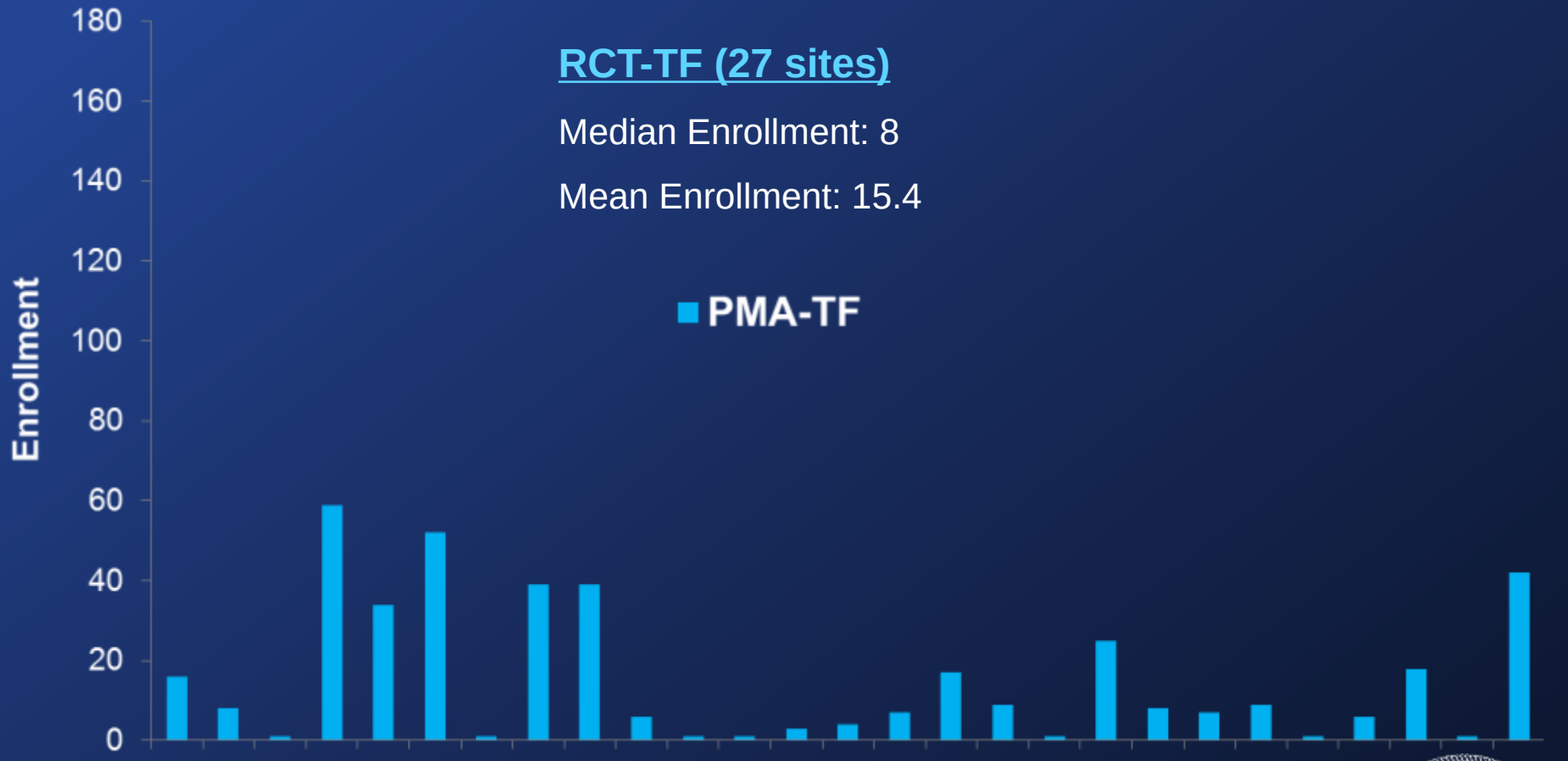
PARTNER Trial Timelines



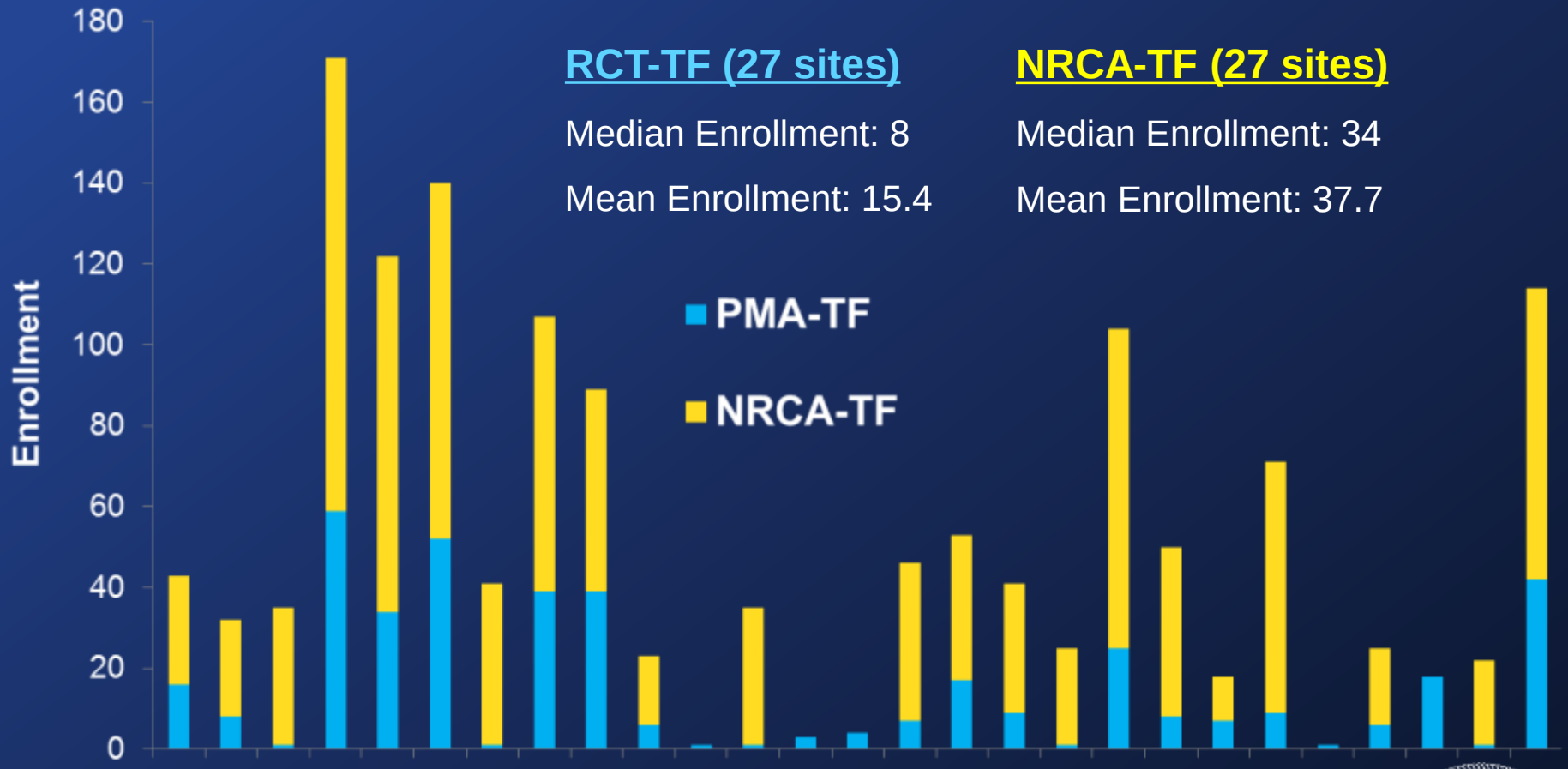
As Treated Study Population



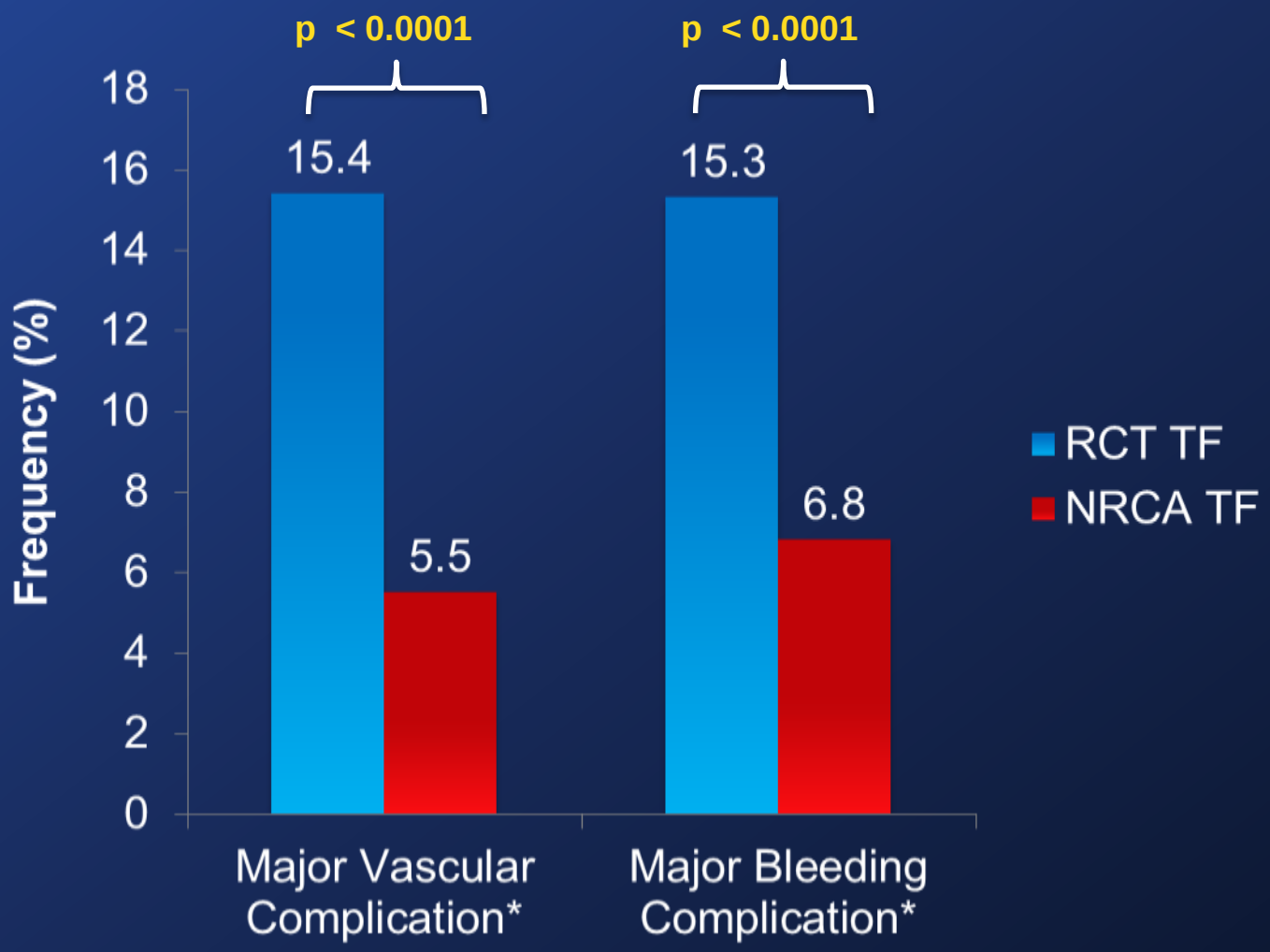
Transfemoral Implants per Site



Transfemoral Implants per Site

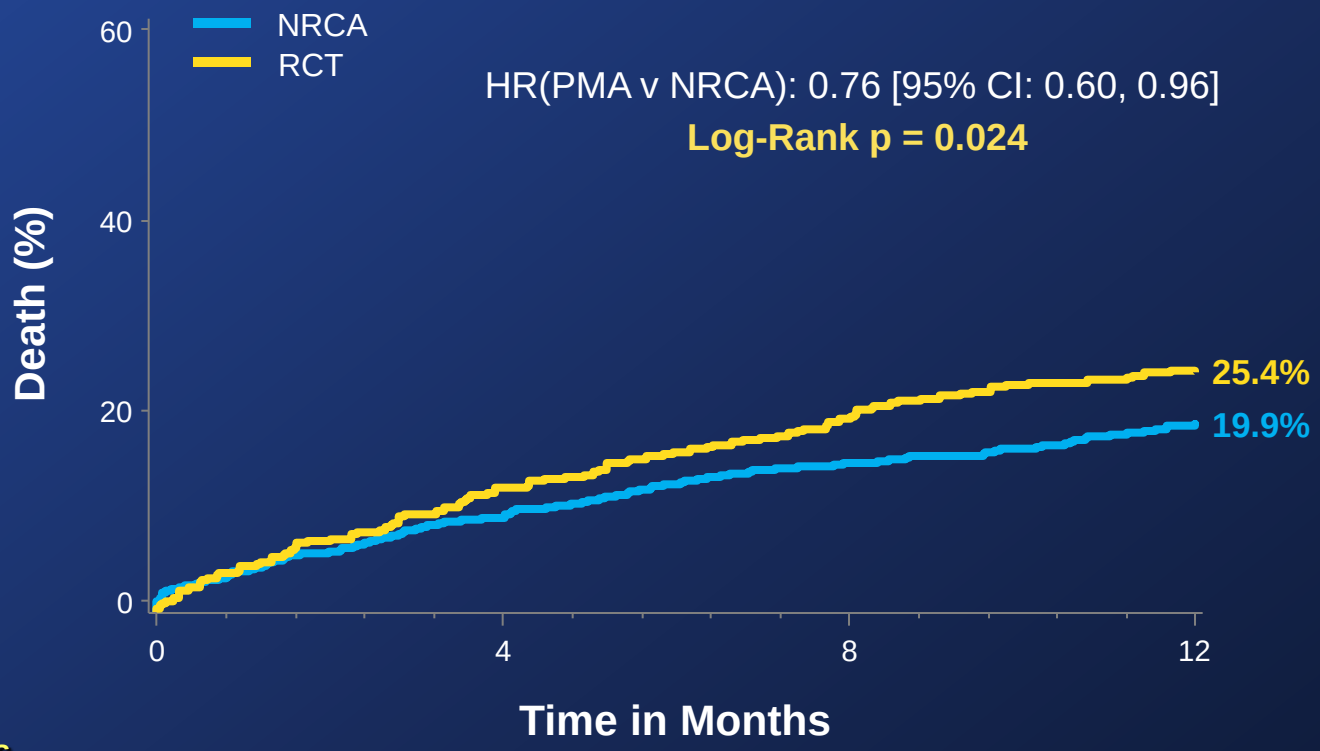


Procedural Complications



*Based on Modified VARC 1 Definitions

Mortality Following TF TAVR



Numbers at Risk

NRCA	1017	904	737	521
RCT	415	361	329	308

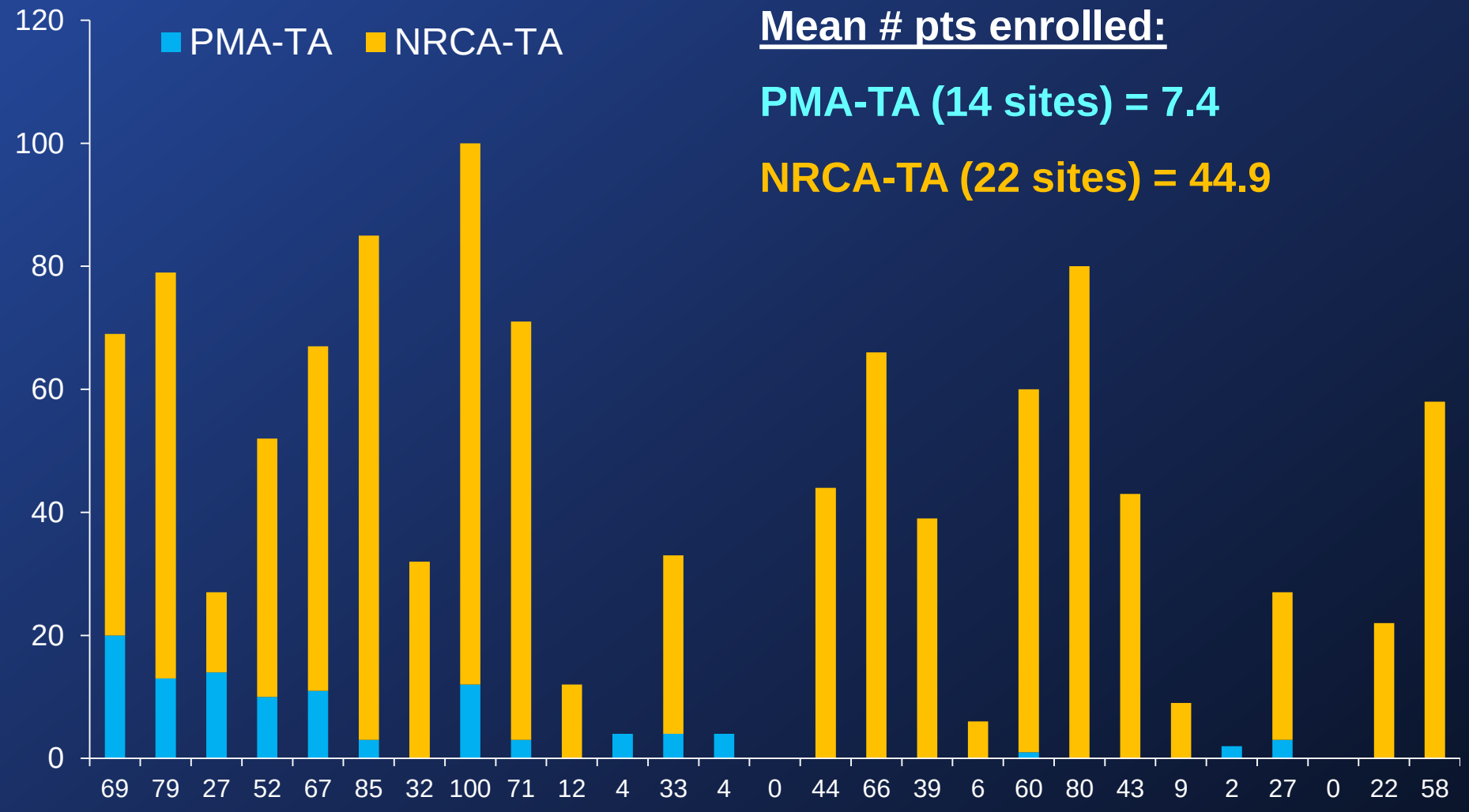
New Data from PARTNER Continued Access (Non-randomized): Transapical Outcomes After TAVR

Todd M. Dewey, MD

TCT 2012 | Miami | October 22, 2012

THE PARTNER TRIAL

Transapical Enrollment per Site

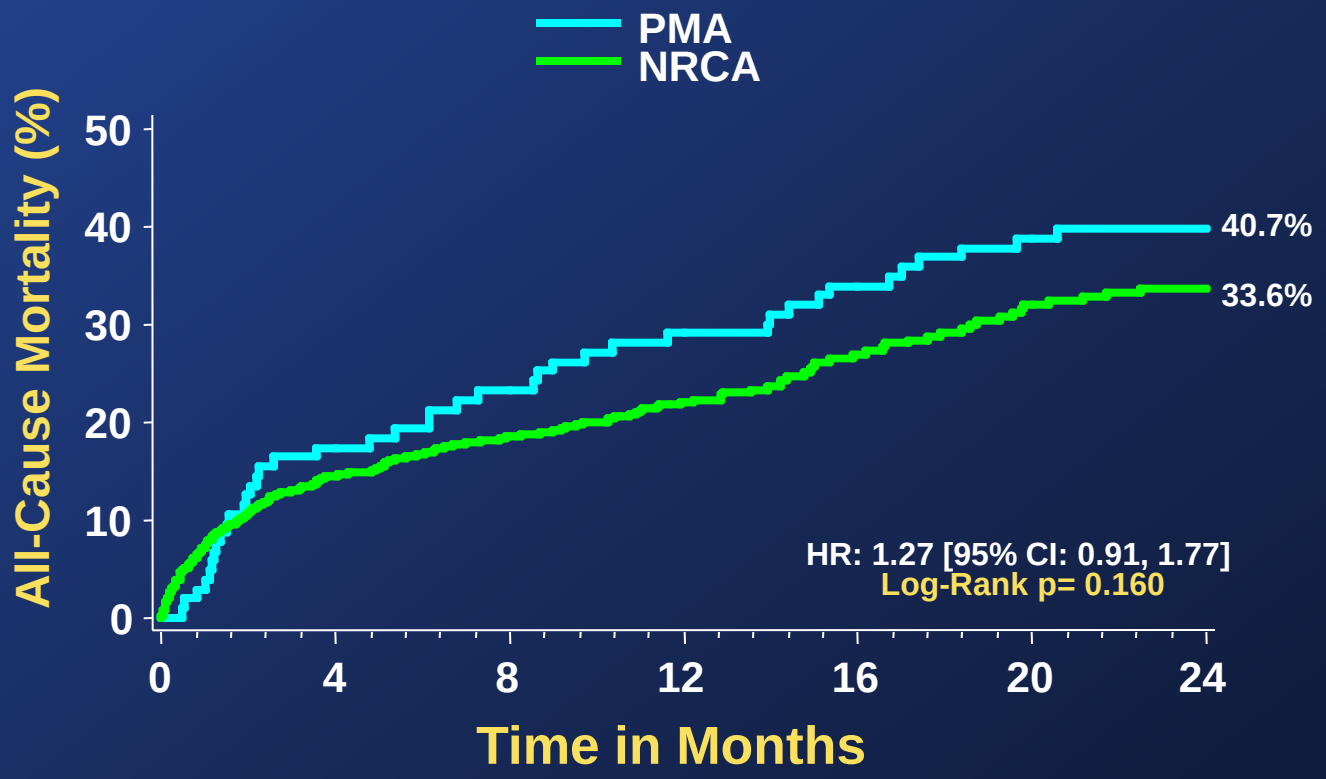


Mean # pts enrolled:

