

Long-Term Outcomes Using a Self-Expanding Bioprosthesis in Patients With Severe Aortic Stenosis Deemed Extreme Risk for Surgery: Two-Year Results From the CoreValve US Pivotal Trial

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For the CoreValve US Clinical Investigators

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- Consultant to Medtronic: member of the CoreValve US Pivotal Trial screening, steering, and publications committees

Medtronic personnel performed all statistical analyses and assisted in the graphical display of the data

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Transcatheter Aortic Valve Replacement Using a Self-Expanding Bioprosthesis in Patients With Severe Aortic Stenosis at Extreme Risk for Surgery

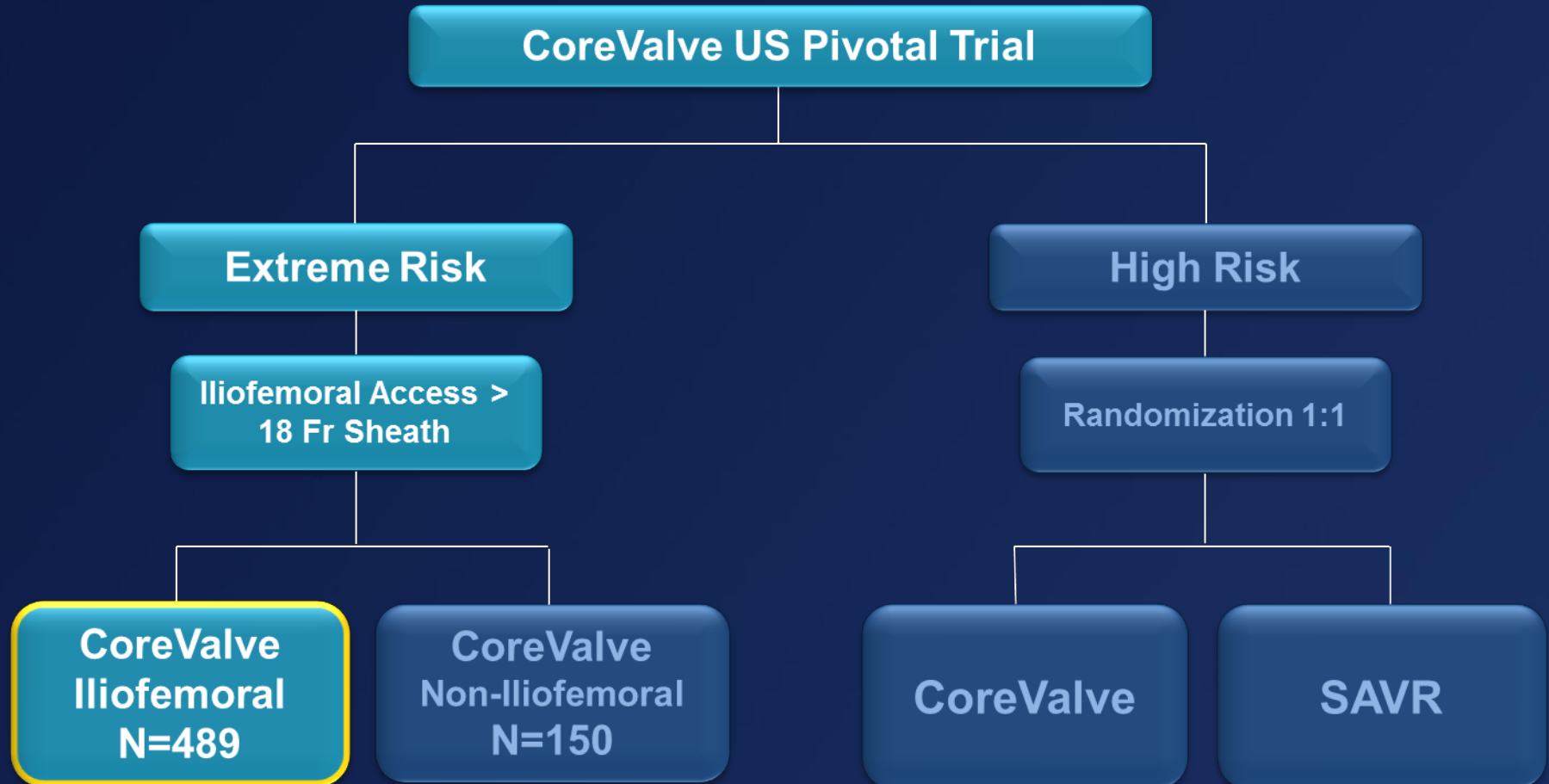


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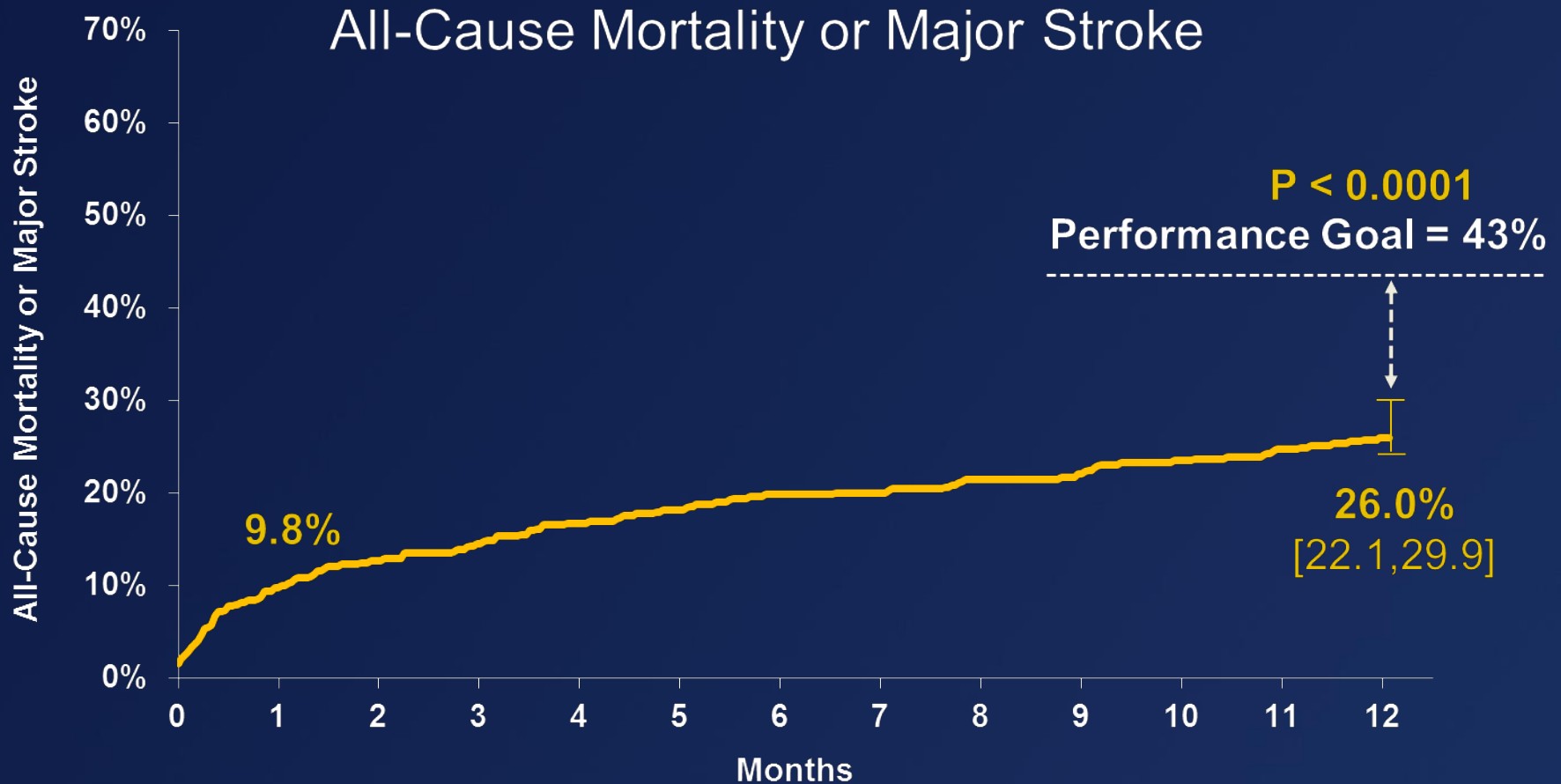
Popma JJ, et al. Transcatheter aortic valve replacement using a self-expanding bioprosthesis in patients with severe aortic stenosis at extreme risk for surgery. *J Am Coll Cardiol* 2014; 63: 1972-81.