PMA-TA (14 sites) = 7.4

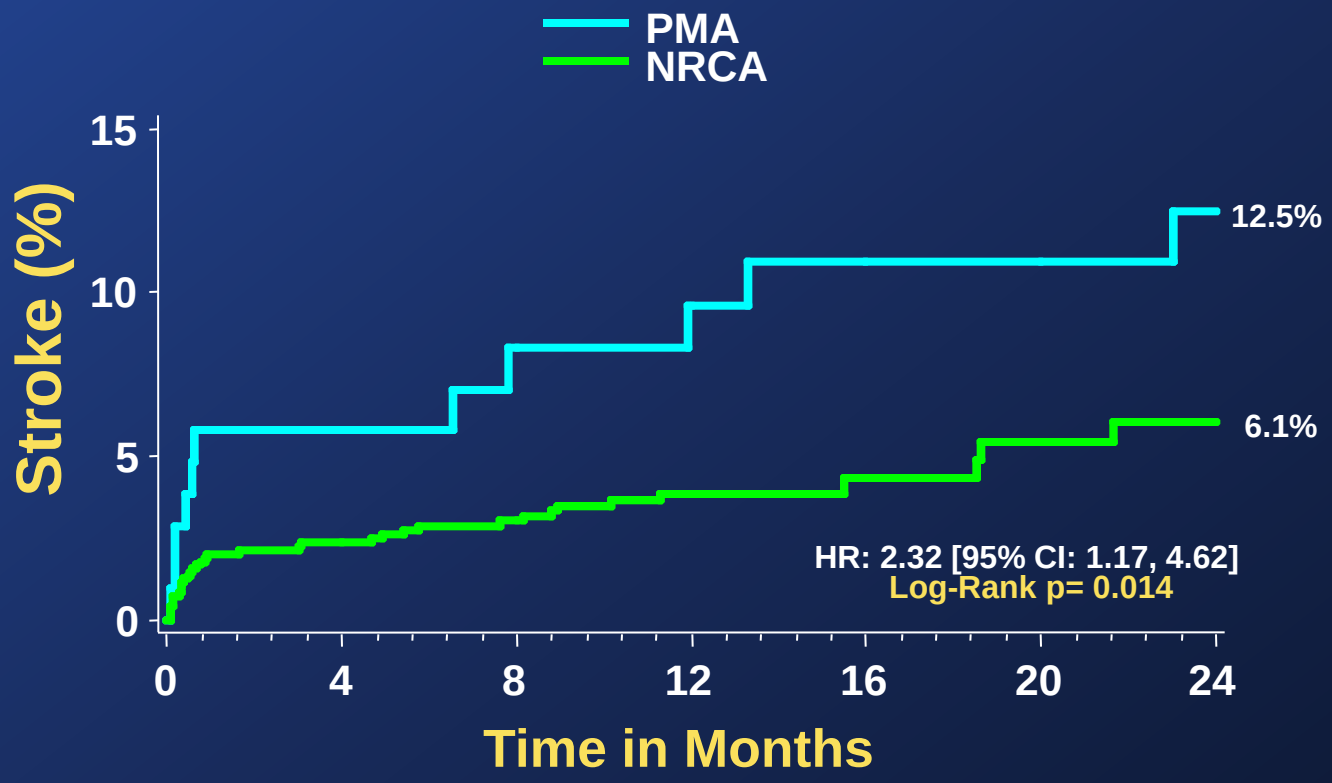
NRCA-TA (22 sites) = 44.9

2 Year Mortality following TA-TAVR



Number at risk							
PMA	104	85	79	73	68	63	60
NRCA	988	808	638	456	194	171	116

2 Year Stroke following TA-TAVR



Number at risk							
PMA	104	80	73	68	63	59	55
NRCA	988	789	620	439	187	164	109

Agenda…in 8 minutes!

- *Update*
  - PARTNER cohort 1B 3 years
  - PARTNER cohort 1A 3 years
  - PARTNER cohort 2B 1 year
  - Continued Access Registries
- *Latest publications from PARTNER*
  - Vascular Complications, Bleeding Complications, Arrhythmias, Sex Gender, Diabetics, Cost-effectiveness…and PVL
- *PARTNER 2A update*

A Randomized Comparison of Vascular Complications after TAVR Comparing the SAPIEN vs. The Lower-Profile SAPIEN XT System in Inoperable Aortic Stenosis Patients

A PARTNER 2B Substudy Analysis

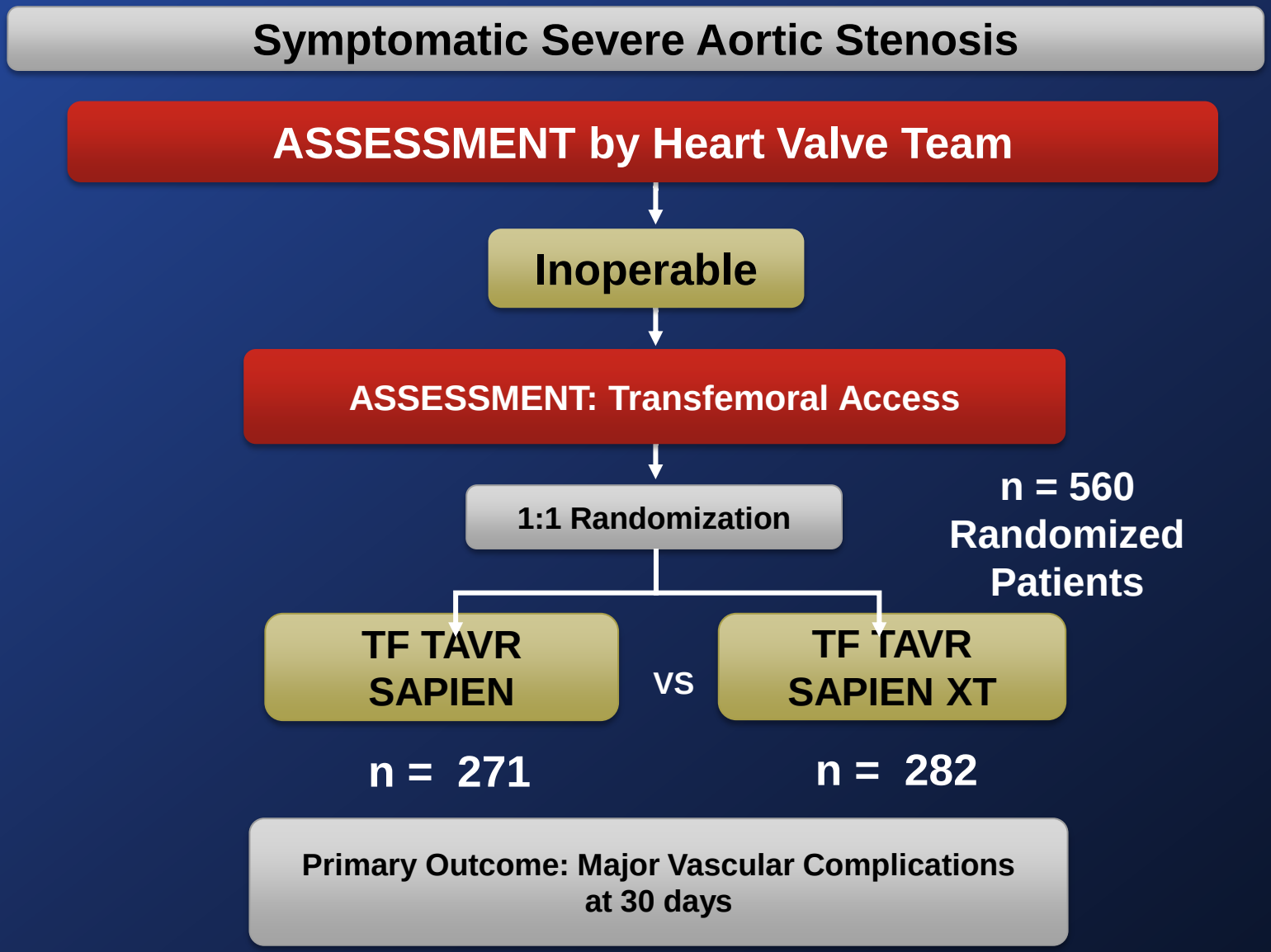
Augusto D. Pichard, MD

on behalf of The PARTNER Trial Investigators
and The PARTNER Publications Office

ACC 2014 | Washington, D.C. | March 29, 2014

The PARTNER II Inoperable Cohort

As-Treated Population Study Flow



Sheath Size Comparison

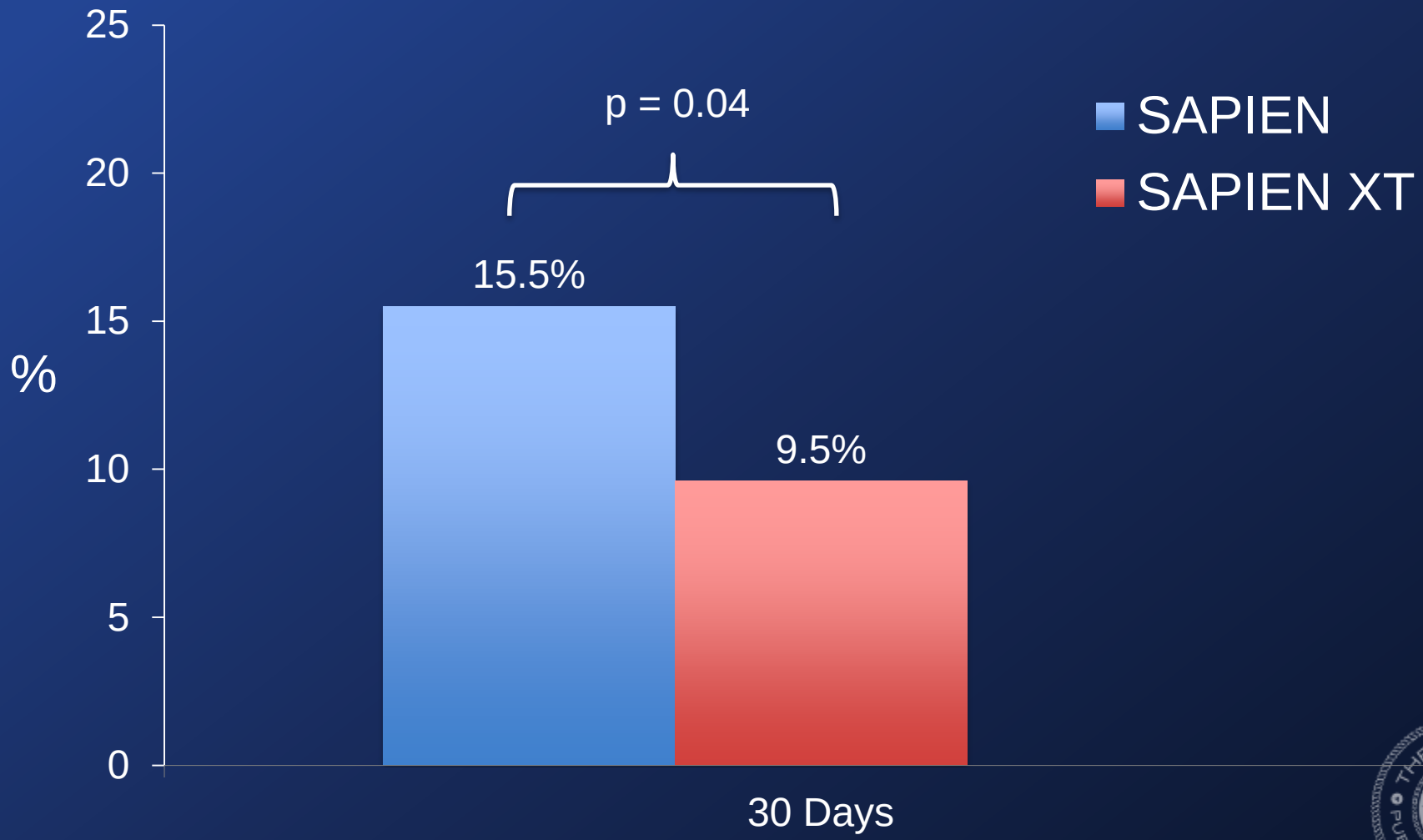
Valve	Valve Size	Sheath ID	Sheath OD	Minimum Vessel Diameter
SAPIEN THV	23mm	22F	25F (8.4mm)	7.0mm
SAPIEN XT THV	23mm	18F	22F (7.2mm)	6.0mm
SAPIEN THV	26mm	24F	28F (9.2mm)	8.0mm
SAPIEN XT THV	26mm	19F	23F (7.5mm)	6.5mm

33% reduction in CSA

RetroFlex 3

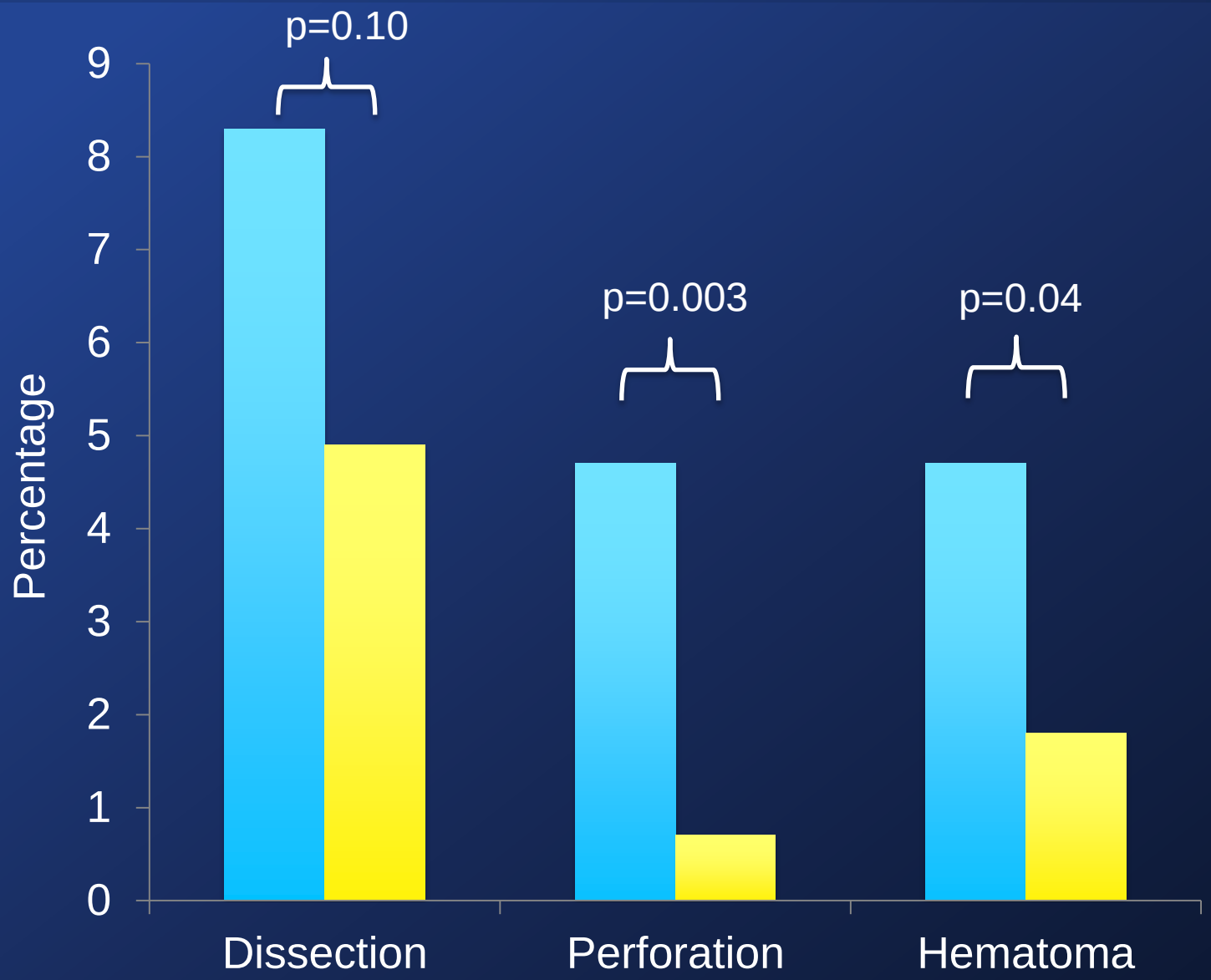
NovaFlex

30 Day Outcomes – Major Vascular Complications



Généreux et al. *JACC* 2012

Vascular Complications by Valve Type



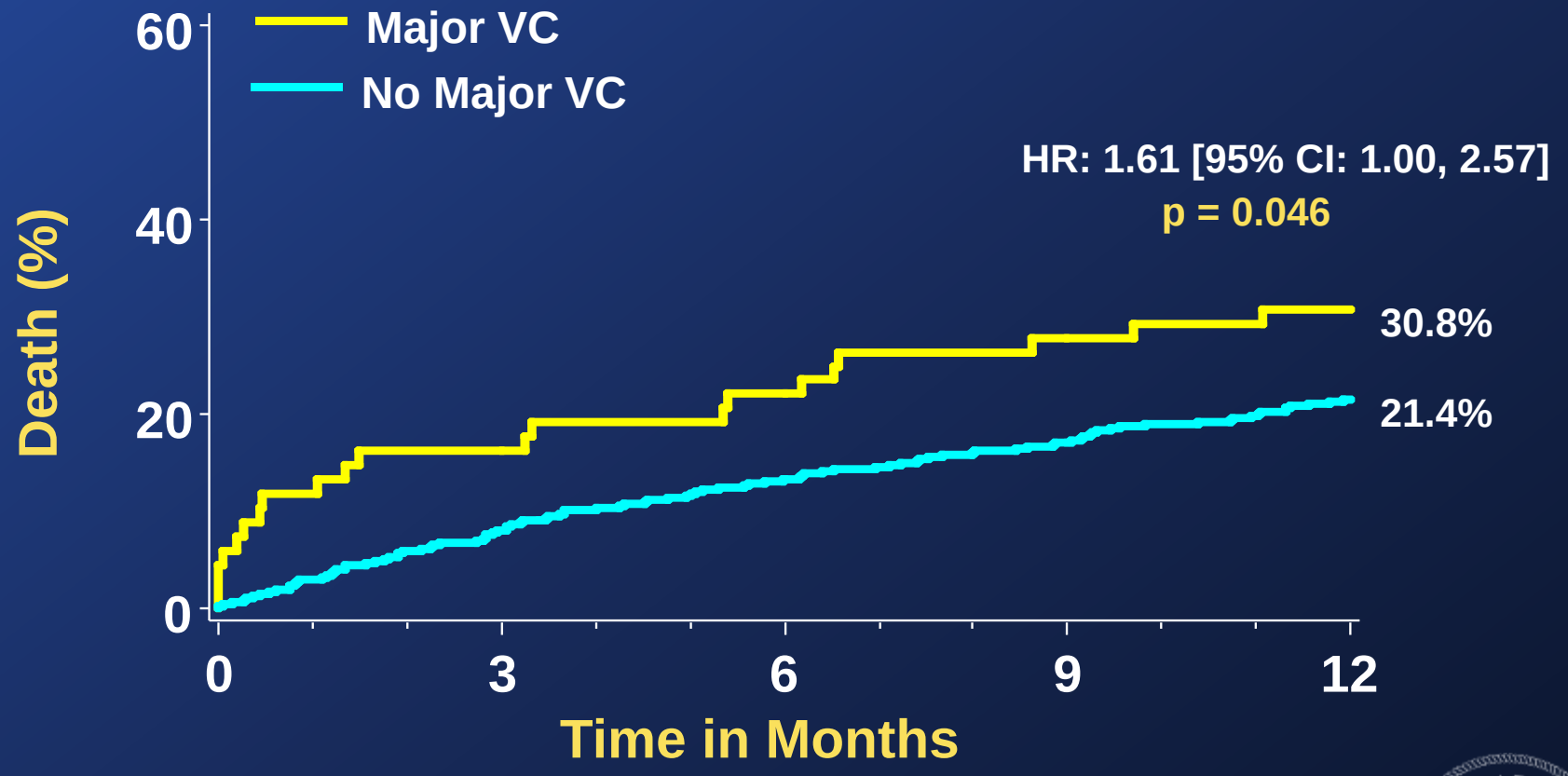
Predictors of 30 Day Major Vascular Complications

- Multivariable analysis* demonstrated only two statistical significant predictors:
  - Female sex (HR 2.34, CI 1.40-3.91, p=0.0001)
  - SAPIEN THV (HR 1.64, CI 1.01-2.67, p=0.043)

- Interaction testing between gender and device type was not statistically significant for 30 day major vascular complications.