Pivotal Trial Design

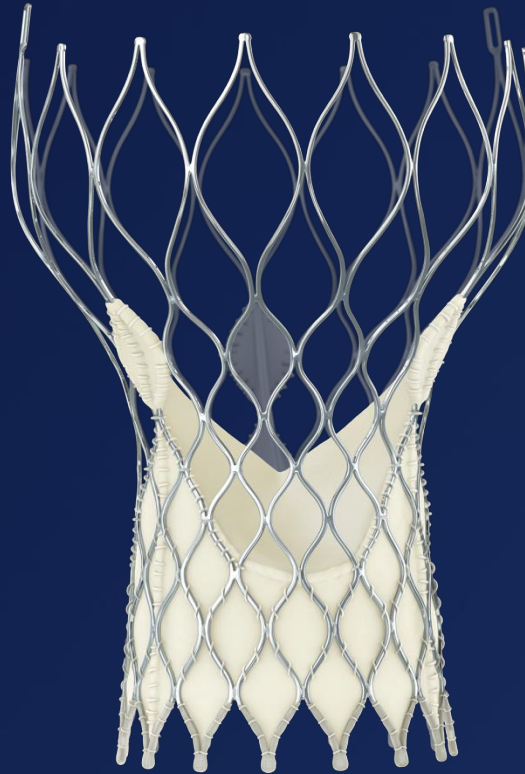


Primary Endpoint

1-Year All-Cause Mortality or Major Stroke



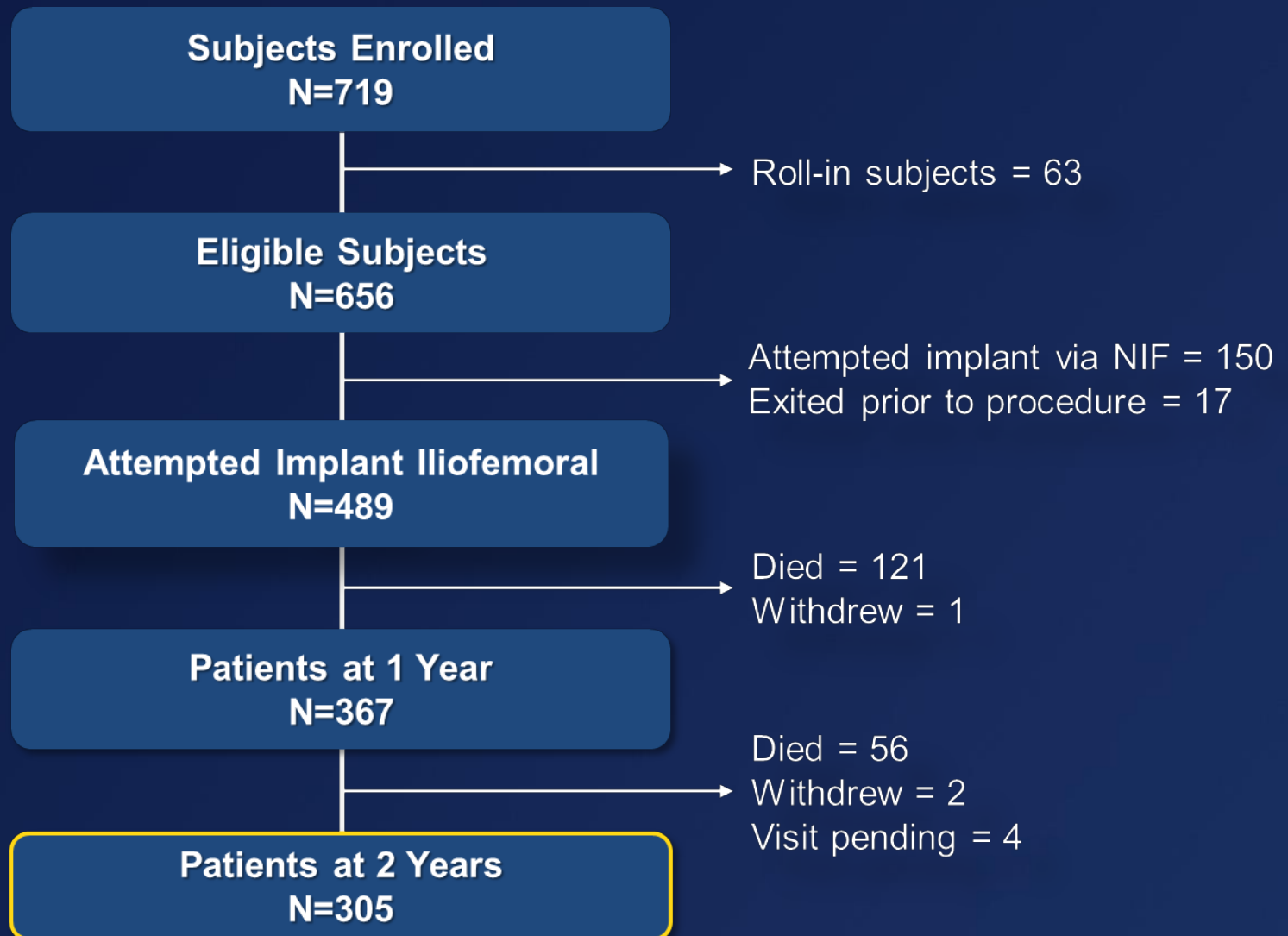
Study Device



4 Valve Sizes
(18–29 mm annular diameter)

18F Delivery System

Study Disposition



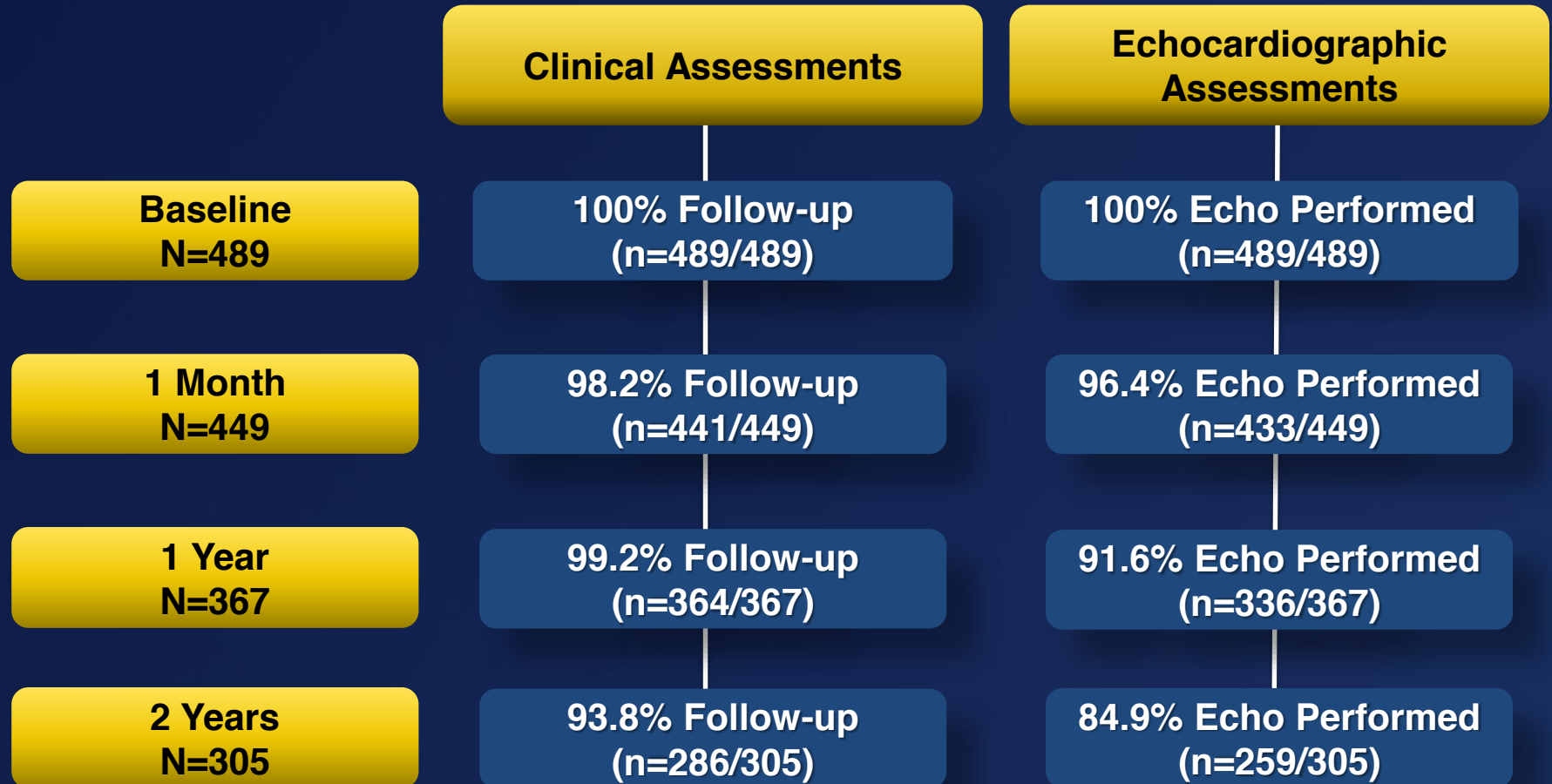
Analysis Cohort

- Primary Analysis was performed using the “Attempted Implant” population: all enrolled subjects with a documented attempt for an iliofemoral implant procedure—defined when subject was brought into the procedure room and any of the following have occurred: anesthesia administered, vascular line placed, TEE placed or any monitoring line placed

Participating Sites



Study Compliance



National Screening Committee

Chairman: Michael J. Reardon, MD

- Two clinical site cardiac surgeons and one interventional cardiologist determined patient eligibility
- All patients were reviewed on web-based conference calls with site investigators to confirm eligibility and access route
- Detailed portfolio included:
 - STS PROM and all other risk factors
 - Independent review of transthoracic echocardiogram
 - Independent review of chest/abdominal CTA findings