**Baseline Covariates:* Age, gender, BMI, STS score, diabetes, smoker, peripheral arterial disease, renal insufficiency, and device type

1 Year Mortality for Major Vascular Complications



Number at risk:					
Major VC	69	57	53	49	47
No 30D Major VC	484	444	417	398	372

Update:
Bleeding Complications

THE PARTNER TRIAL

Bleeding in PARTNER 1A trial?
SAVR vs. TAVR

Bleeding Complications After Surgical Aortic Valve Replacement Compared With Transcatheter Aortic Valve Replacement

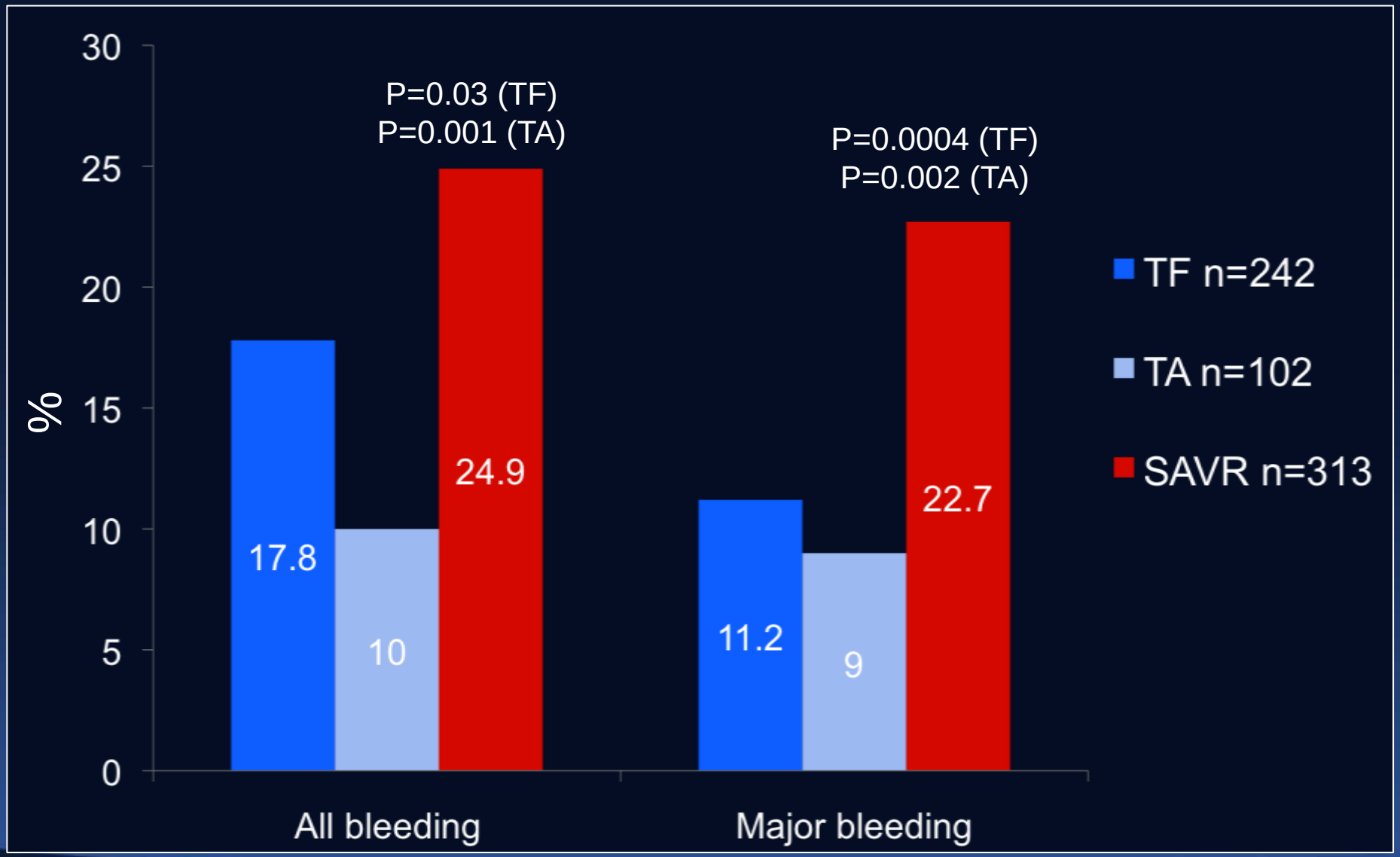
Insights From the PARTNER I Trial (Placement of Aortic Transcatheter Valve)

Philippe Généreux, MD,*†‡ David J. Cohen, MD, MSc,§ Mathew R. Williams, MD,* Michael Mack, MD,‖ Susheel K. Kodali, MD,*† Lars G. Svensson, MD, PhD,¶ Ajay J. Kirtane, MD, SM,*† Ke Xu, PhD,† Thomas C. McAndrew, MS,† Raj Makkar, MD,# Craig R. Smith, MD,* Martin B. Leon, MD*†

New York, New York; Montreal, Quebec, Canada; Kansas City, Missouri; Plano, Texas; Cleveland, Ohio; and Los Angeles, California

Généreux et al. J Am Coll Cardiol 2014;63:1100–9

PARTNER trial 1A-Bleeding at 30 days



P=ns between TF and TA group

Généreux et al. J Am Coll Cardiol 2014;63:1100–9

Transfusions: SAVR vs. TAVR

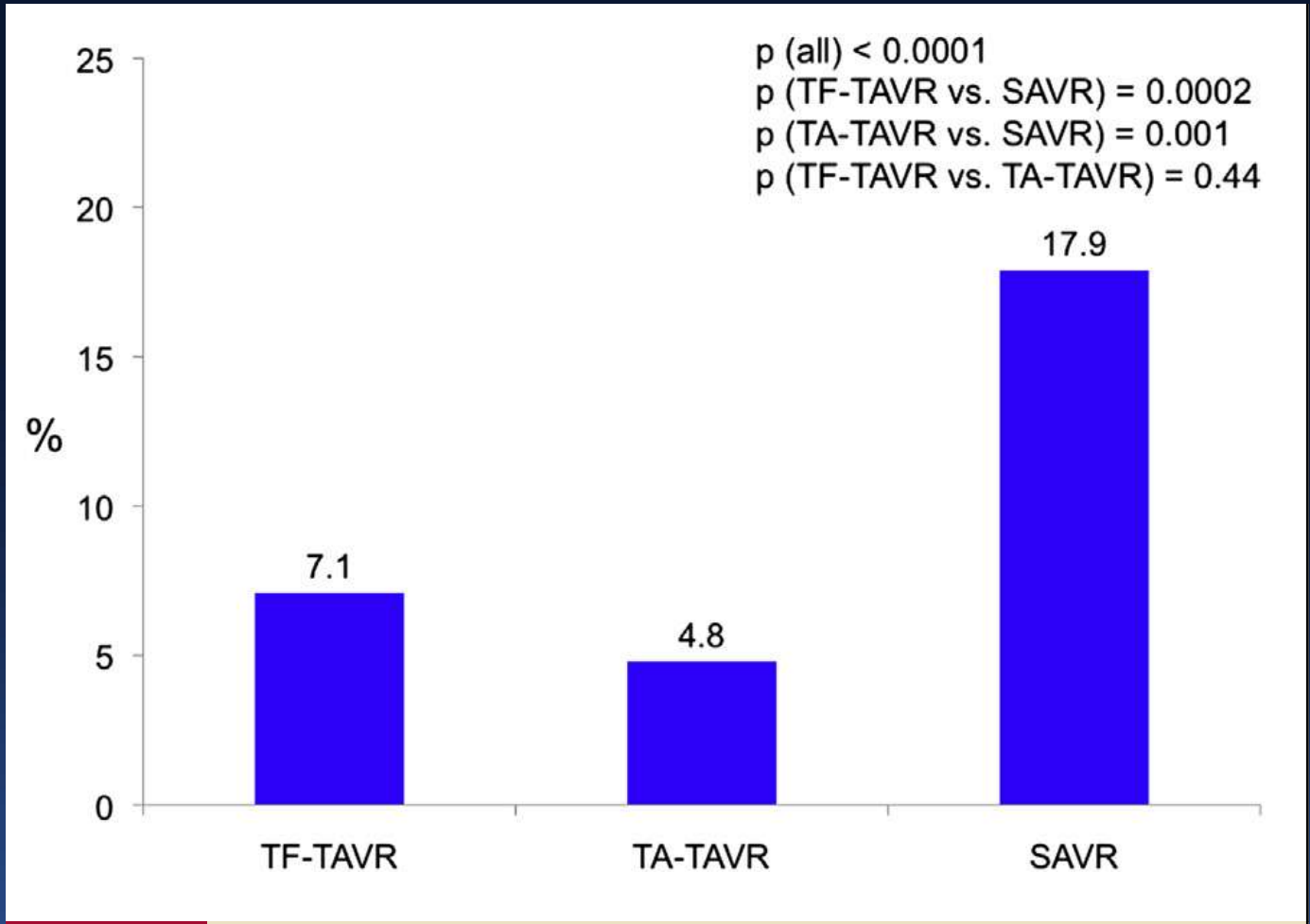


Figure 2 **Patients Receiving at Least 1 Transfusion Within 30 Days Per Treatment Strategy**

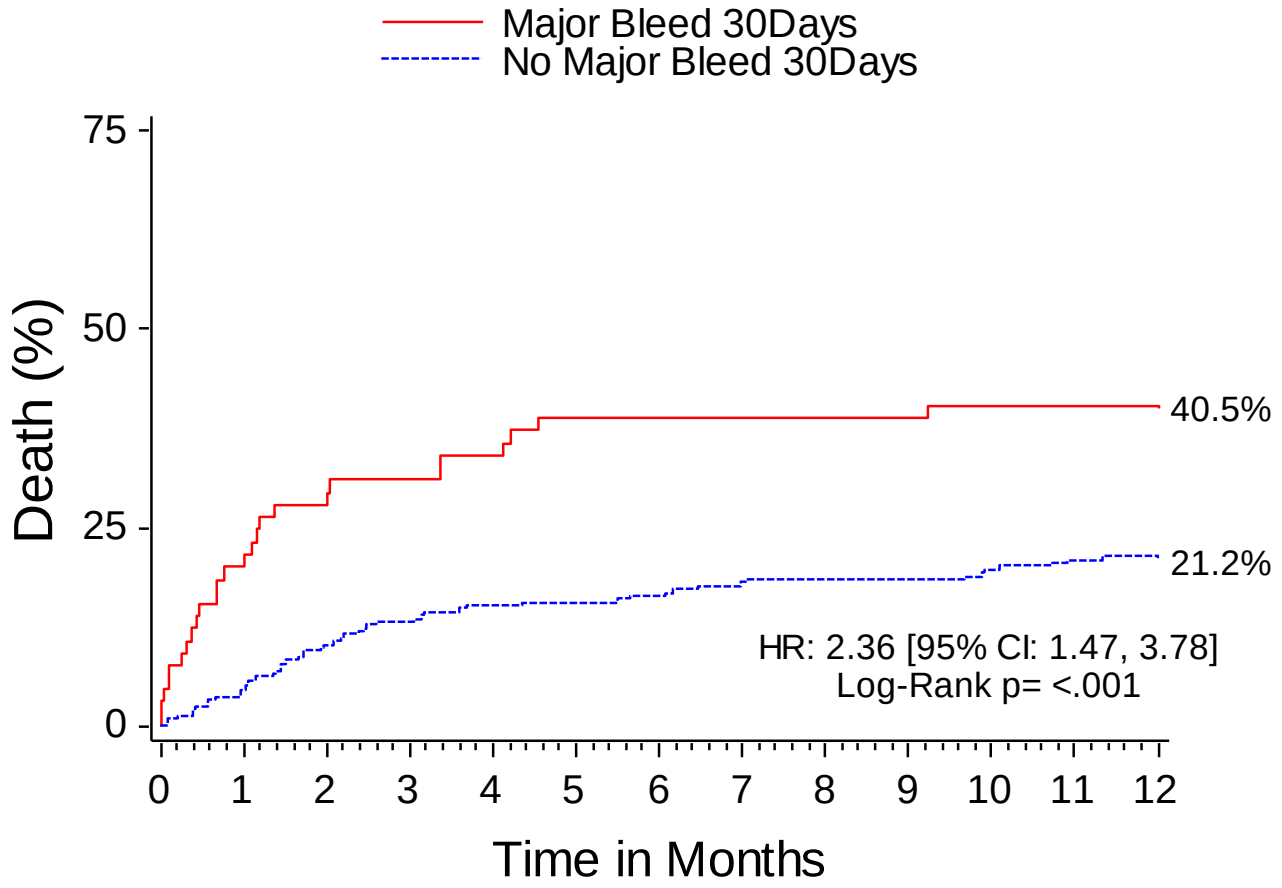
Généreux et al. J Am Coll Cardiol 2014;63:1100–9

Transfusions: SAVR vs. TAVR

- *Among pts receiving transfusions, the % of pts receiving ≥4 transfusions* was
  - *69.6% in the SAVR group* (median: 7.0 [1st, 3rd quartiles: 3.0, 9.0]),
  - *66.7% in the TA-TAVR group* (median: 4.0 [1st, 3rd quartiles: 1.0, 7.0]),
  - *40.5% in the TF-TAVR group* (median: 3.5 [1st, 3rd quartiles: 2.0, 5.0];
  - p for trend = 0.0002).

Généreux et al. J Am Coll Cardiol 2014;63:1100–9

AT - Cohort A - Surgery

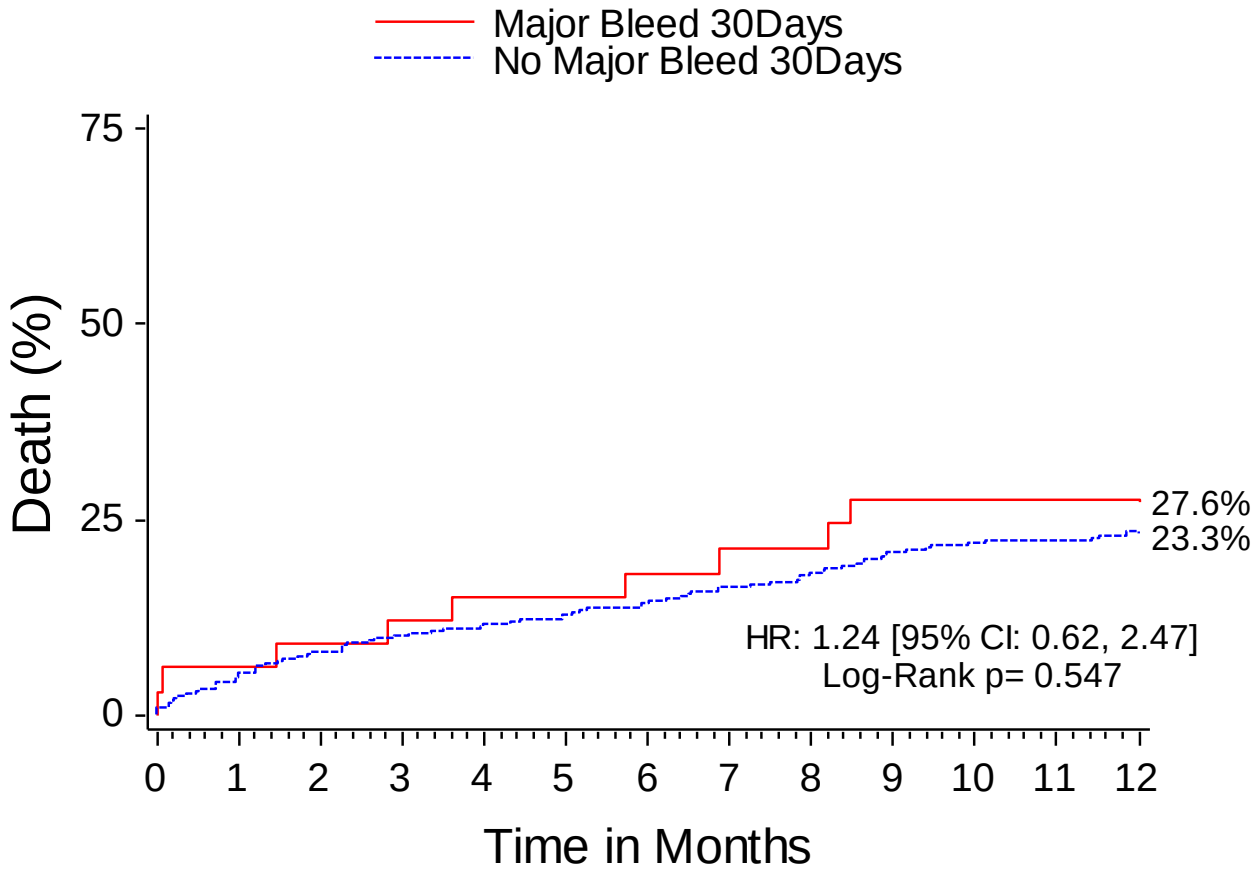


Number at risk

Major Bleed	50	42	38	37
No Major Bleed	234	208	199	192

Généreux et al. J Am Coll Cardiol 2014;63:1100–9

AT - Cohort A - TF & TA

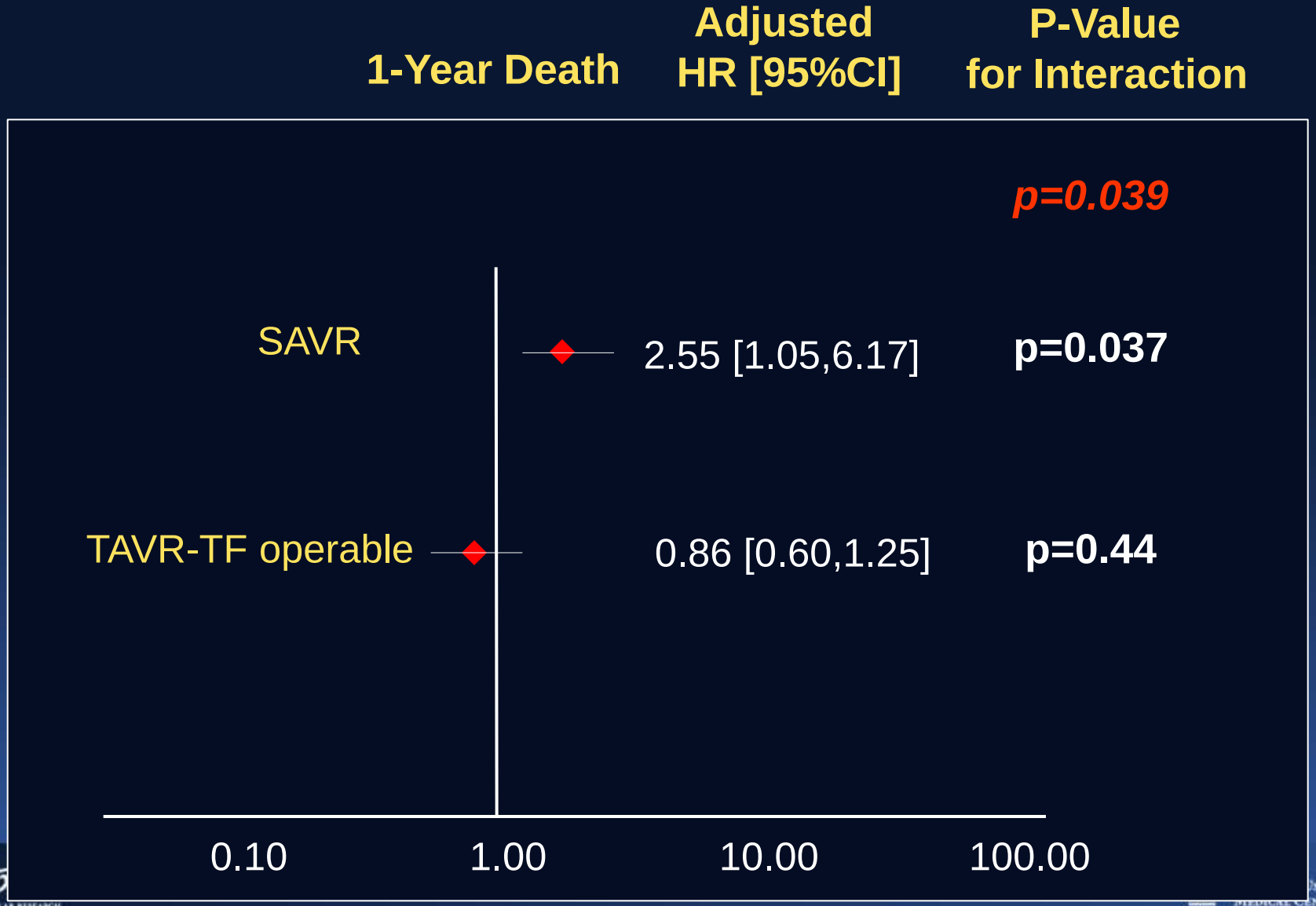


Number at risk

Major Bleed	31	28	25	23
No Major Bleed	294	275	254	236

Généreux et al. J Am Coll Cardiol 2014;63:1100–9

Interaction Major bleeding-SAVR



Généreux et al. JACC, 2014, 63; 11

PARTNER trial A: SAVR and TAVR

Independent predictors of 1-Year Mortality (n=657)

Predictors	Adjusted HR [95% CI]	p value
Major bleeding at 30 days	***2.36 [1.68,3.31]***	***<0.0001***
Stroke	2.14 [1.21,3.80]	0.009
PVL (moderate to severe)	1.35 [0.79,2.29]	0.28
STS risk score	1.07 [1.04,1.11]	<0.0001
Body mass index	0.96 [0.94,0.99]	0.006
Oxygen dependent COPD	1.43 [0.94,2.18]	0.09
Baseline renal disease	1.31 [0.95,1.80]	0.10

Candidate variables for the model were age, gender (female), body mass index, STS, prior coronary artery bypass graft, permanent pacemaker, renal disease, malignant tumors, liver disease, chronic obstructive pulmonary disease oxygen dependent, left ventricular ejection fraction, baseline hemoglobin, baseline platelet; Major bleeding, Stroke at 30 days, and PVL (moderate to severe) ≤7 day or at discharge if earlier (as time dependent co-variable).
COPD=chronic obstructive pulmonary disease; STS=society of society of thoracic surgeons

Généreux et al. JACC, 2014, 63; 11

Update: Arrhythmias

THE PARTNER TRIAL

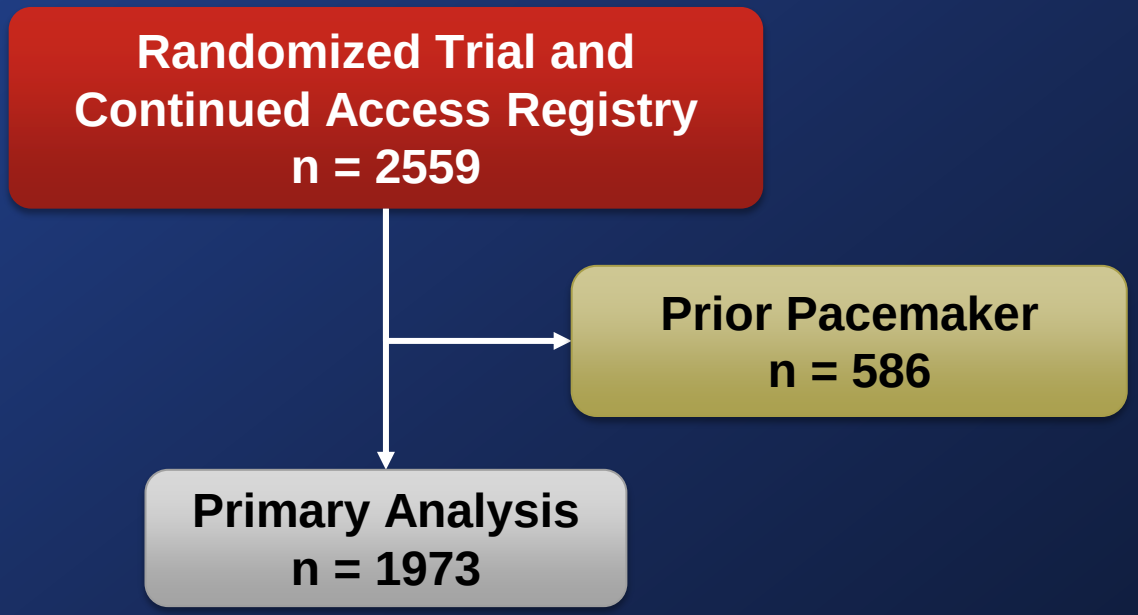
Predictors and Clinical Consequences of Permanent Pacemaker Implantation after TAVR: The PARTNER Experience

Tamim Nazif, MD

on Behalf of The PARTNER Trial Investigators
and The PARTNER Publications Office

TCT 2013 | San Francisco | October 29, 2013

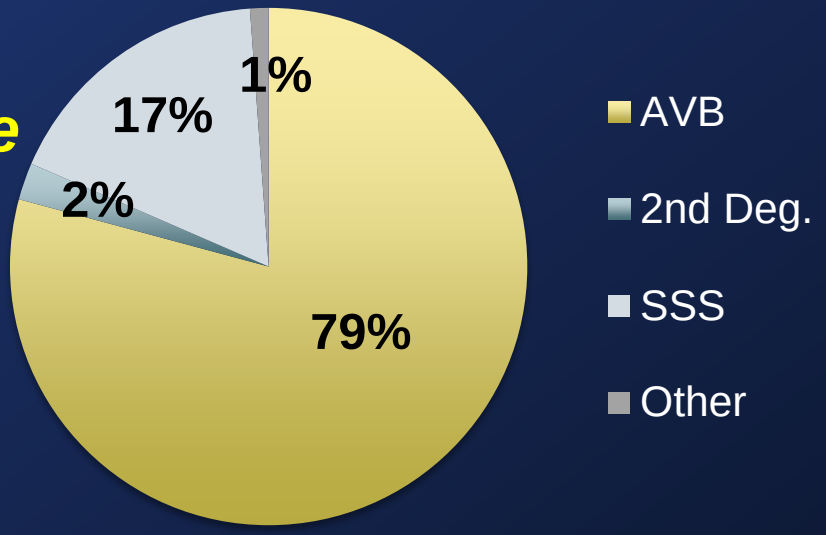
Study Population



Tamim Nazif TCT 2013

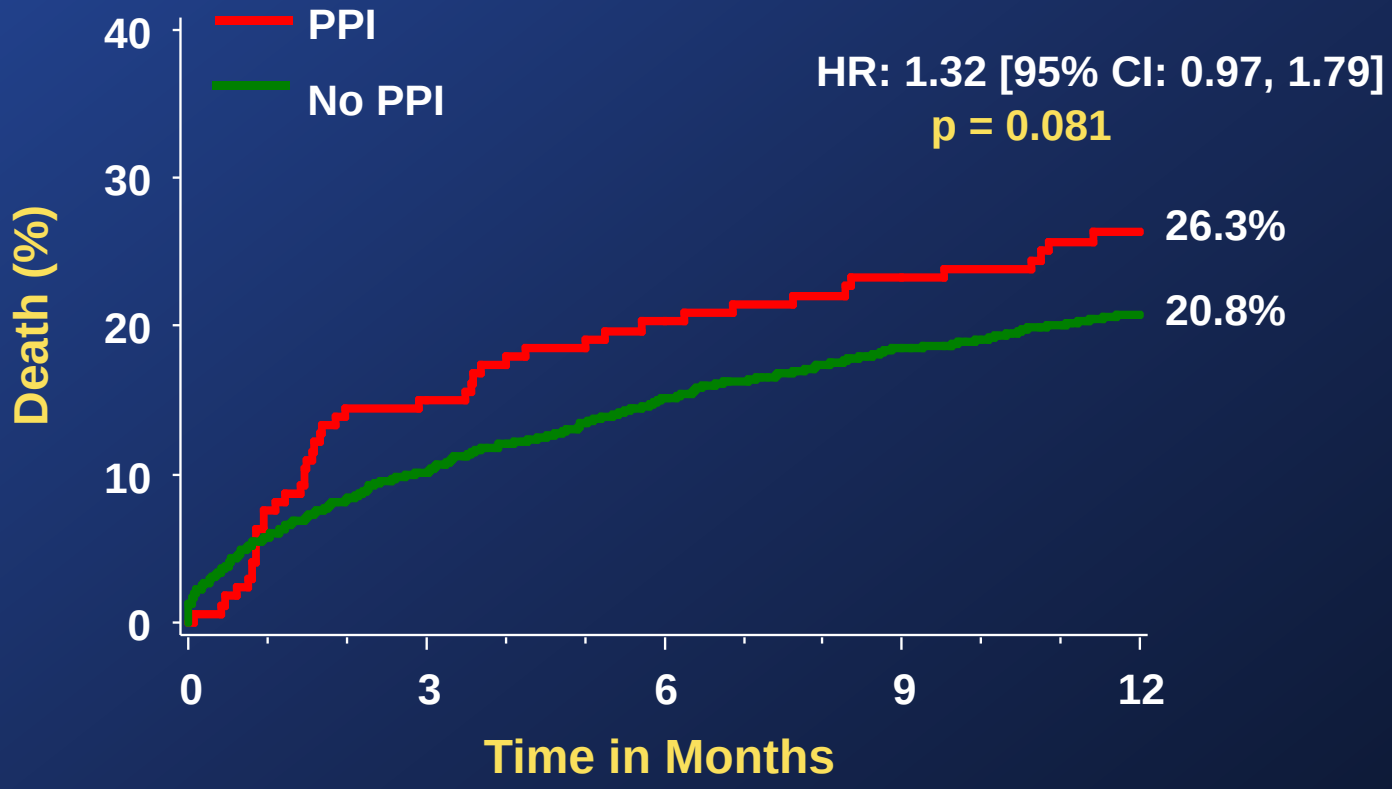
Incidence of PPI after TAVR

- ***Incidence of PPI within 30 days of TAVR:***
  - ***8.8% (173/1973)***
- ***Indication for PPI complete or high-degree AV block*** in the significant majority.



Tamim Nazif TCT 2013

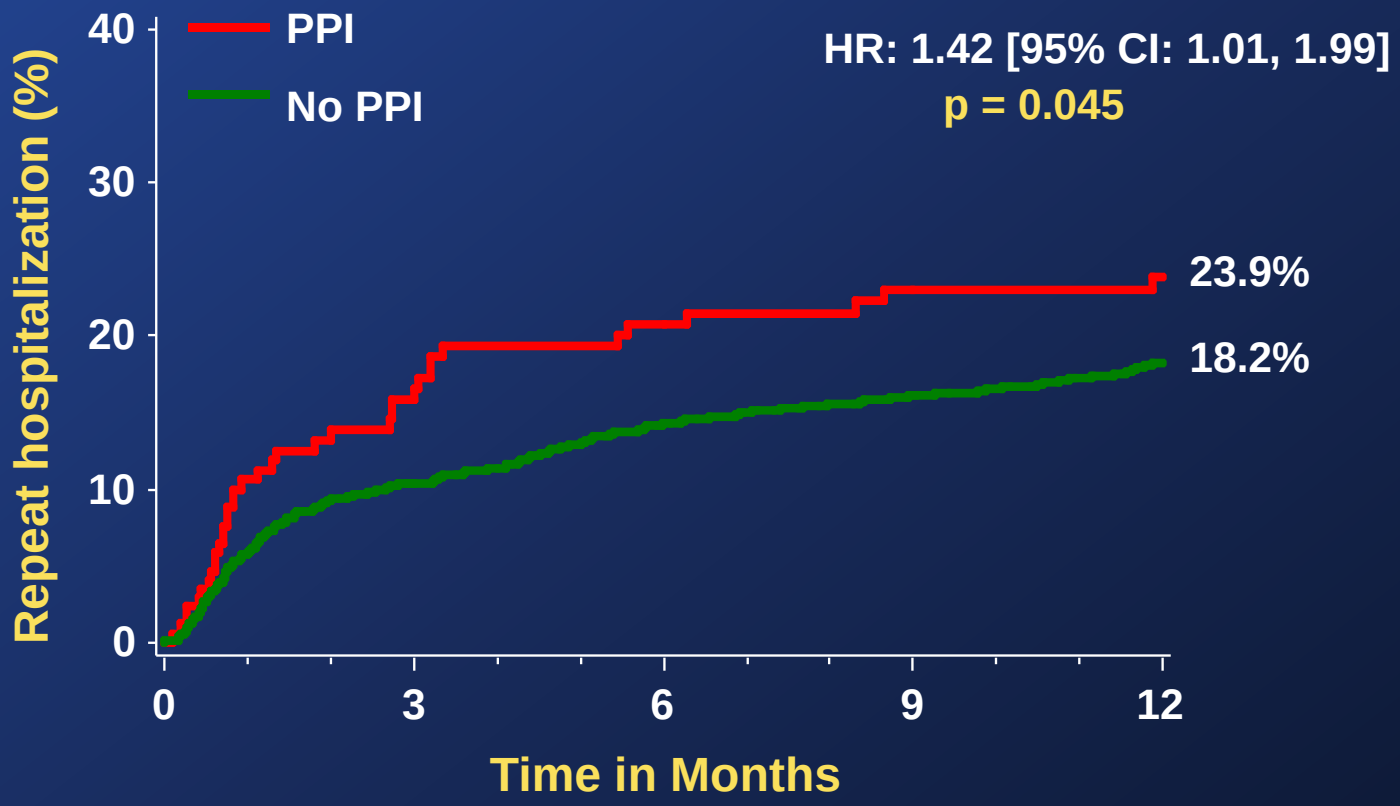
All-Cause Mortality



Number at risk:					
PPI	173	147	134	129	103
No PPI	1800	1606	1502	1429	1274

Tamim Nazif TCT 2013

Repeat Hospitalization

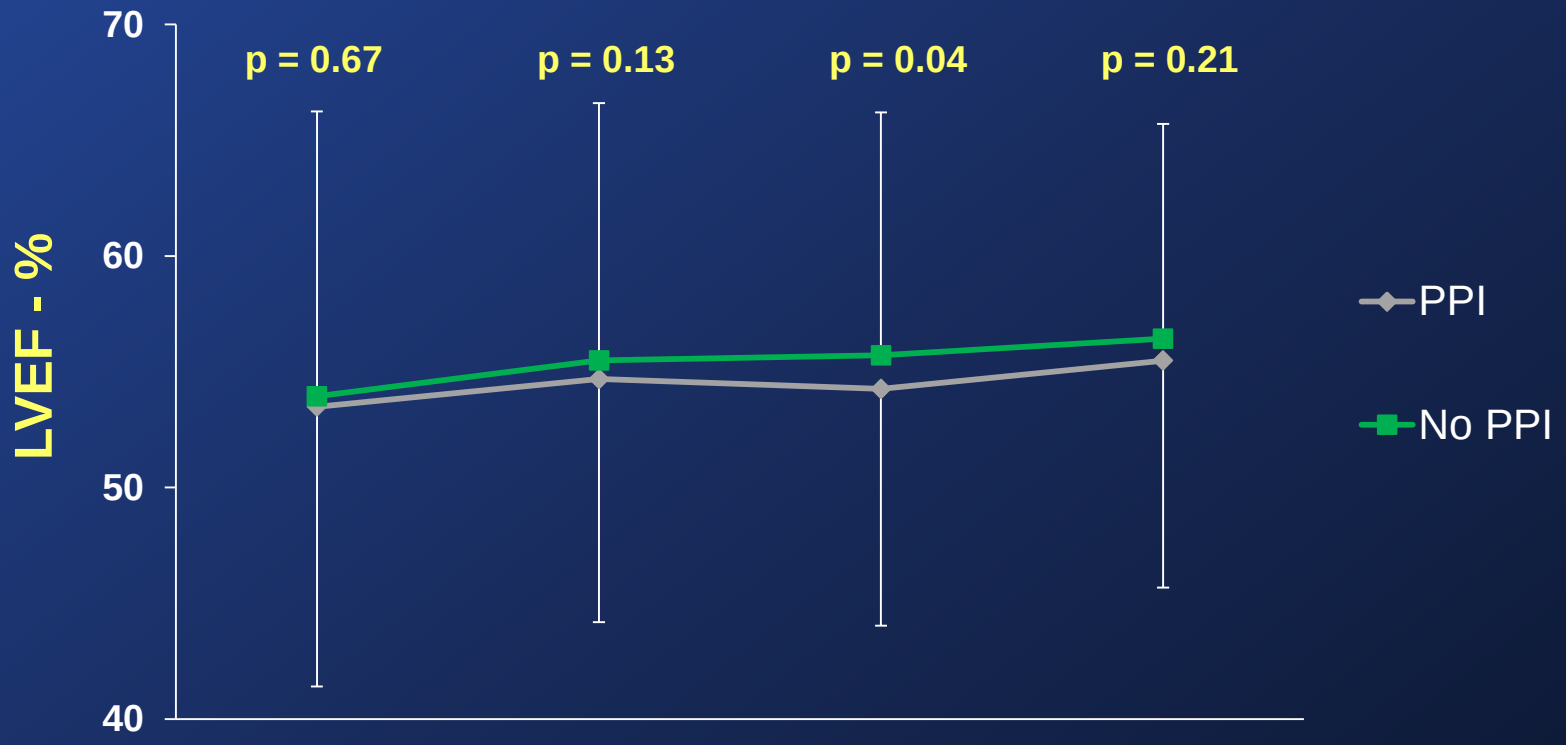


Number at risk:

PPI	173	123	108	103	82
No PPI	1800	1450	1317	1243	1082

Tamim Nazif TCT 2013

Impact of PPI on Evolution of LVEF



Numbers at Risk:	Baseline	Discharge	30-days	Late
PPI	172	170	146	125
No PPI	1764	1705	1577	1384

Tamim Nazif TCT 2013

Clinical Implications of New Left Bundle Branch Block:

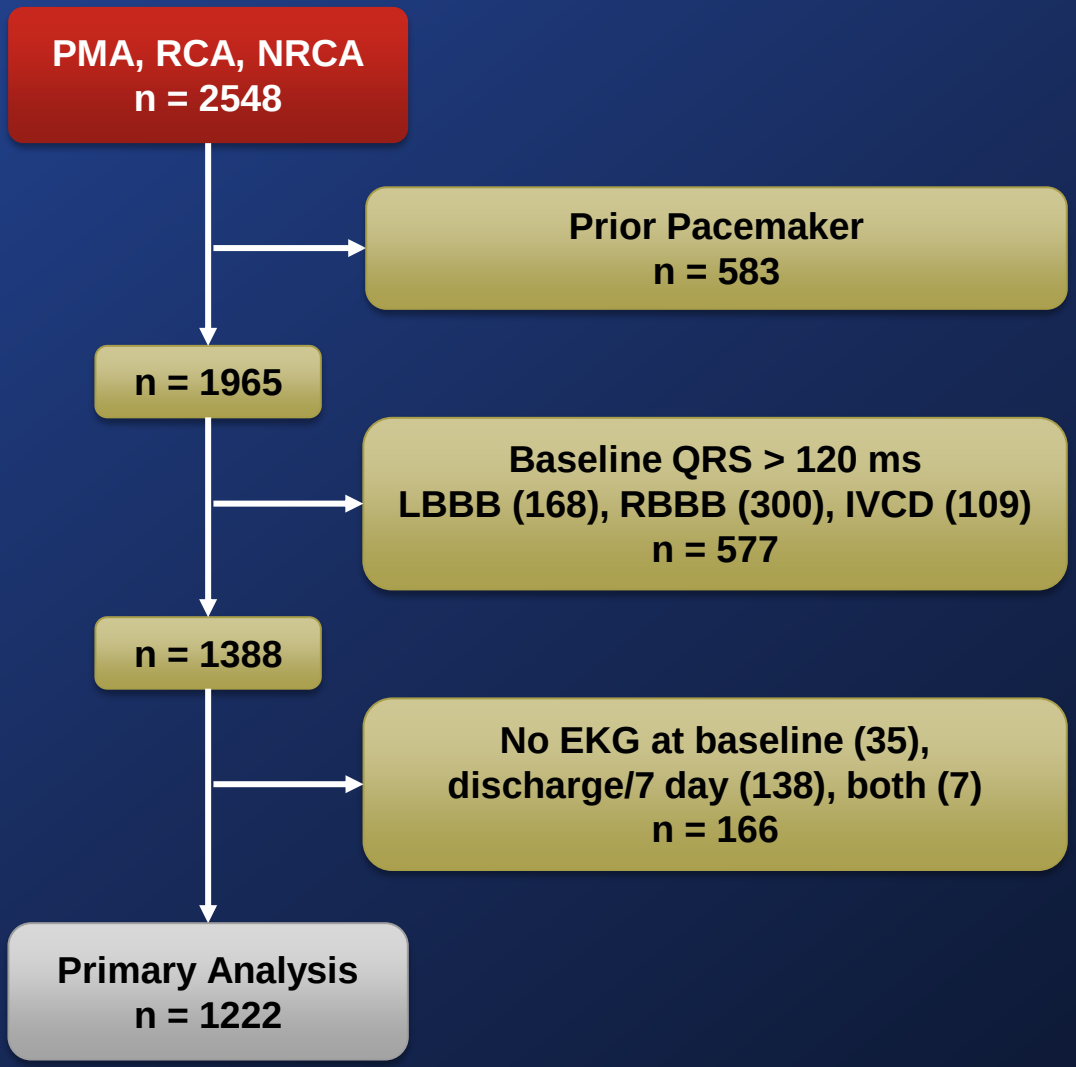
Sub-Analysis from The PARTNER Experience