- Two senior surgeons and one cardiologist on the screening committee had to concur with the local heart team assessment to qualify the patient for trial enrollment

Baseline Demographics

Characteristic, %	N=489
Age, years	83.2 ± 8.7
Male	47.9
STS Predicted Risk of Mortality	10.3 ± 5.5
Logistic EuroSCORE	22.6 ± 17.1
New York Heart Association class III/IV	91.8
Diabetes mellitus	41.5
Insulin requiring diabetes	18.4
Prior stroke	13.7
Coronary artery disease	81.8
Prior coronary artery bypass grafting	39.5
Prior percutaneous coronary intervention	37.0
Prior balloon aortic valvuloplasty	20.4

Comorbidities, Frailty, Disabilities

Characteristic, %	N=489
<i>Prohibitive Anatomy</i>	
Severe aortic calcification*	17.2
Hostile mediastinum	11.9
<i>Comorbidities</i>	
Severe chronic lung disease	23.5
Home oxygen	29.9
<i>Frailty</i>	
Anemia with prior transfusion	22.8
Albumin < 3.3 g/dL	18.2
5-Meter gait speed > 6 secs	84.2
<i>Disabilities</i>	
Assisted living	27.6
≥ 2 Katz ADL deficits	20.9
Wheelchair bound	16.6

*Aorta calcification measured on screening CTA

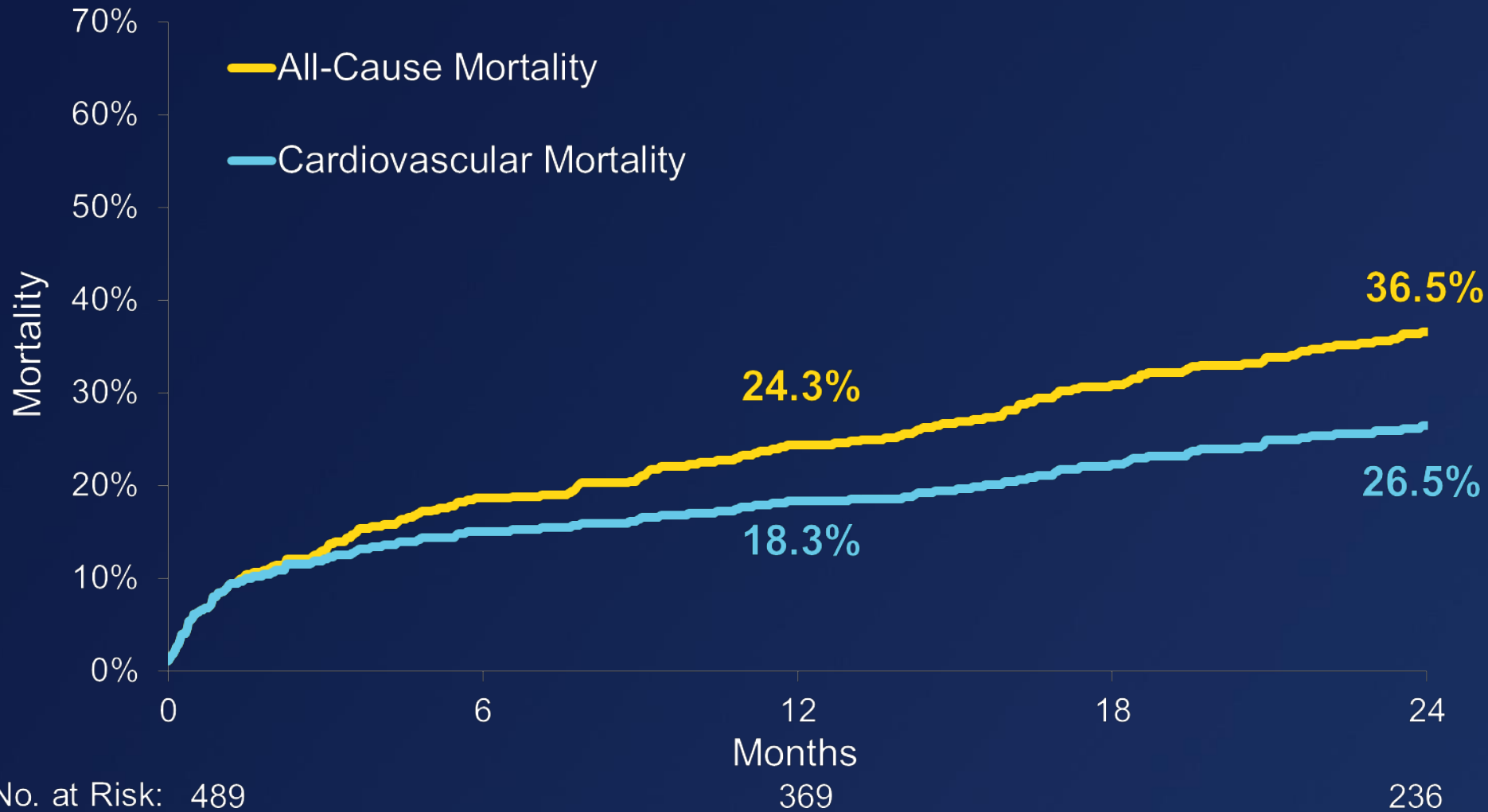
CoreValve US Pivotal Trial Extreme Risk Iliofemoral 2-Year Results