Tamim Nazif, MD

on behalf of The PARTNER Trial Investigators
and The PARTNER Publications Office

ACC 2013 | San Francisco | March 11, 2013

Study Population



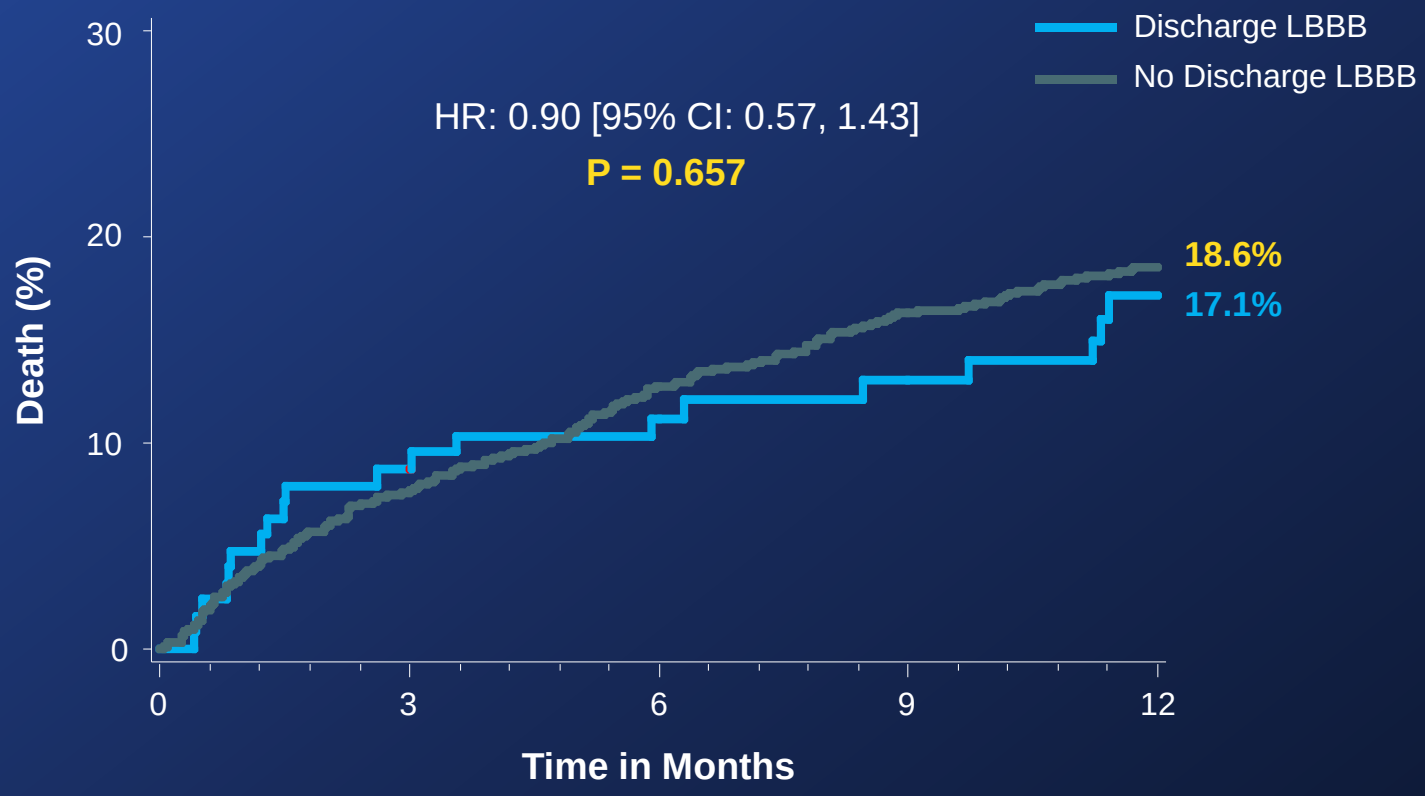
Tamim Nazif ACC 2013

Incidence and Persistence of New-onset LBBB

- Incidence of ***new LBBB at discharge / 7-days***
  - ***10.4% (127/1222)***

- ***Persistence of LBBB***
  - 57.7% (64/111) at 30-days (6.0% of total)
  - ***58.5% (55/94) at 6 months to 1 year*** (5.9% of total)

All-Cause Mortality

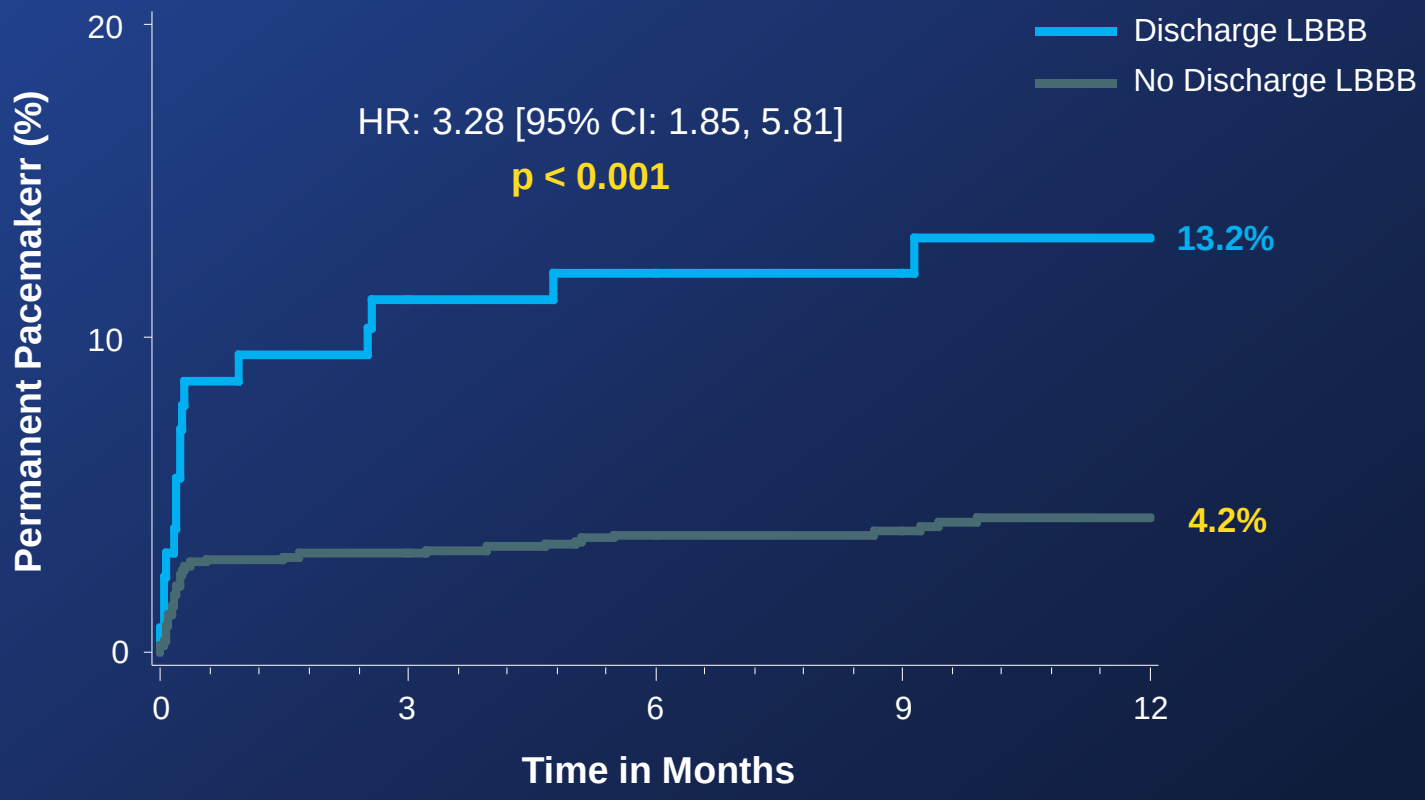


Numbers at Risk

Discharge LBBB	127	114	102	94	71
No LBBB	1095	998	891	798	617

Tamim Nazif ACC 2013

Permanent Pacemaker

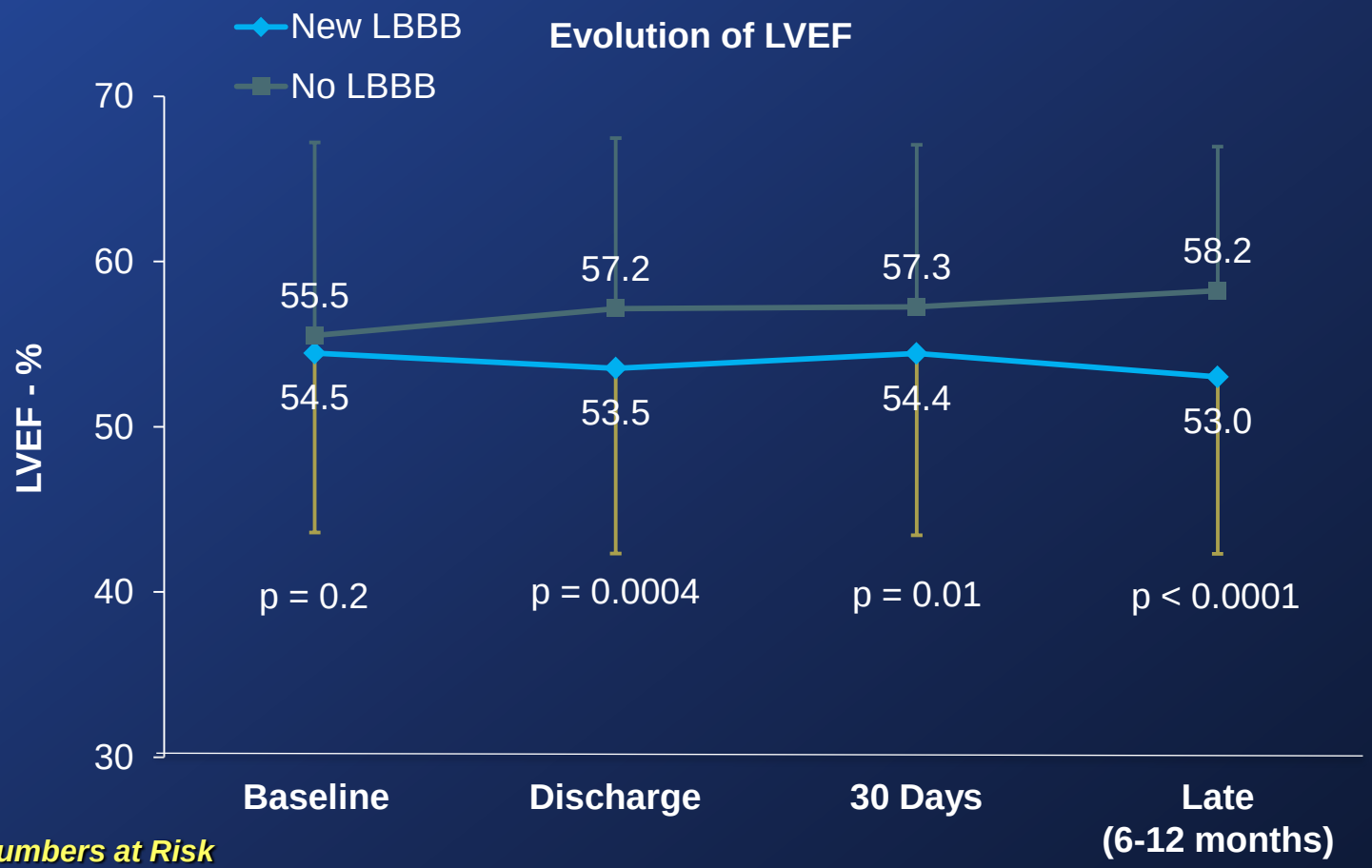


Numbers at Risk

Discharge LBBB	127	102	88	80	62
No LBBB	1095	970	858	766	595

Tamim Nazif ACC 2013

Impact of New-Onset LBBB on Evolution of LVEF



Numbers at Risk

New LBBB	121	119	113	82
No LBBB	1039	1034	957	682

Tamim Nazif ACC 2013

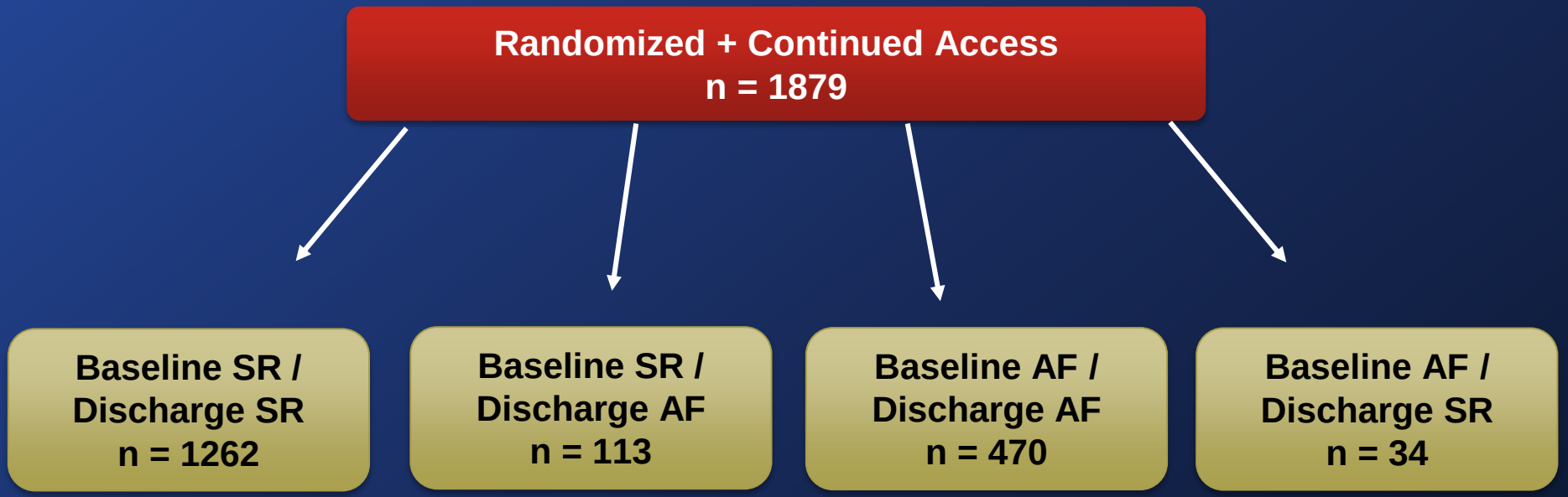
Atrial Fibrillation is Associated with Increased Mortality in Patients Undergoing TAVR: Insights from The PARTNER Trial

Angelo Biviano, MD, MPH
New York-Presbyterian Hospital
Columbia University Medical Center
on behalf of The PARTNER Trial Investigators
and The PARTNER Publications Office:

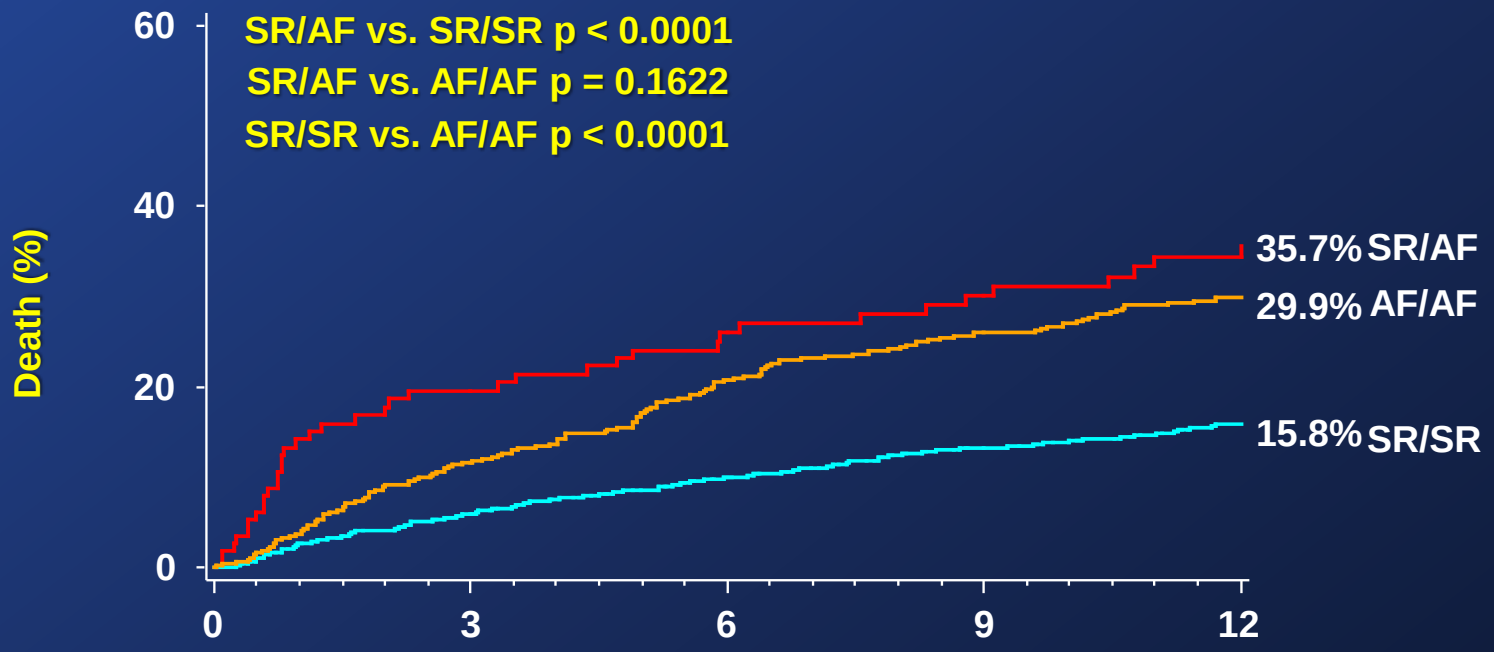
Angelo B. Biviano, Jose Dizon, Tamim Nazif, Samir Kapadia, Vasilis Babaliaros, Ke Xu, Josep Rodes-Cabau, Wilson Y. Szeto, William F. Fearon, Danny Dvir, Todd Dewey, Mathew Williams, Michael Mack, John G. Webb, D. Craig Miller, Craig Smith, Martin B. Leon, Susheel Kodali

ACC 2014 | Washington, DC | March 29, 2014

Study Population



Mortality



Number at risk					
Group A	113	89	76	67	51
Group B	1262	1174	1064	962	747
Group C	470	412	337	290	212

Multivariable Analysis: Predictors of 1-Year Outcomes

THE PARTNER TRIAL

DEATH	p-value	Hazard Ratio (95% CI)
Bleeding event that requires transfusion	0.0018	1.74 [1.23, 2.46]
Male	0.0093	1.33 [1.07, 1.64]
Renal Failure (Dialysis required)	<0.0001	3.95 [2.80, 5.58]
STS Risk Score	0.0089	1.03 [1.01, 1.05]
Stroke	<0.0001	2.18 [1.57, 3.02]
Baseline SR / Discharge AF (vs. Baseline SR / Discharge SR)	<0.0001	2.27 [1.59, 3.23]
Baseline AF / Discharge AF (vs. Baseline SR / Discharge SR)	<0.0001	1.81 [1.44, 2.27]

CARDIOVASCULAR DEATH	p-value	Hazard Ratio (95%CI)
LVEF	0.0014	0.98 [0.97, 0.99]
Bleeding event that requires transfusion	0.003	1.96 [1.26, 3.06]
Renal Failure (Dialysis required)	<0.0001	3.87 [2.41, 6.24]
Stroke	<0.0001	2.89 [1.94, 4.31]
Age	0.0626	1.02 [1.00, 1.04]
Baseline SR / Discharge AF (vs. Baseline SR / Discharge SR)	0.0016	2.19 [1.35, 3.57]
Baseline AF / Discharge AF (vs. Baseline SR / Discharge SR)	<0.0001	2.20 [1.64, 2.96]

REHOSPITALIZATION	p-value	Hazard Ratio (95%CI)
Bradyarrhythmic Event	0.0157	1.57 [1.09, 2.25]
Renal Failure (Dialysis required)	<0.0001	3.32 [2.14, 5.15]
STS Risk Score	0.0608	1.02 [1.00, 1.05]
Baseline SR / Discharge AF (vs. Baseline SR / Discharge SR)	0.0297	1.62 [1.05, 2.51]
Baseline AF / Discharge AF (vs. Baseline SR / Discharge SR)	<0.0001	1.73 [1.36, 2.20]

* TAVR type not independent predictor of outcomes

Transcatheter versus Surgical Aortic Valve Replacement in Patients with Diabetes and Severe Aortic Stenosis at High Risk for Surgery

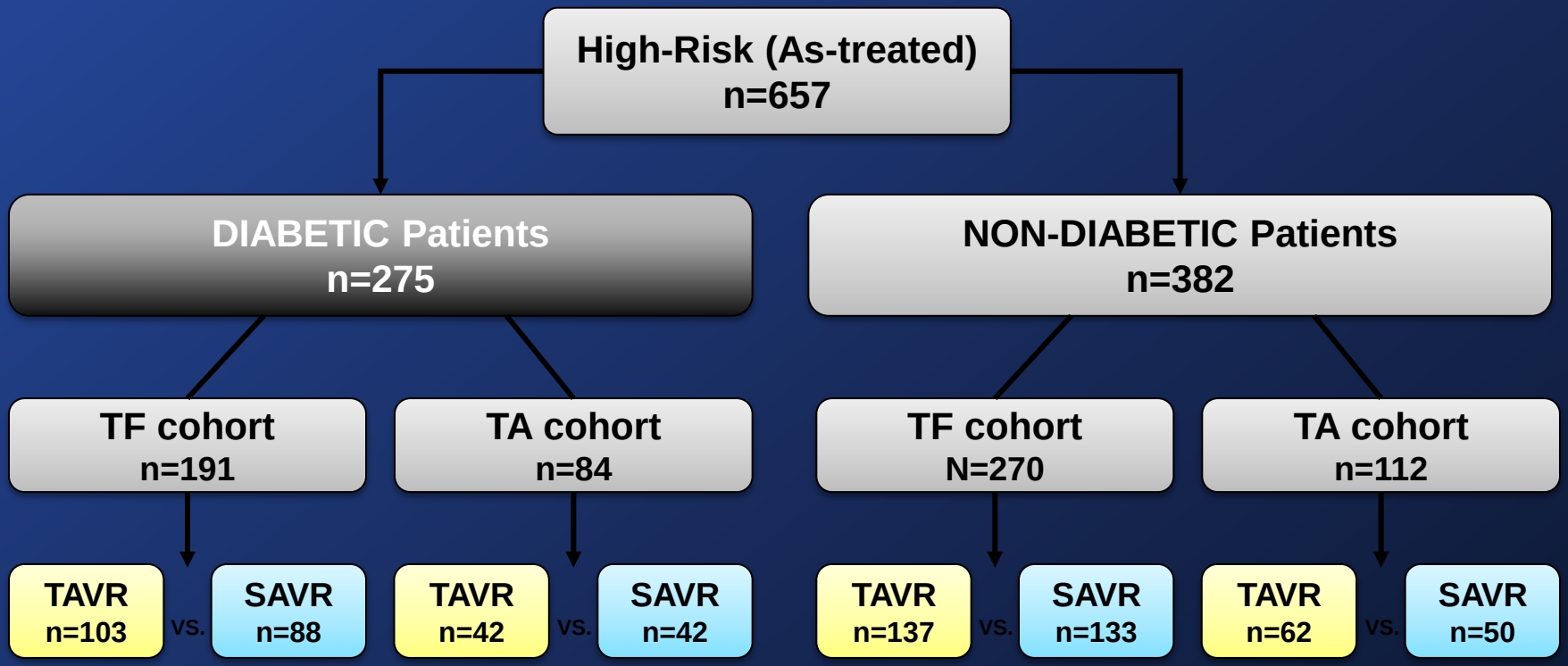
PARTNER I, High-risk Cohort

Brian R. Lindman, MD

on behalf of The PARTNER Trial Investigators

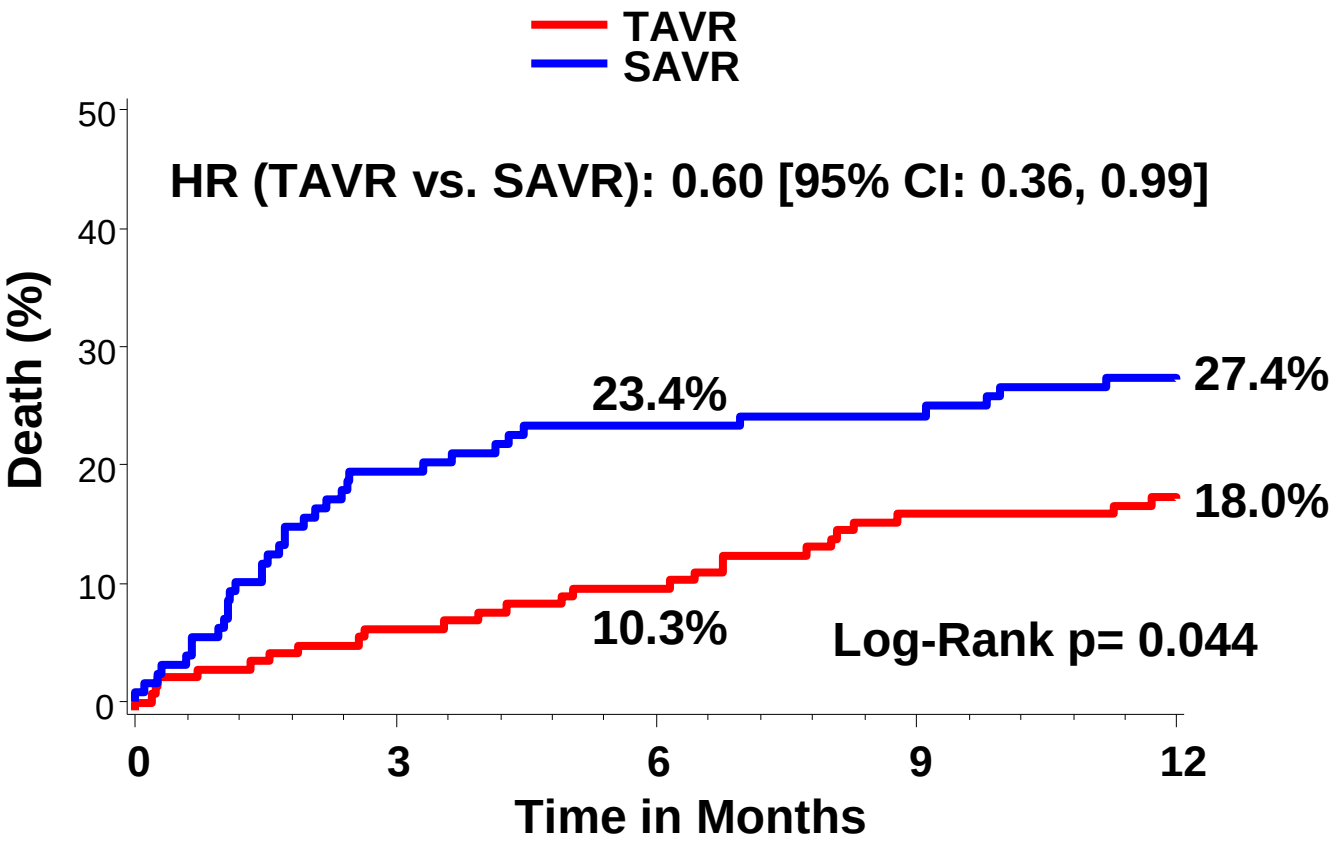
ESC 2013 | Amsterdam | September 3, 2013

Study Flow by Diabetes Status



All-Cause Mortality

Diabetics – All (as-treated cohort, n=275 patients)

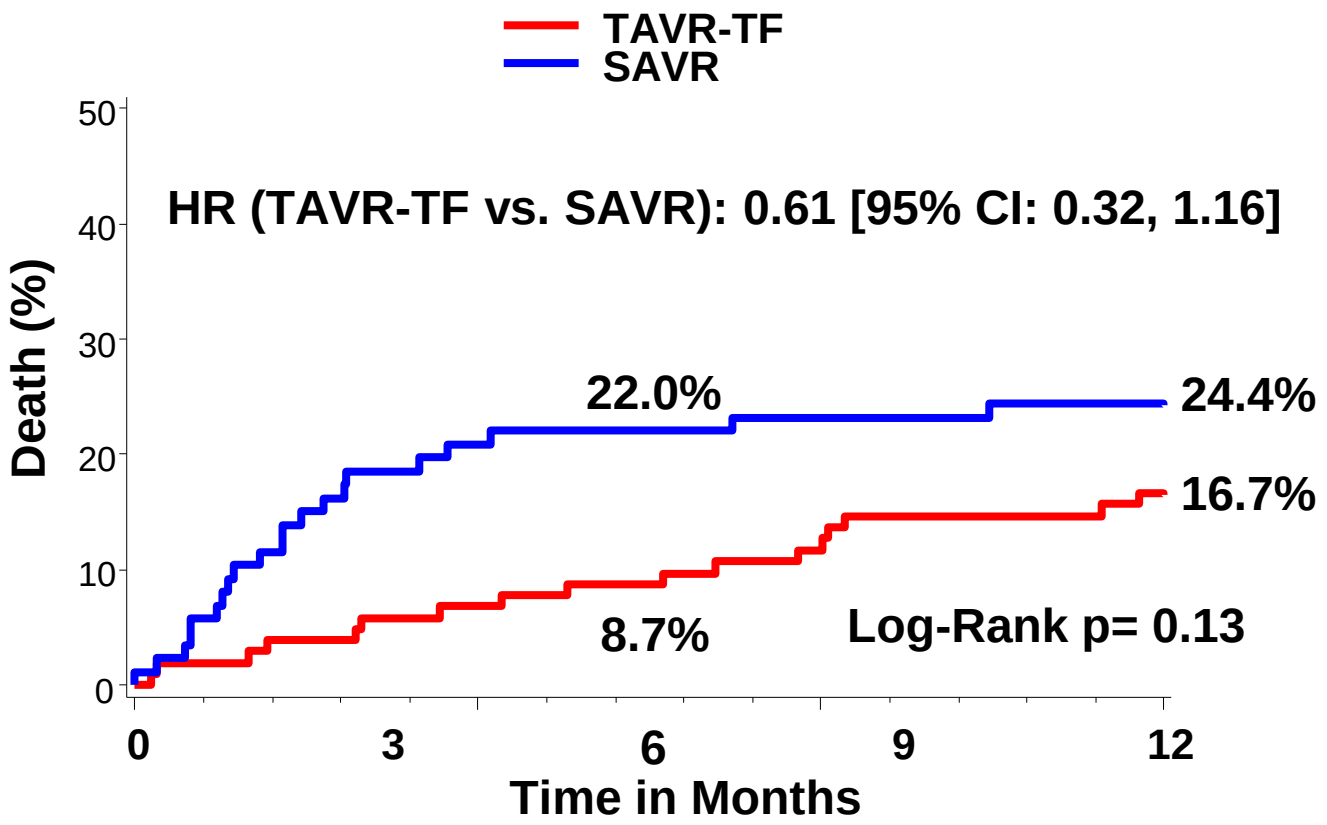


Number at risk

TAVR	145	135	129	119	117
SAVR	130	103	97	95	91

All-Cause Mortality: Diabetics

TF cohort (n=191 patients)

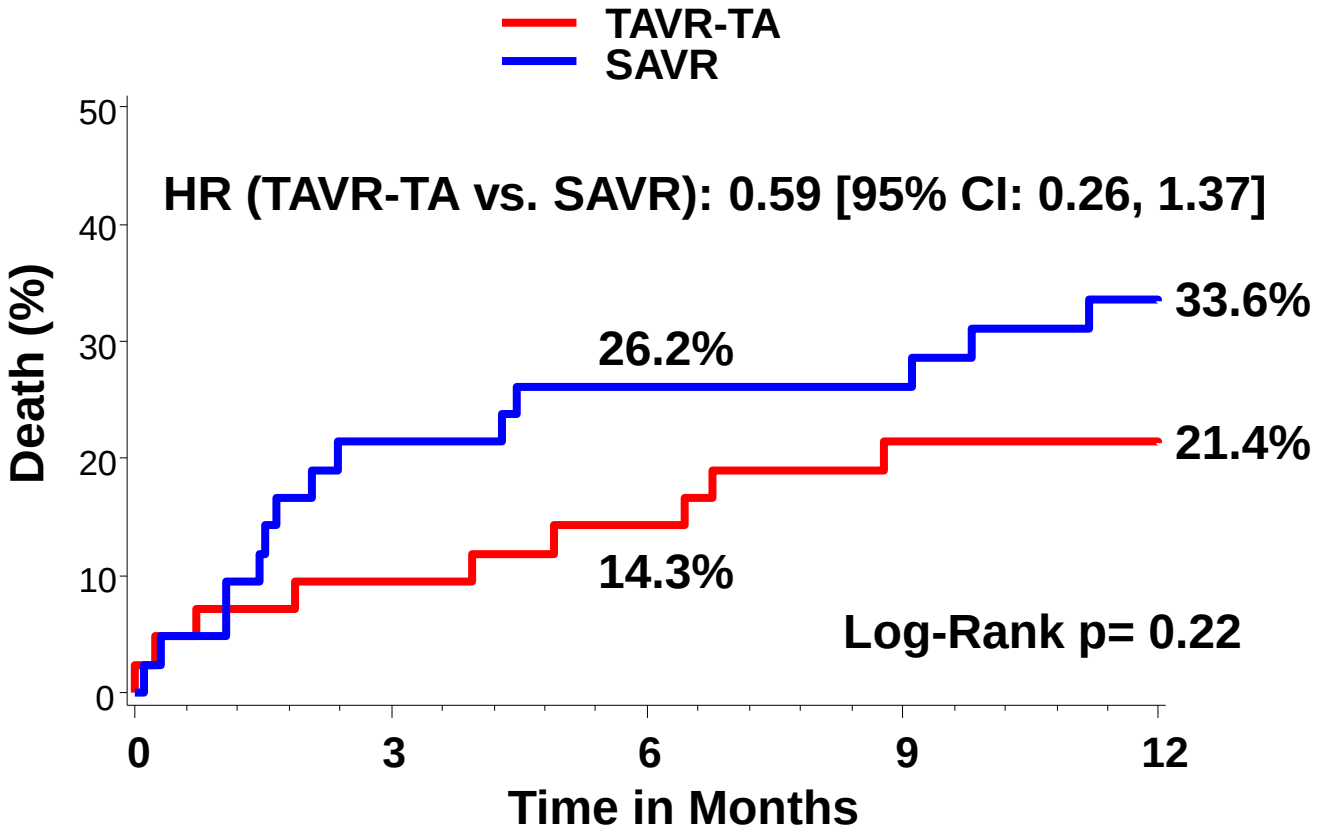


Number at risk

TAVR-TF	103	97	93	86	84
SAVR	88	70	67	65	64

All-Cause Mortality: Diabetics

TA cohort (n=84 patients)



Number at risk

TAVR-TA	42	38	36	33	33
SAVR	42	33	30	30	27

Other Clinical Outcomes at 1 Year
Diabetics – All

Clinical Outcome	TAVR % (no.)	SAVR % (no.)	HR (95% CI)	p-value
Stroke (any)	3.5% (5)	3.5% (4)	1.11 [0.30,4.12]	0.88
Renal Failure ***(dialysis required)***	***4.2% (6)***	***10.6% (13)***	***0.39 [0.15,1.03]***	***0.05***
Dialysis lasting >30 days	0.0% (0)	6.1% (7)	---	0.003
Bleeding ***(major)***	***15.1% (21)***	***26.9% (34)***	***0.52 [0.30,0.89]***	***0.01***
Vascular complications (major)	11.7% (17)	2.3% (3)	5.10 [1.50,17.4]	0.003

Differences in Outcomes in Females Undergoing Transcatheter Aortic Valve Replacement Compared to Surgical Aortic Valve Replacement from the PARTNER Randomized Trial

Mathew R. Williams, MD
on behalf of The PARTNER Trial Investigators

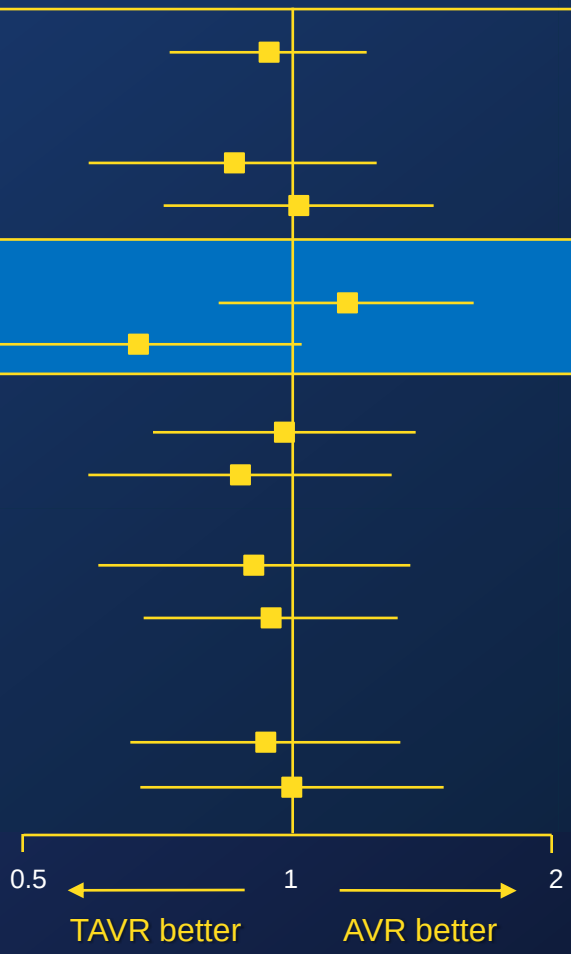
AATS 2013 | Minneapolis | May 2013

THE PARTNER TRIAL

Subgroup Analyses (High-Risk Pts)
All-Cause Mortality at 1 Year

THE PARTNER TRIAL

Subgroup	TAVR (%) n = 348	AVR (%) n = 351	RR (95% CI)	p value for interaction
Overall	24.1	25.4	0.95(0.73-1.23)	
Age				
<85	21.6	24.9	0.87(0.60-1.27)	0.52
>85	27.0	26.1	1.03(0.72-1.47)	
Sex				
Male	28.4	24.2	1.17(0.84-1.63)	0.045
Female	18.4	27.2	1.17(0.84-1.63)	
BMI				
<26	27.3	27.4	0.68(0.44-1.04)	0.66
>26	21.0	23.8	0.99(0.71-1.40)	
STS score				
<11	19.9	21.7	0.88(0.59-1.31)	0.87
>11	28.1	29.3	0.92(0.61-1.38)	
LV ejection fraction				
<55	26.2	27.7	0.96(0.69-1.34)	0.80
>55	22.4	22.1	1.01(0.68-1.50)	