All-Cause Mortality or Major Stroke

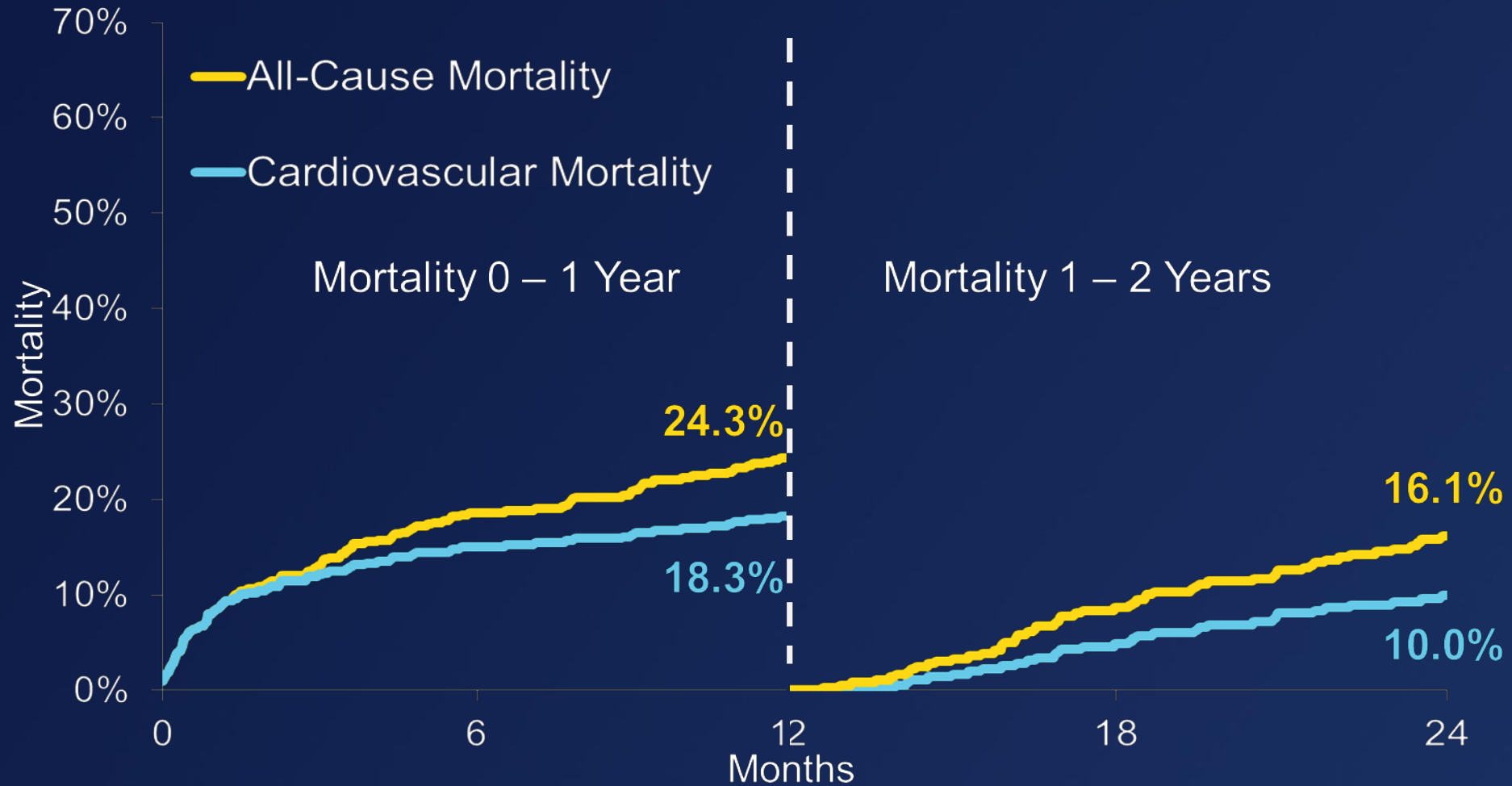


* Calculated rate for 117 events in 179 patients (65.4%, lower confidence bound of 57.9% by Exact method) (Makkar RR, et al, New Engl J Med, 2012)