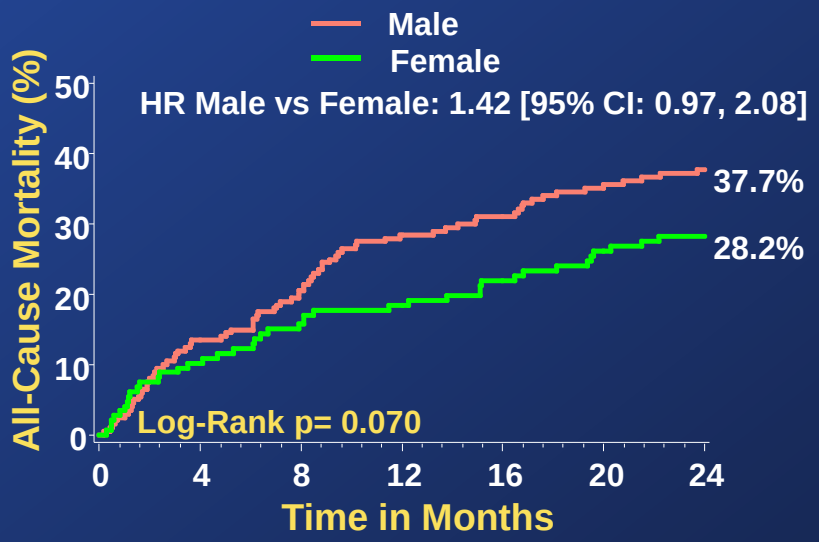


Smith C et al, NEJM 2011

2 year All-Cause Mortality ITT Population

THE PARTNER TRIAL

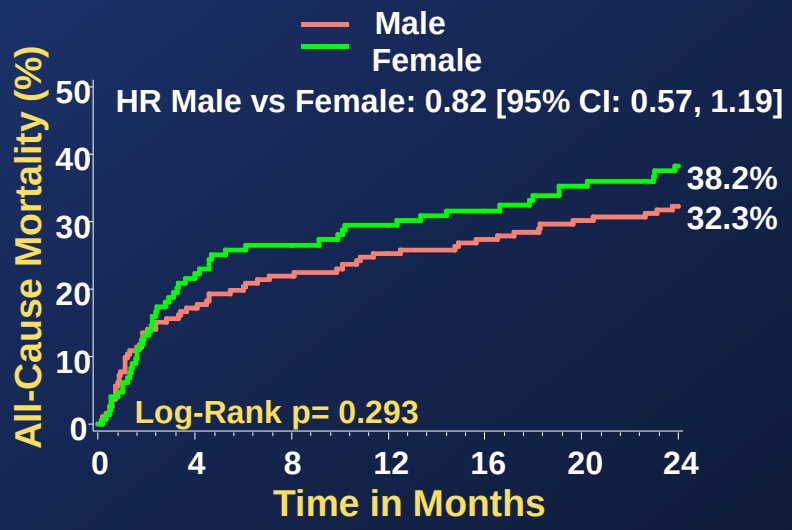
TAVR



Number at risk

Male	201	173	159	143	135	126	117
Female	147	132	122	118	112	106	101

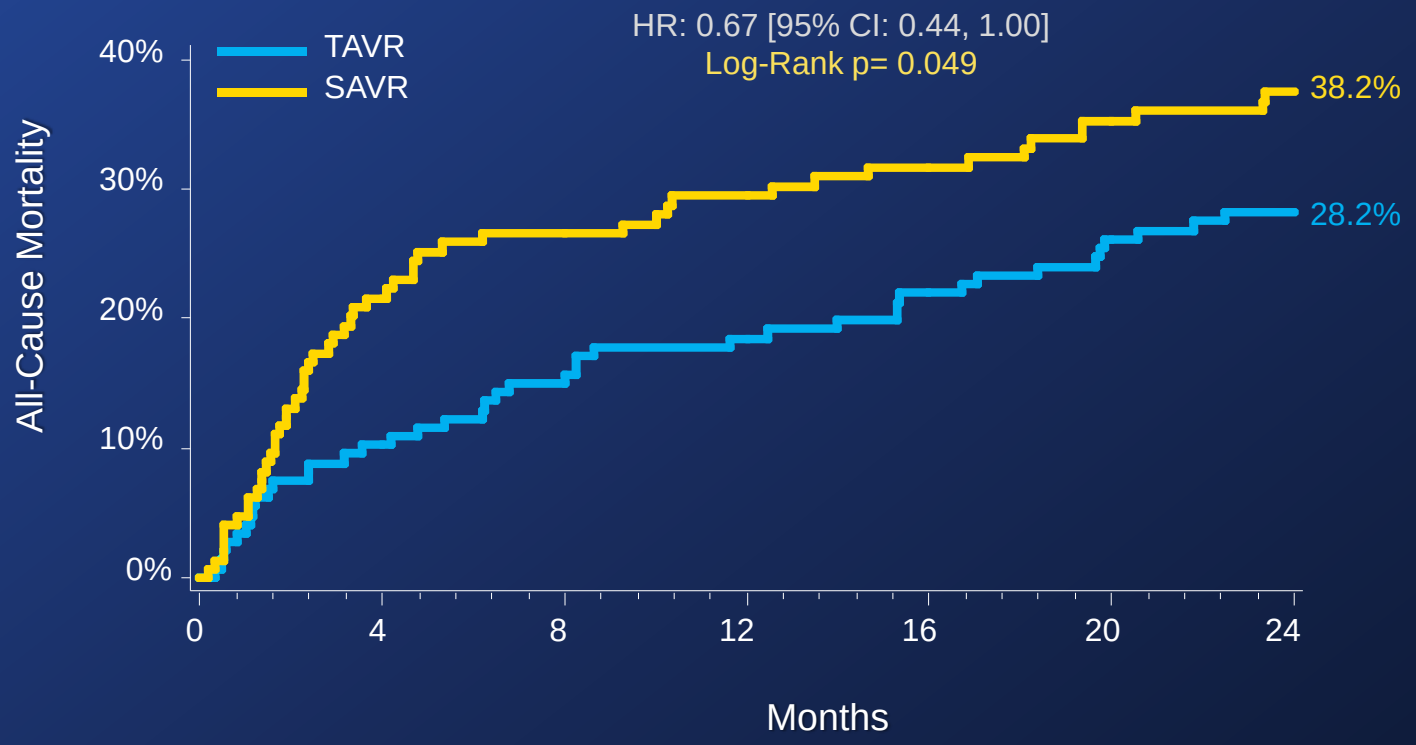
SAVR



Number at risk

Male	198	156	145	139	133	128	119
Female	153	110	101	97	94	89	80

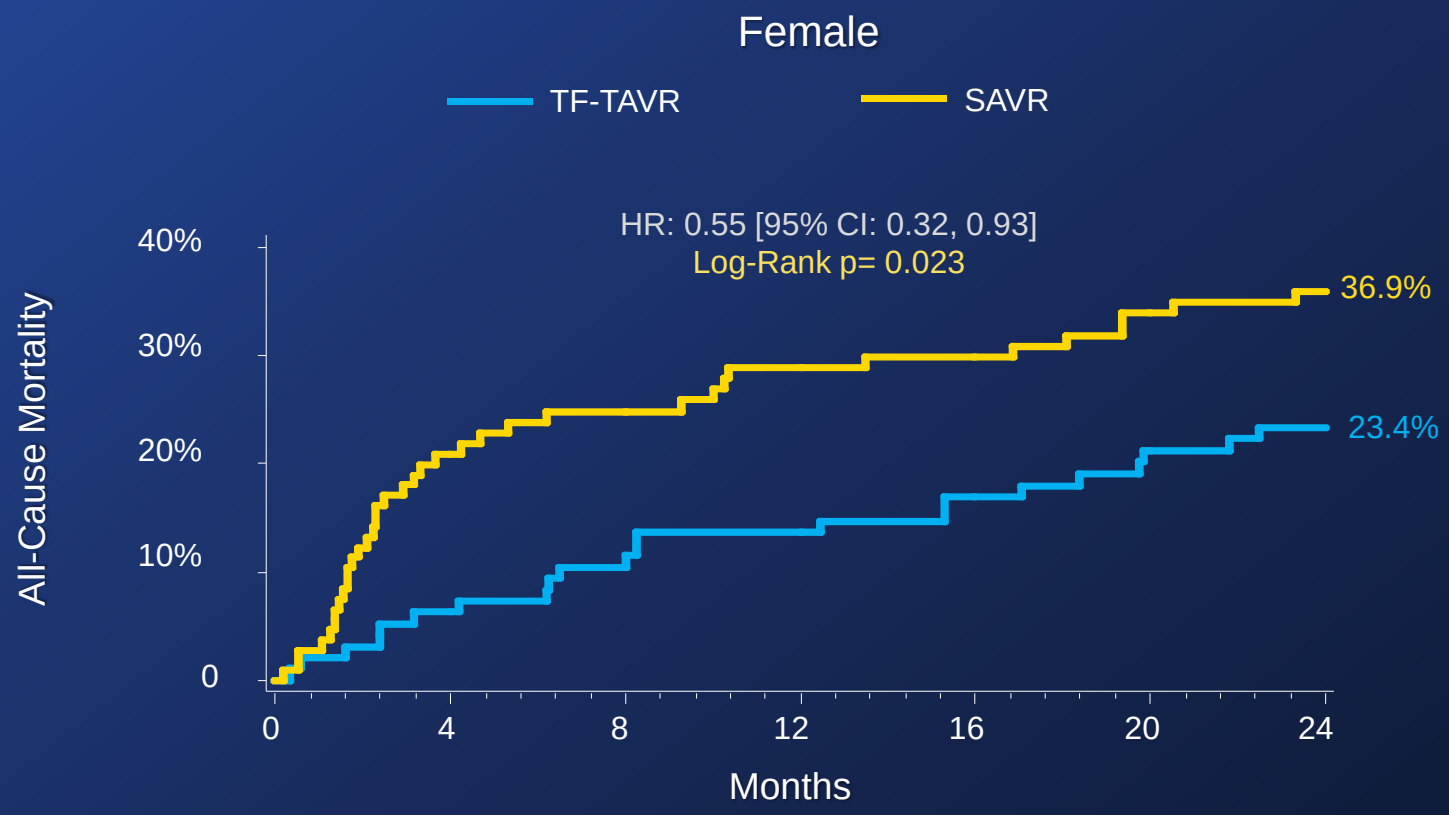
Female Mortality Stratified by Treatment – ITT



Numbers at Risk

TAVR	147	132	123	118	112	106	103
AVR	153	110	101	97	94	89	83

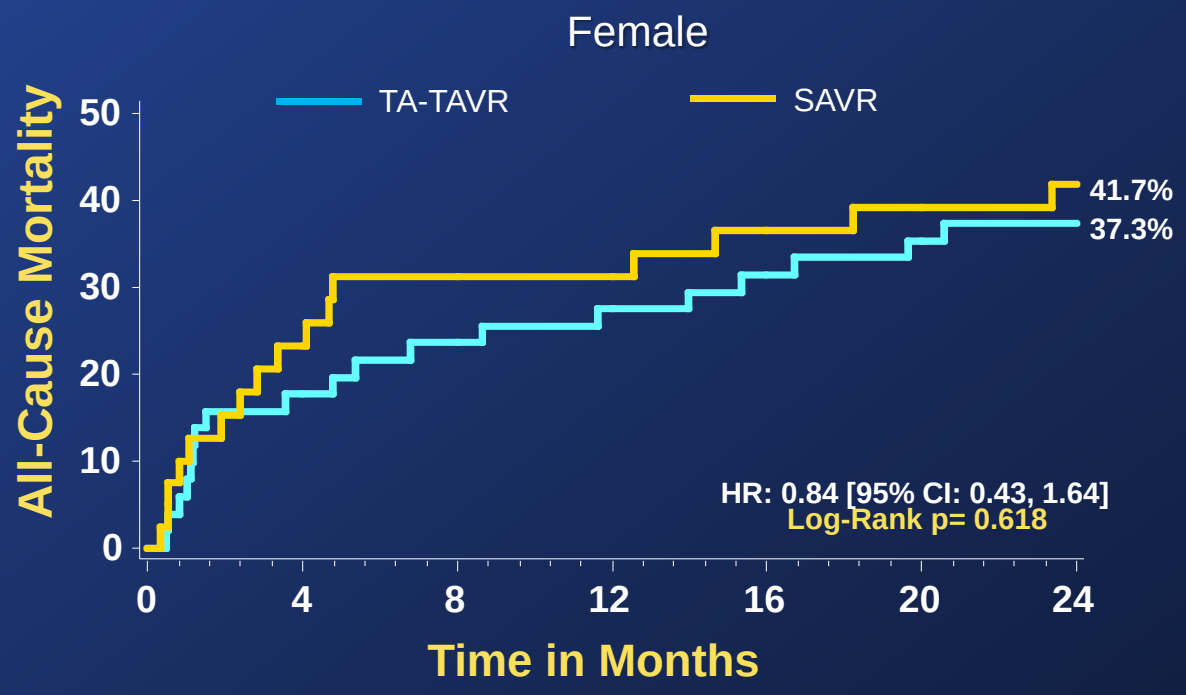
Transfemoral Arm



Numbers at Risk

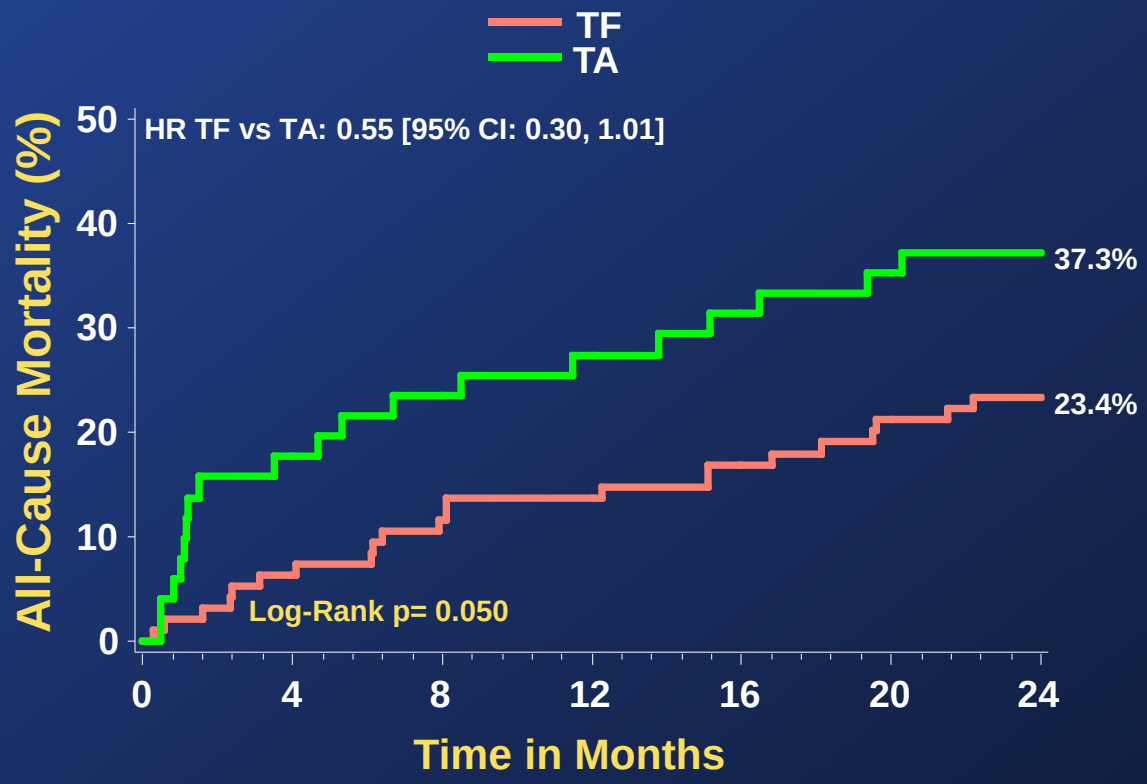
TF-TAVR	**96**	**90**	**84**	**81**	**77**	**73**	**71**
TF-SAVR	**112**	**81**	**75**	**71**	**70**	**66**	**61**

Transapical Arm



Number at risk							
TA-TAVR	51	42	39	37	35	33	32
TA-SAVR	41	29	26	26	24	23	22

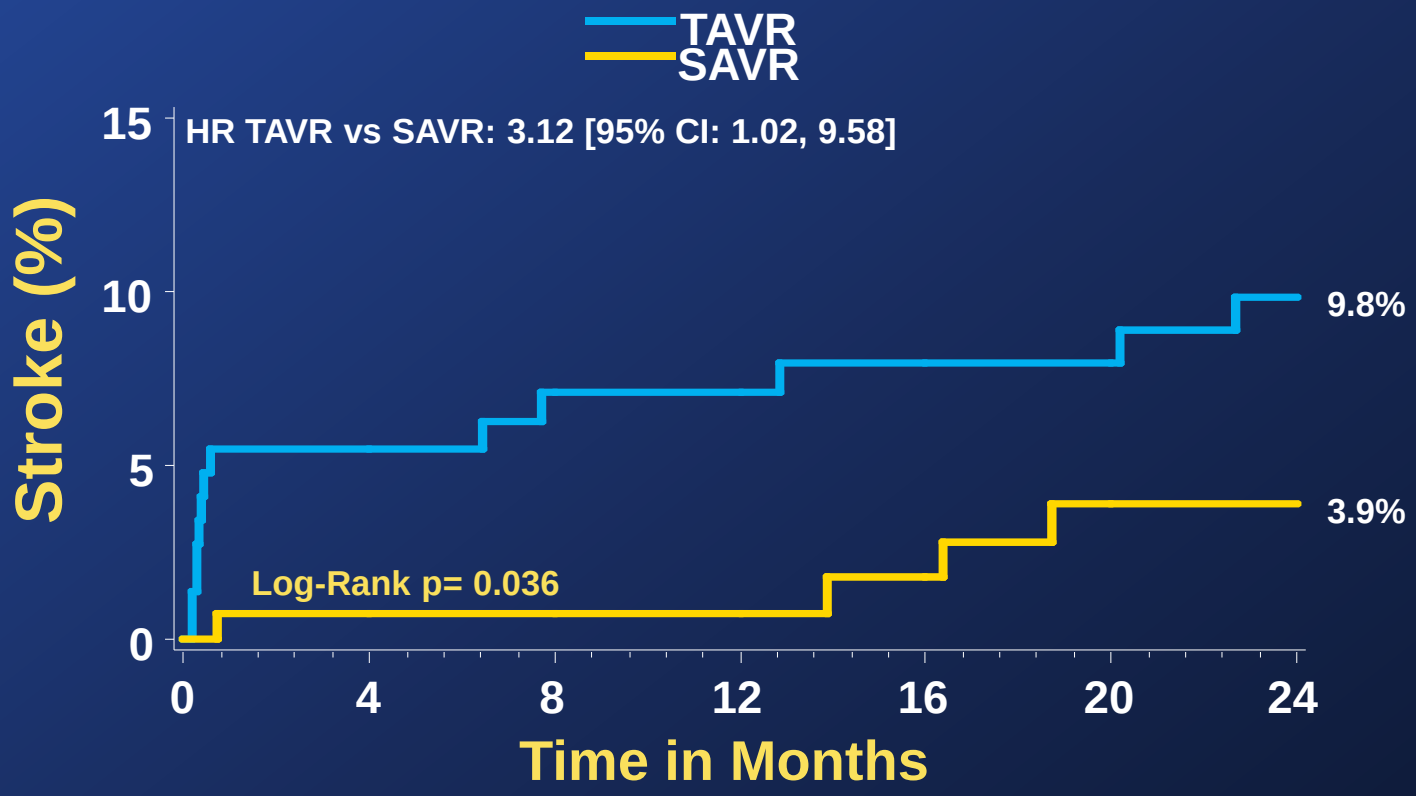
TF-TAVR vs TA-TAVR
ITT – Females only



Number at risk

TF	96	90	83	81	77	73	69
TA	51	42	39	37	35	33	32

Stroke to 2 years-Female only



Number at risk

TAVR	147	124	113	111	104	99	93
SAVR	153	110	101	97	94	88	79

Impact of Paravalvular Leak Following Transcatheter Aortic Valve Replacement on One-Year Mortality

Analysis of the Combined PARTNER Cohorts

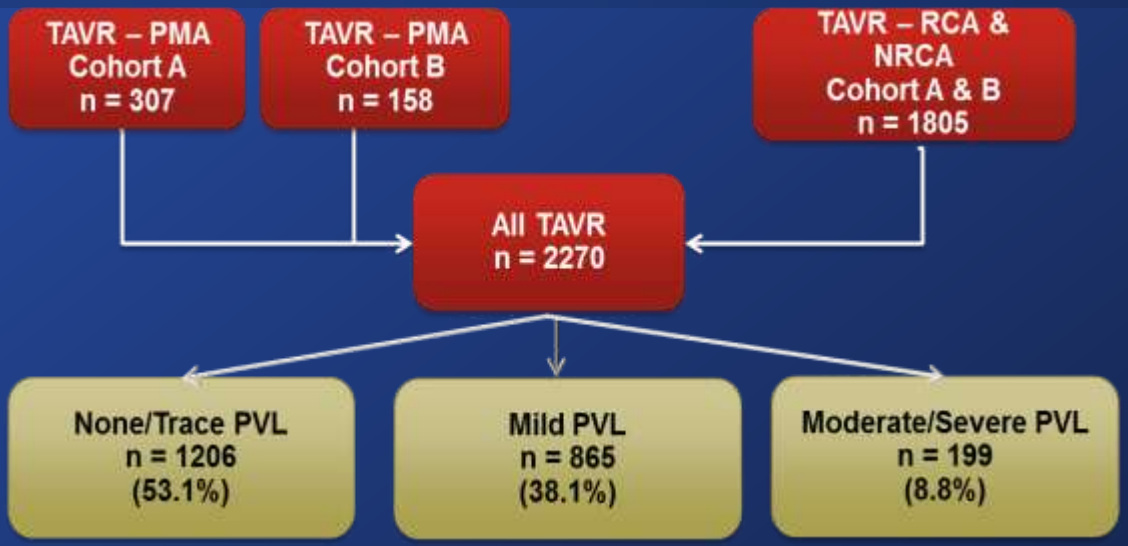
Susheel K. Kodali

on behalf of The PARTNER Publications Office and the PARTNER Trial Investigators

ESC 2013 | Amsterdam | September 2, 2013

THE PARTNER TRIAL

Introduction & Methodology



219 TAVR patients excluded from this analysis:

- 67 died in-hospital
- 73 died before 30 days
- 79 did not have evaluable echocardiograms