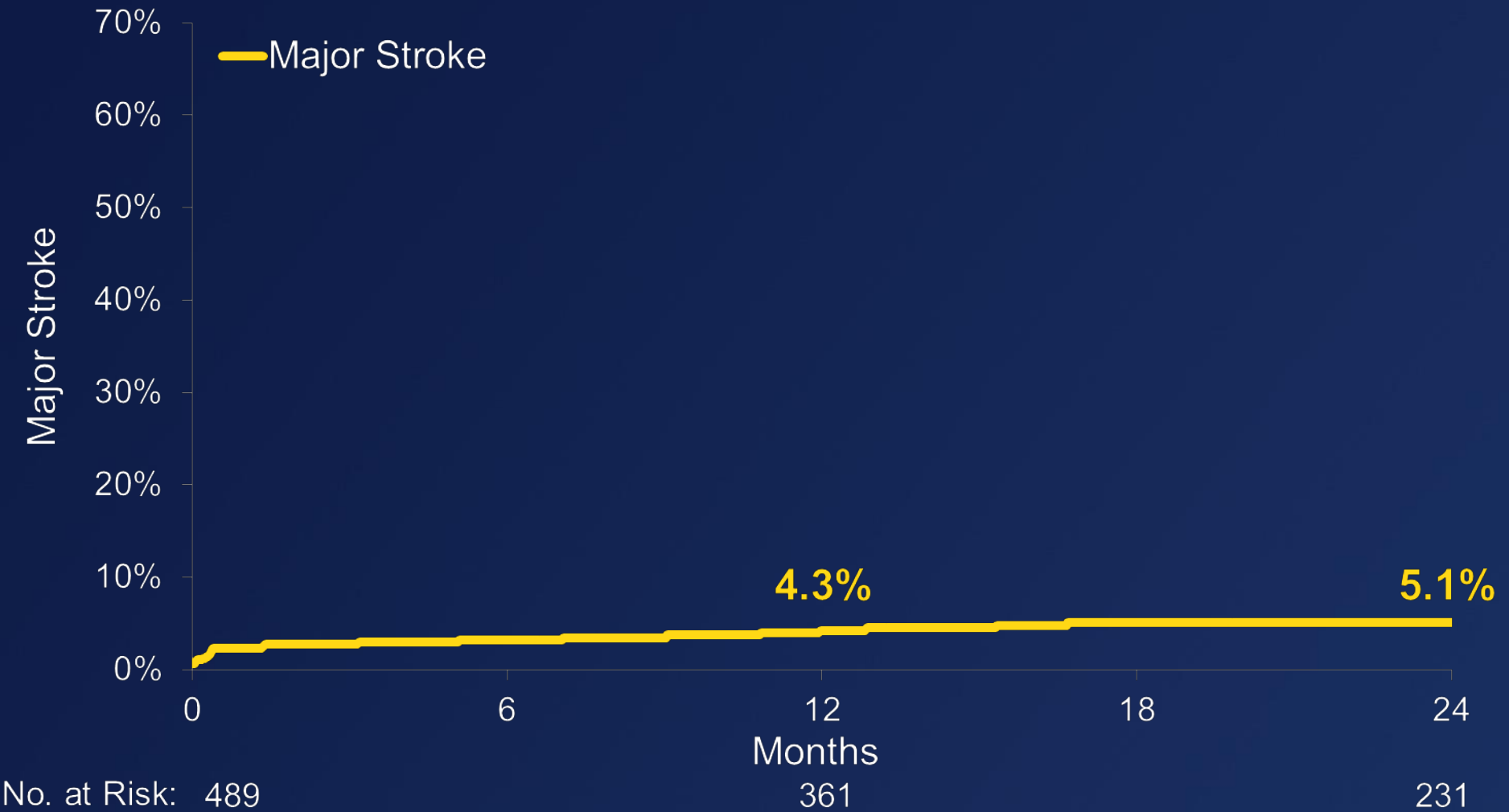
2-Year Mortality



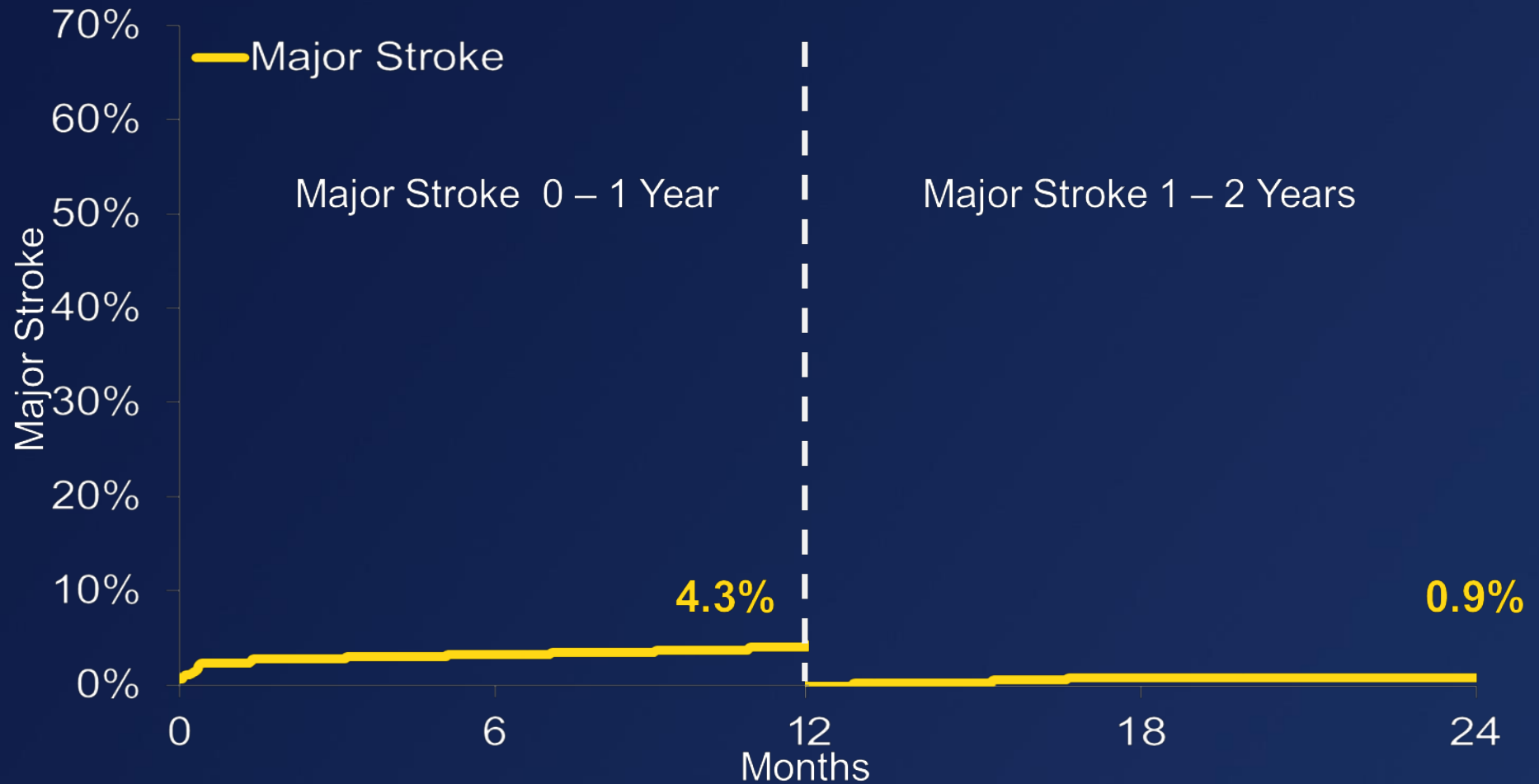
2-Year Mortality Landmark Analysis



2-Year Major Stroke



2-Year Major Stroke Landmark Analysis



Secondary Endpoints

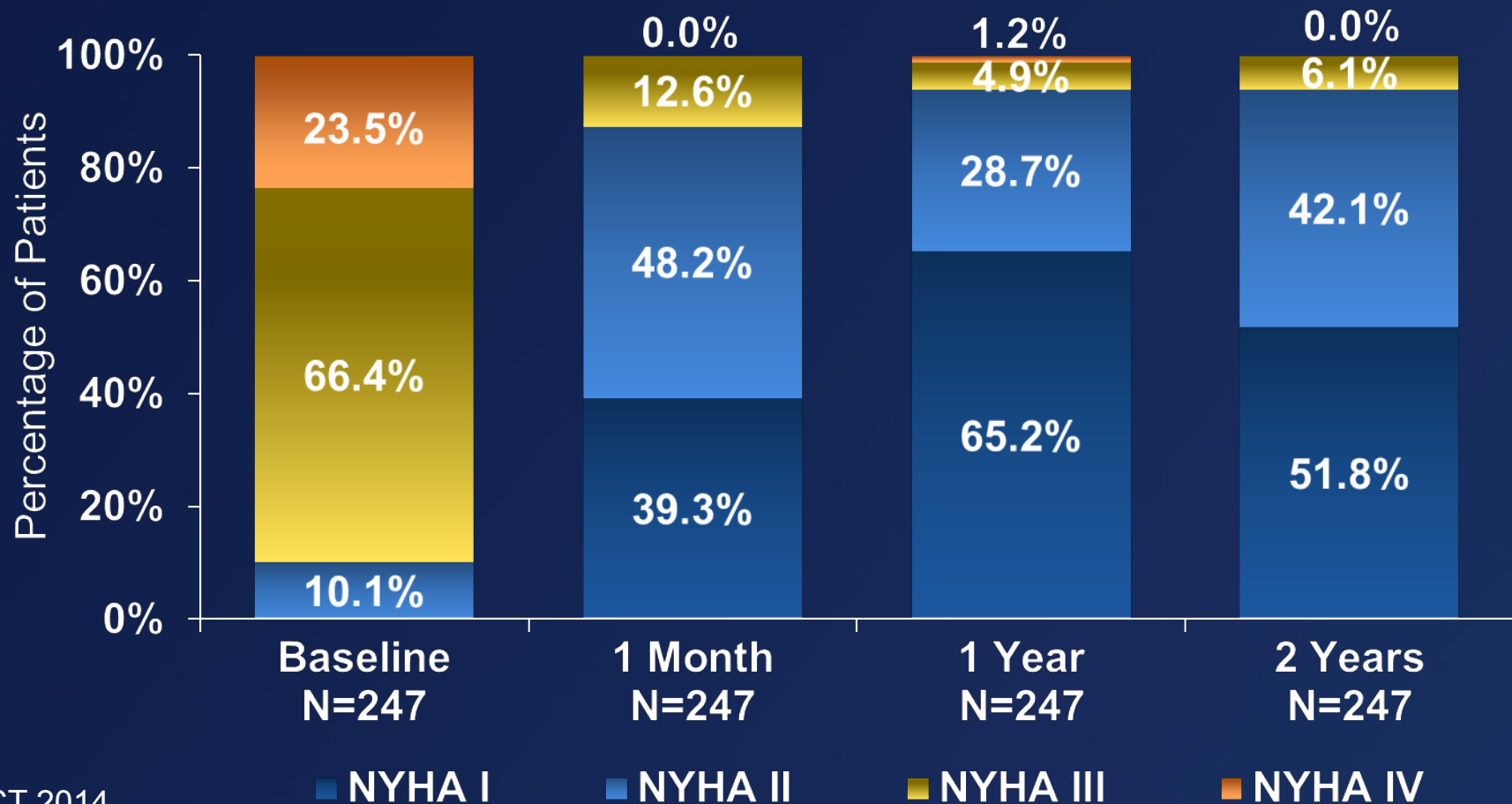
Events*, %	1 Year	2 Years
Any stroke	7.0	8.7
Major	4.3	5.1
Minor	3.2	4.1
Myocardial infarction	2.0	2.8
Reintervention	1.8	1.8
VARC bleeding	42.8	45.3
Life threatening or disabling	18.0	20.8
Major	28.3	29.1
Major vascular complications	8.4	8.4
Permanent pacemaker implant	26.4	28.9
Per ACC guidelines	19.5	22.0

* Percentages obtained from Kaplan Meier estimates

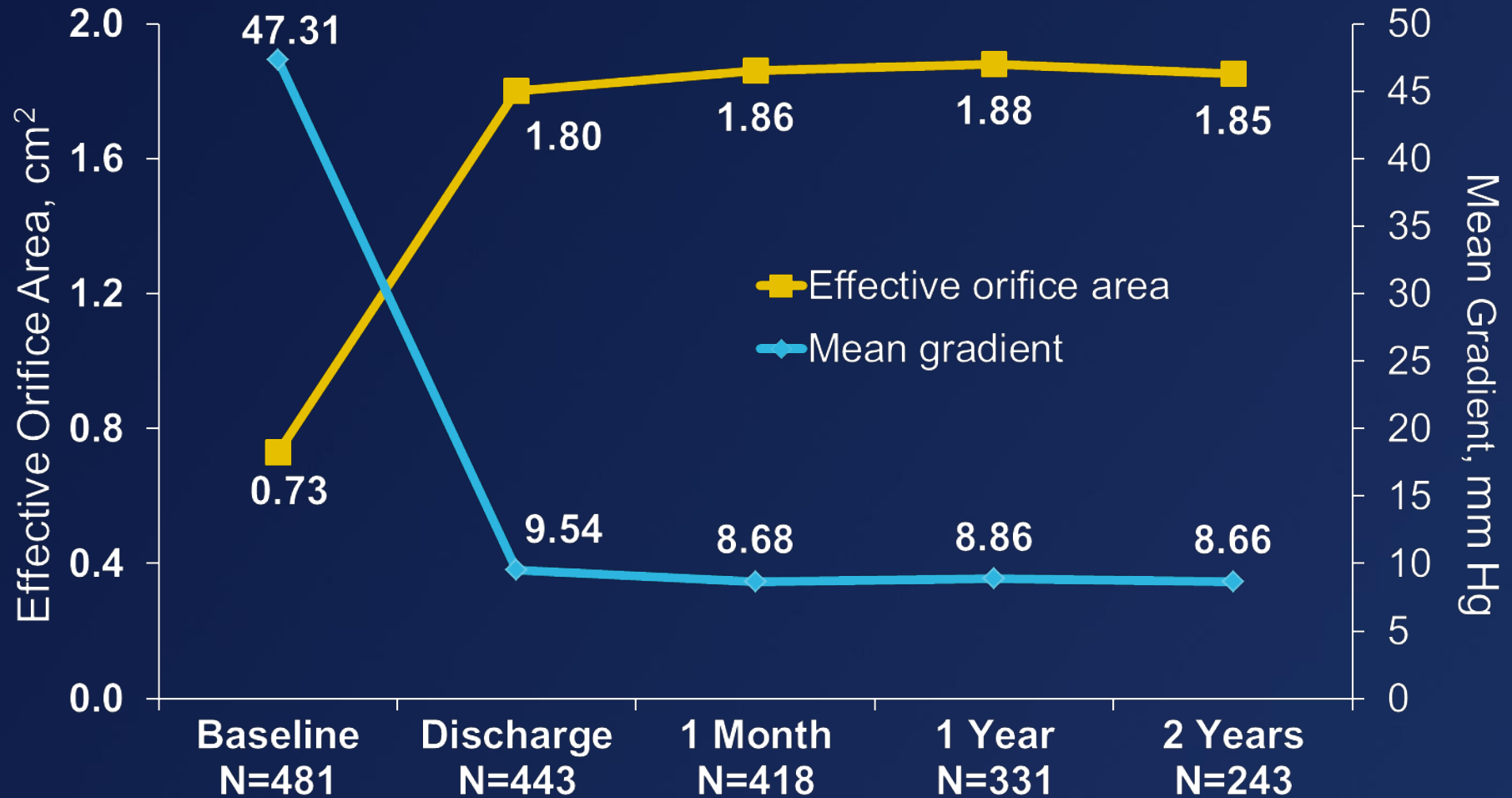
NYHA Class in 2-Year Survivors

Paired Analysis

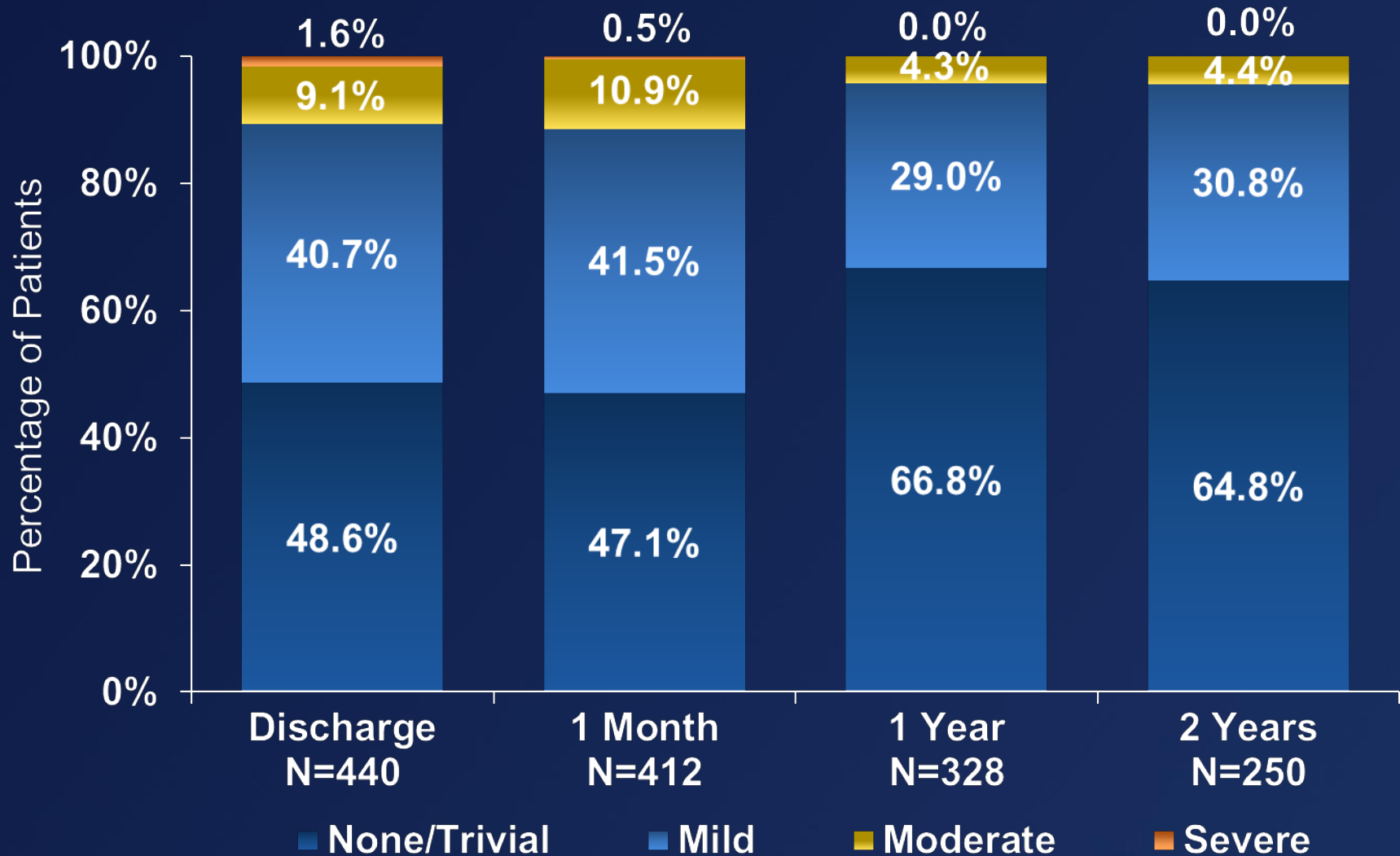
92% of Patients Improved at Least 1 NYHA Class by 2 Years
58% of Patients Improved at Least 2 NYHA Classes by 2 Years