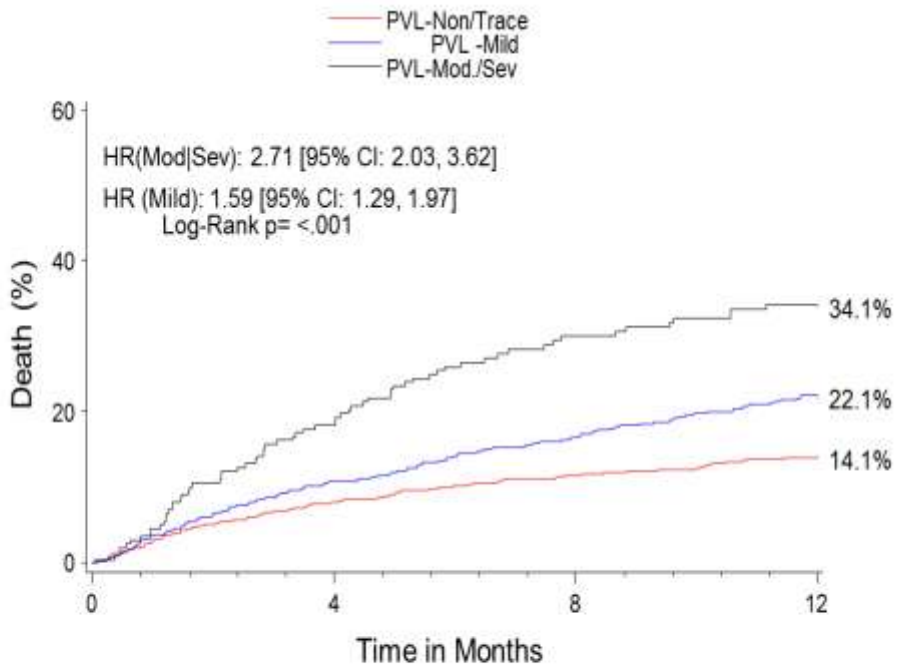
PVL assessments aligned with VARC-2

Doppler Parameters	Mild (1+)	Moderate	Severe (4+)
Semi-quantitative Parameters			
Diastolic flow reversal in the descending aorta—PW	Absent or brief early diastolic	Intermediate	Prominent, holodiastolic
Circumferential Extent of AR (%)	<10	10-30	>30
Quantitative Parameters			
Regurgitant Volume (ml/beat)	<30	30-59	≥60
Regurgitant Fraction (%)	<30%	30-49	≥50
EROA (cm2)	0.10	0.10-0.29	≥0.30

Kappetein et al. J Am Coll Cardiol 2012;60:1438–54

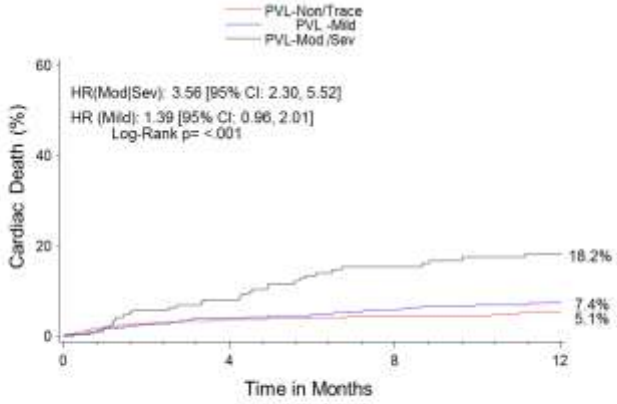
Clinical Outcomes

THE PARTNER TRIAL



Number at risk

PVL-Non/Trace	1206	1083	892	677
PVL -Mild	865	754	625	450
PVL-Mod./Sev	199	160	122	98



Number at risk

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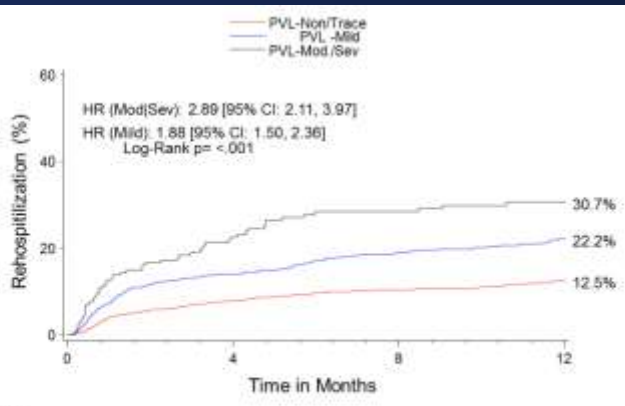


Number at risk

PVL-Non/Trace	1206	1008	811	597
PVL -Mild	865	690	525	370
PVL-Mod./Sev	199	126	97	79

Predictors of Mortality

THE PARTNER TRIAL

Multivariable Analysis – Predictors of One Year Mortality

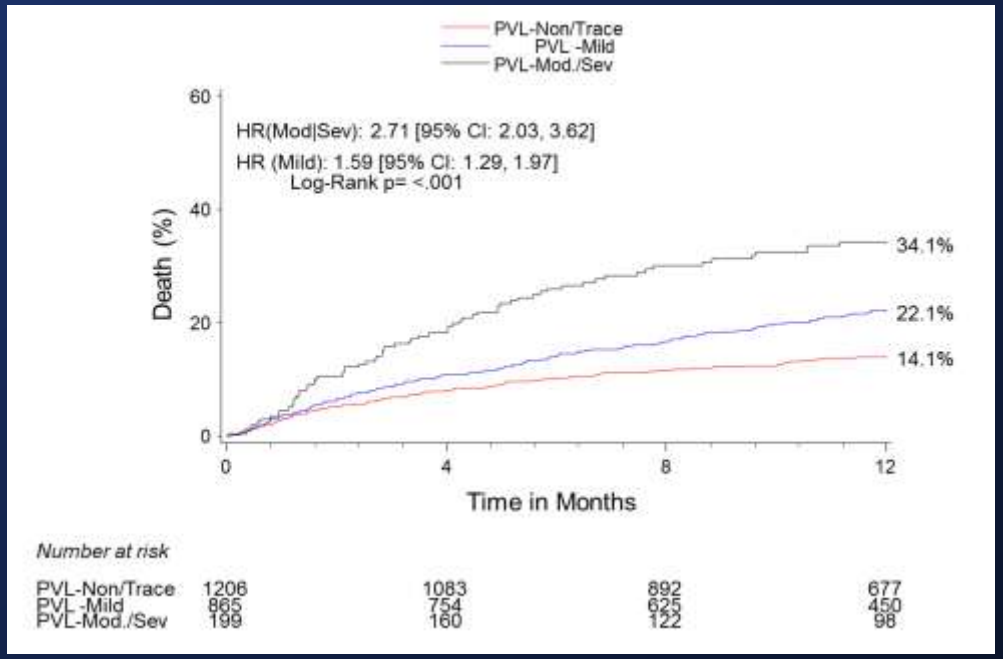
Variable	Hazard Ratio	p value
TF vs. TA	0.70 [0.55, 0.88]	0.0029
AV Annulus Diameter (cm)	2.35 [1.56, 3.53]	<0.0001
BMI	0.95 [0.93, 0.97]	<0.0001
Total Distance Walked imputing 0 for those who could not perform (per 10m)	0.97 [0.96, 0.98]	<0.0001
AV Mean Gradient (mmHg)	0.98 [0.97, 0.99]	0.0001
PVL (Mild vs. None/Trace)	1.47 [1.14, 1.90]	0.0034
PVL (Moderate/Severe vs. None/Trace)	2.38 [1.69, 3.35]	<0.0001
Renal disease (CR >=2)	1.37 [1.05, 1.81]	0.0226

Multivariate predictors using stepwise Cox regression with entry/stay criteria of 0.1/0.1

Potential Covariates include:
Forced-In Variables: PVL, TF vs TA
Baseline Characteristics: sex, BMI, STS score, DM, Smoking, Prior CABG, Prior BAV, Frailty, renal disease, major arrhythmia, pacemaker, COPD, anemia, 6 min walk, total distance walking (imputing 0 time for those who do not walk), LVES volume, LV ejection fraction, LV Mass, LVED dimensions, LVES dimensions, AV annulus diameter, AV mean gradient.

Key Messages

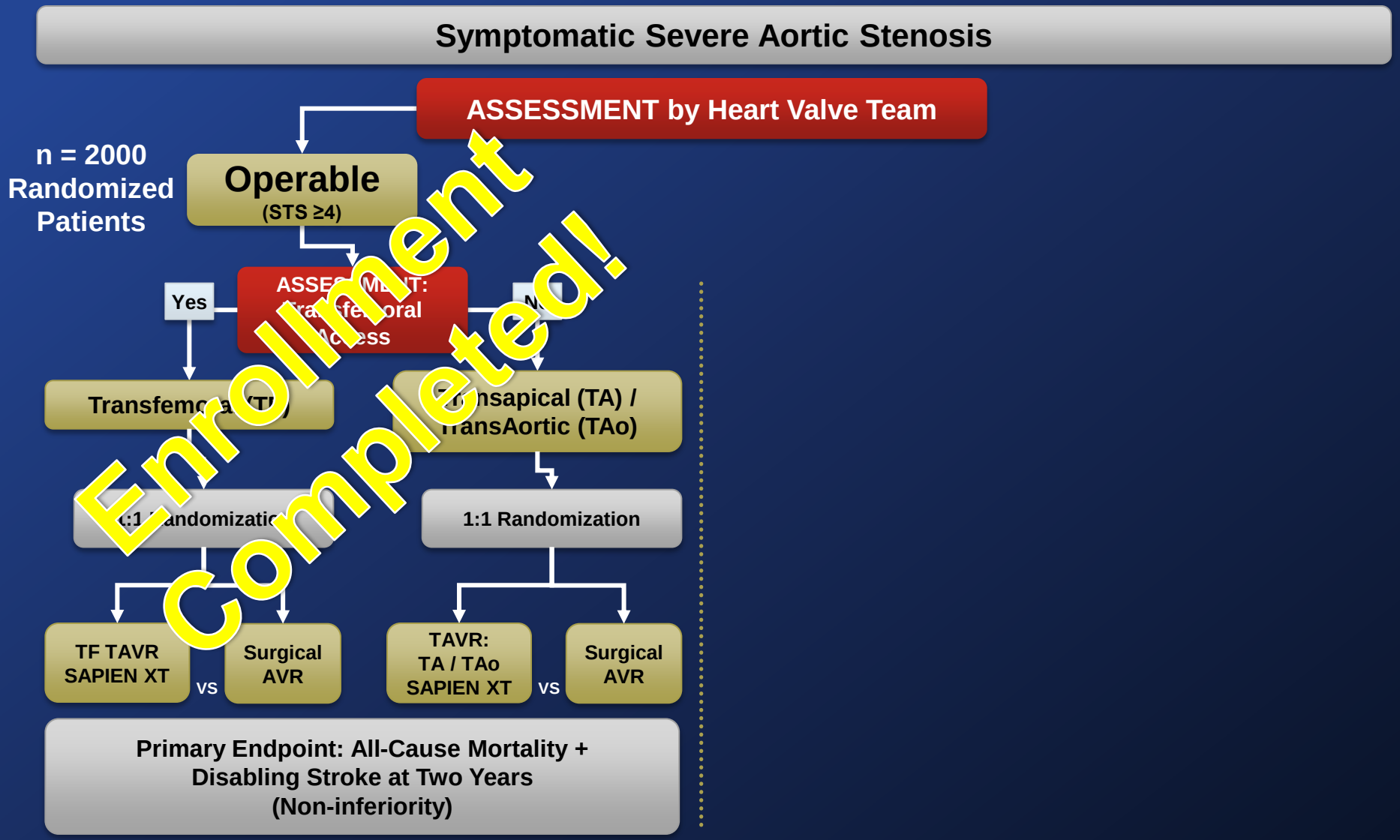
- PVL after TAVR remains a frequent occurrence
- None/Trace (53.1%), Mild (38.1%), Mod/Sev (8.8%)
- Baseline characteristics (clinical and echo) differ significantly between the groups
- Presence of either mild or mod/sev PVL impacts late mortality



Agenda…in 8 minutes!

- *Update*
  - PARTNER cohort 1B 3 years
  - PARTNER cohort 1A 3 years
  - PARTNER cohort 2B 1 year
  - Continued Access Registries
- *Latest publications from PARTNER*
  - Vascular Complications, Bleeding Complications, Arrhythmias, Sex Gender, Diabetics, Cost-effectiveness…and PVL
- *PARTNER 2A update-Intermediate risk*

The PARTNER IIA Trial
Study Design

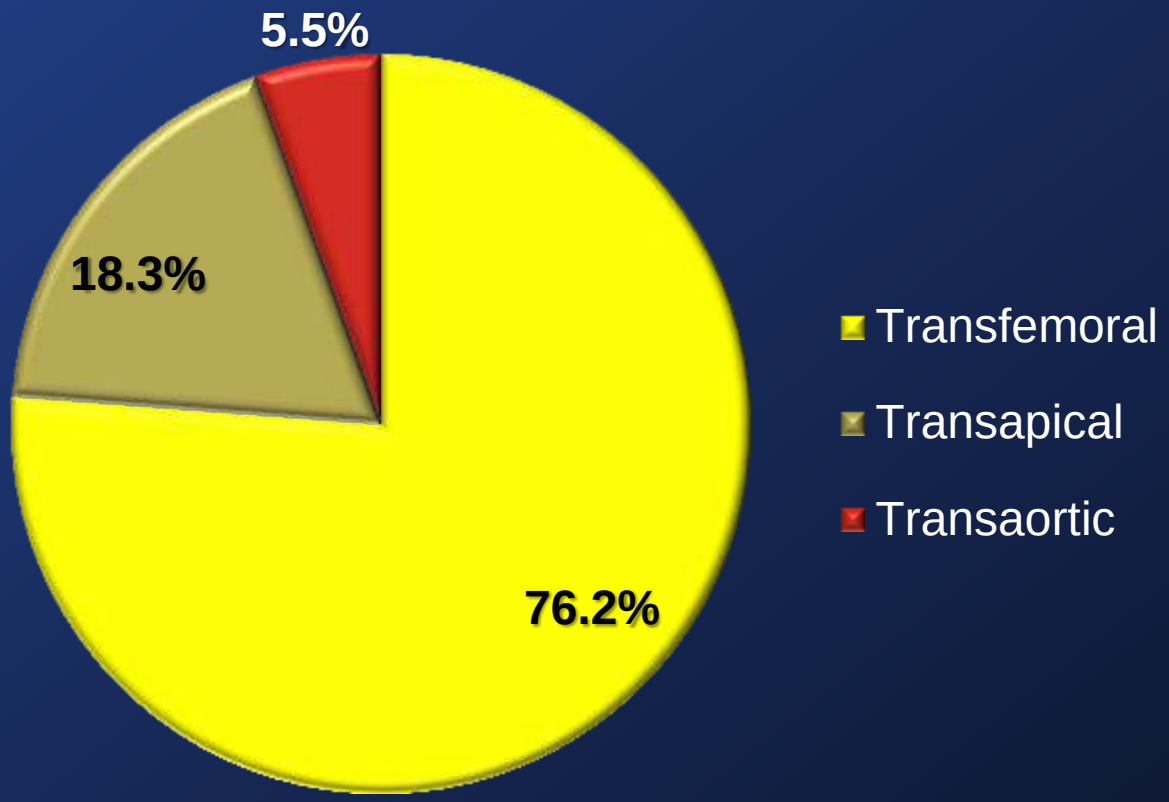


PARTNER IIA - Intermediate Risk
Study Design Details

- Study hypothesis is *non-inferiority of test (TAVR-Sapien XT) vs. control (AVR)* for the primary endpoint for the duration of the study *(all patients followed for at least 2 years)*
- Primary endpoint is a nonhierarchical *composite of all-cause mortality and disabling stroke* (defined as modified Rankin score ≥ 2 @ 90 days with neurology assessments)
- 1:1 randomization between TAVR (Sapien XT) vs. surgical AVR
- Separate analyses of transfemoral vs. non-transfemoral (TA and TAo) cohorts and in patients receiving treatment for concomitant CAD (PCI or CABG)

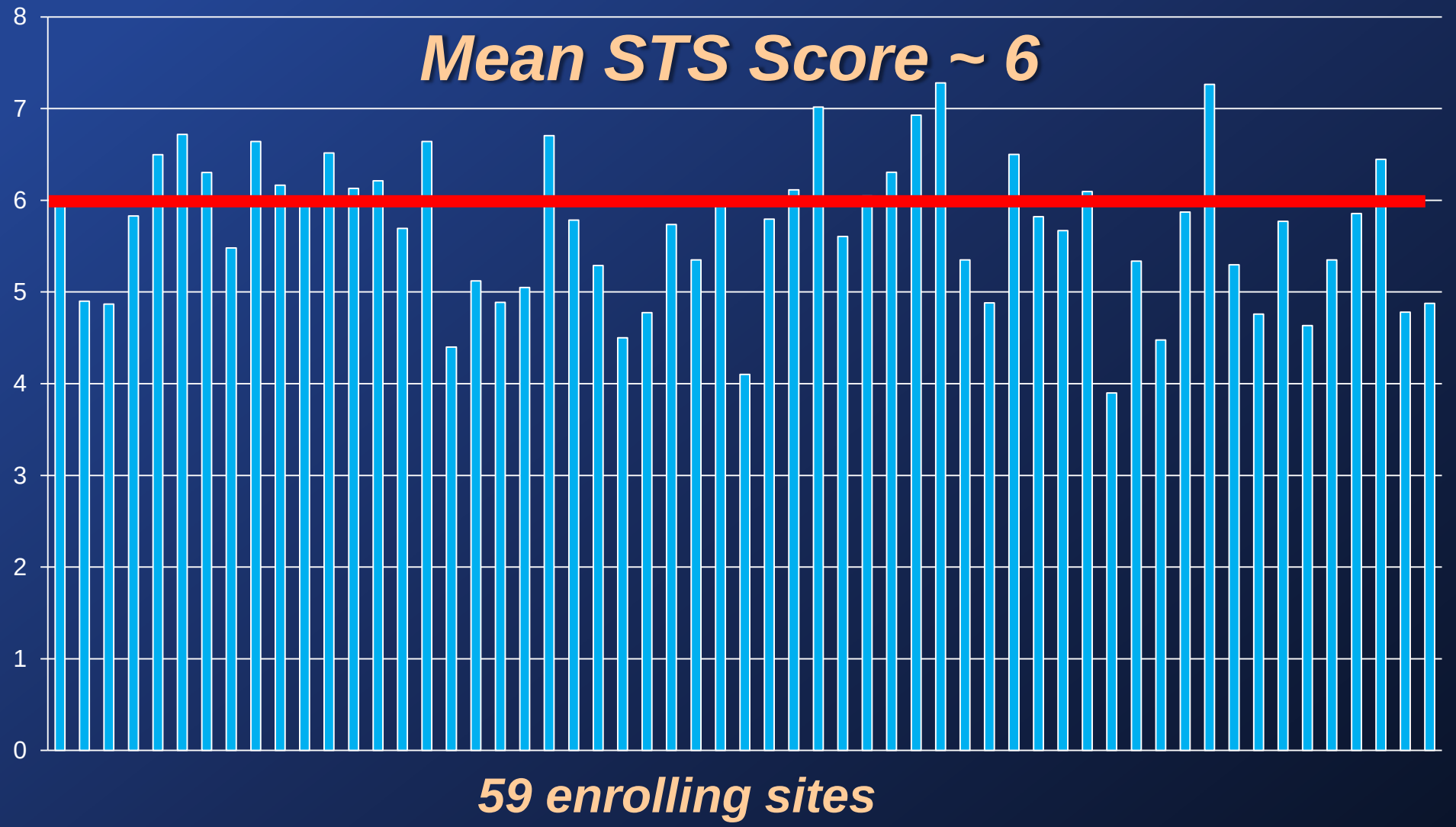
PARTNER IIA - Intermediate Risk
Vascular Access Sites

> 75% Patients with Trans-femoral Access



PARTNER IIA - Intermediate Risk

Mean STS Score by Site



In Conclusion…PARTNER simplified

- ***Inoperable patients:*** **TAVR when possible and appropriate**
- ***High-Risk:*** **TAVR vs. SAVR at 3 years**
  - ***Death:*** **TAVR = SAVR**
  - ***Stroke:*** **TAVR = SAVR**
  - ***Bleeding:*** **TAVR <<< SAVR**
  - ***PVL:*** **TAVR >>SAVR**
- **Smaller devices and increase experience = lower vascular complications**
- ***A. Fib*** **(especially new onset) is bad**
- ***New LBBB*** **is bad**
- ***PPM*** **is annoying, should be avoid, but not that bad**
- ***PVL*****…is very annoying…is bad…should be avoid**
- ***Female and diabetics:*** **TAVR better**

In Conclusion…

- ***PARTNER 2A:***
  - ***Intermediate Risk…We are coming!***
  - ***Thank you to TCTAP work force!***