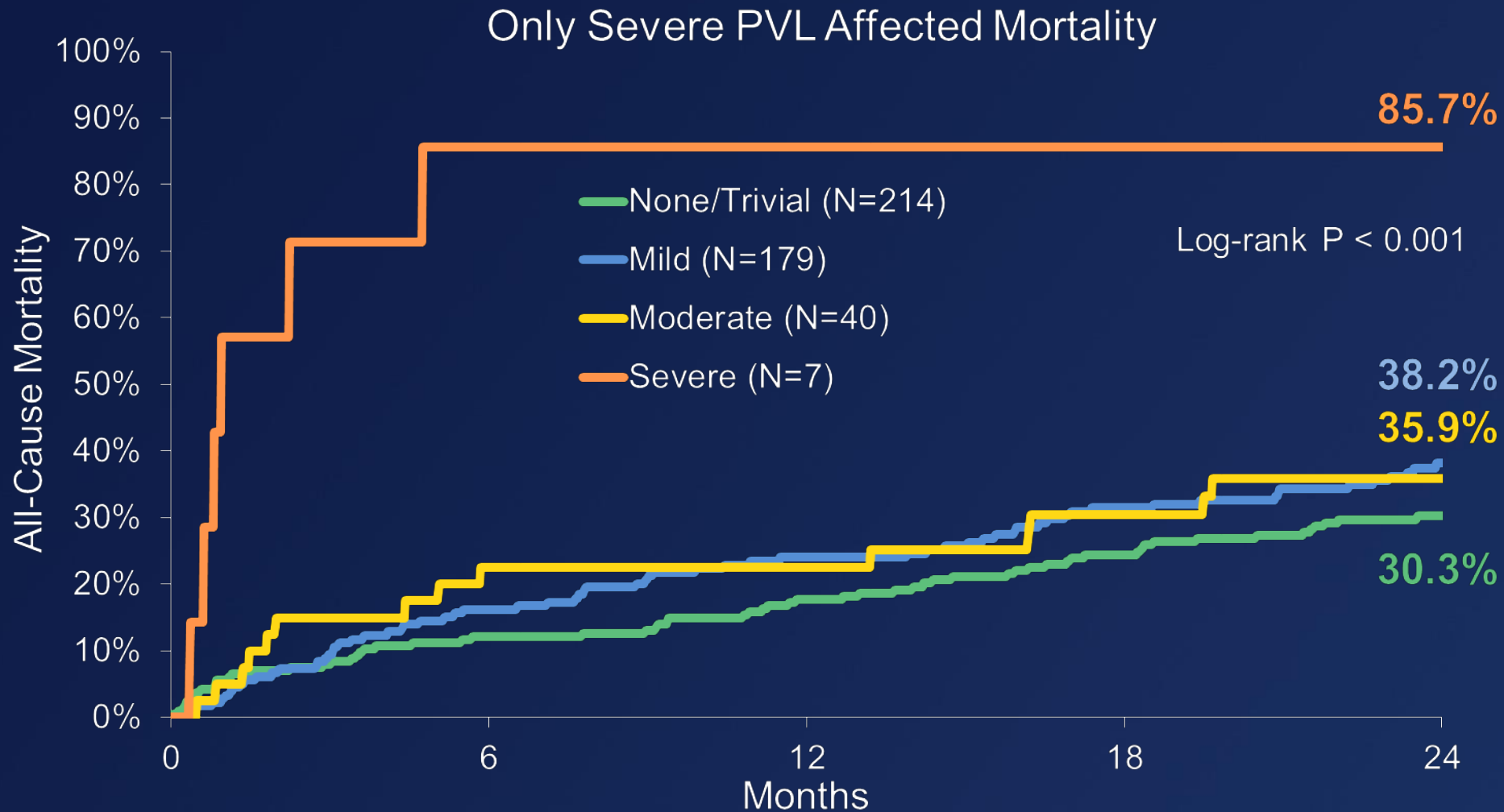
Echocardiographic Findings



Paravalvular Regurgitation

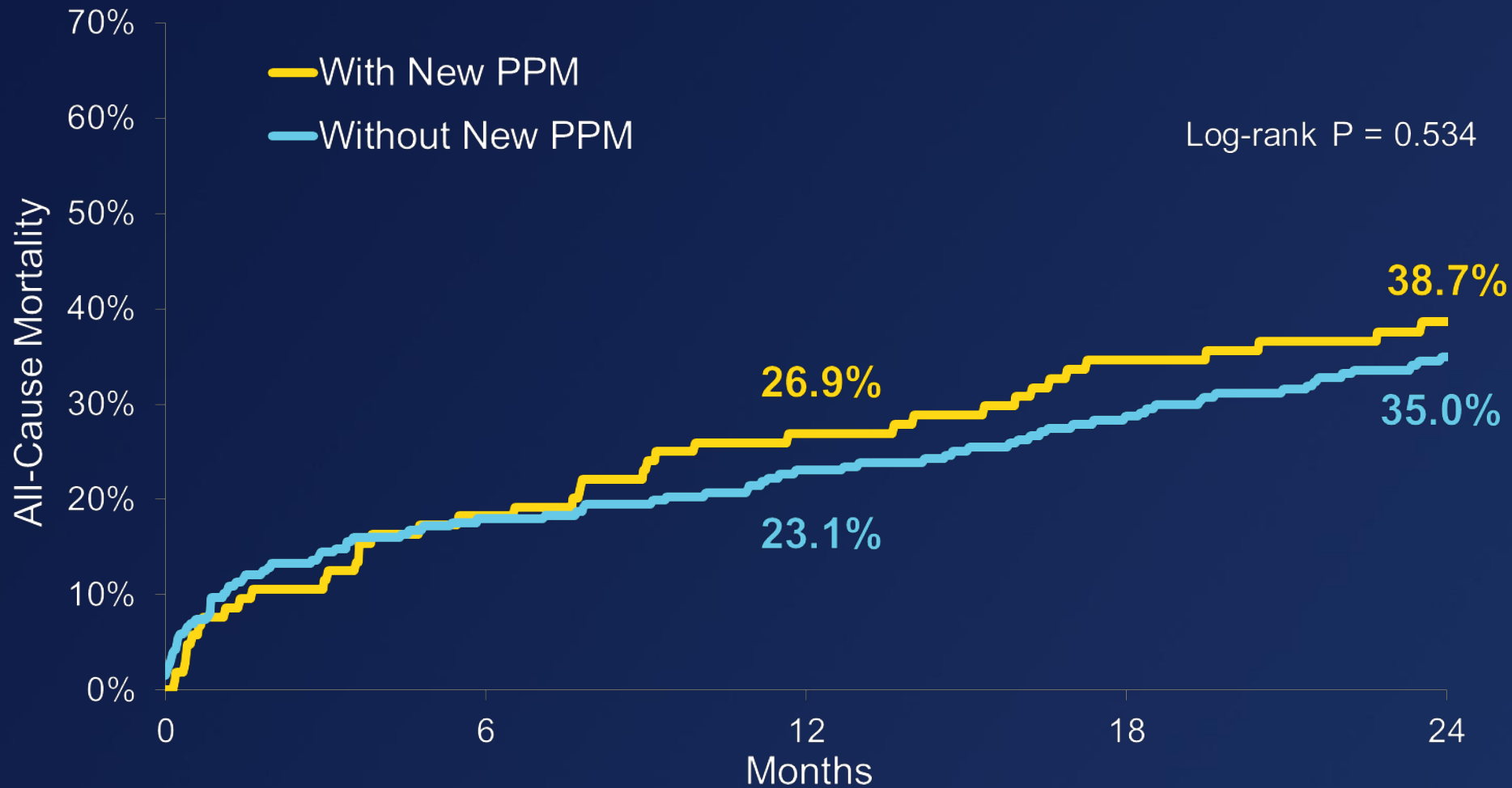


PVL and All-Cause Mortality















Pacemaker and All-Cause Mortality

Pacemaker Implantation Did Not Affect Mortality











Subgroup Analysis

2-Year All-Cause Mortality or Major Stroke

	Patients	KM (%) 2-Yr (95% CI)	All-Cause Mortality or Major Stroke (38.0% at 2 Years)	P Value
Gender				0.1809
Female	255	35.1 (29.2, 41.0)		
Male	234	41.0 (34.7, 47.4)		
Age				0.4647
≤85	263	36.9 (31.0, 42.8)		
>85	226	39.2 (32.8, 45.7)		
NYHA				
II	40	30.3 (15.9, 44.6)		
III	313	38.1 (32.7, 43.6)		0.3805
IV	136	39.9 (31.7, 48.2)		0.3282
LVEF				0.1706
≥40%	404	36.8 (32.0, 41.5)		
<40%	83	43.6 (32.9, 54.3)		
STS Score				
<10%	272	35.8 (30.1, 41.6)		
10-15%	133	34.4 (26.2, 42.5)		0.8008
>15%	84	50.7 (39.9, 61.5)		0.0120

Subgroup Analysis

2-Year All-Cause Mortality or Major Stroke

	Patients	KM (%) 2-Yr (95% CI)	All-Cause Mortality or Major Stroke (38.0% at 2 Years)	P Value
Hypertension	441	39.1 (34.5, 43.8)		0.1773
Diabetes	203	40.2 (33.4, 46.9)		0.3686
Prior stroke	67	40.3 (28.6, 52.0)		0.5535
Prior MI	151	44.0 (36.1, 52.0)		0.0581
Chronic lung disease/ COPD	288	40.1 (34.4, 45.8)		0.3553
PVD	171	41.4 (34.0, 48.9)		0.1885
CAD	400	41.4 (36.5, 46.3)		0.0019
Assisted living	135	50.7 (42.2, 59.2)		<0.0001

Conclusions

- At 2 years the CoreValve US Pivotal Extreme Risk Study showed:
 - Low rates of all-cause mortality
 - Low rates of major stroke
 - Improvement in NYHA classifications
 - Durable improvement in hemodynamic valve performance (EOA and mean gradients)
 - Low rates of moderate or severe aortic insufficiency
 - No association of mild or moderate paravalvular regurgitation on mortality

Summary

- The 1-year results from the CoreValve US Pivotal Extreme Risk Study support the safety and efficacy of this therapy in patients unsuitable for surgical AVR
- The 2-year results confirm the improved survival benefit in these patients

Thank You

On Behalf of the CoreValve US Investigators