ACC.25

TAVR with JenaValve for Symptomatic Aortic Regurgitation in High Surgical Risk Patients

Outcomes in 500 patients from The ALIGN AR Trial

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THE ALIGN AR TRIAL

AMERICAN COLLEGE of CARDIOLOGY

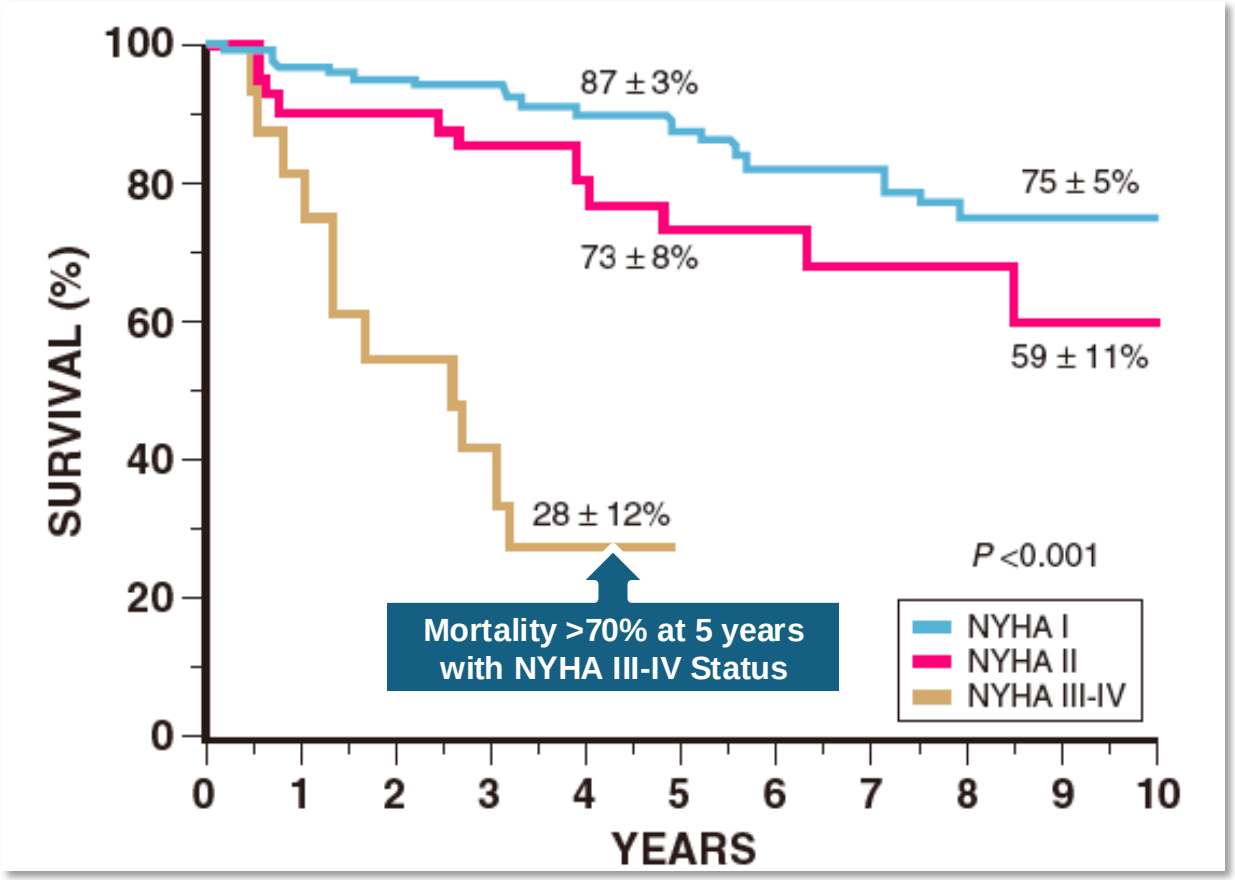
Disclosure of Relevant Financial Relationships

Within the prior 24 months, I have had a relevant financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

Nature of Financial Relationship	Ineligible Company
Grant/Research Support	Edwards Lifesciences, Medtronic, Abbott, Boston Scientific, Jenavalve
Consultant Fees/Honoraria	None
Individual Stock(s)/Stock Options	None
Royalties/Patent Beneficiary	None
Executive Role/Ownership Interest	None
Other Financial Benefit	None

Background

- Untreated severe, symptomatic AR is associated with high mortality especially in those with NYHA III/IV symptoms[1]
- Surgery is the only recommended intervention for patients with native severe AR[2]
- Yet, a significant proportion of patients with severe AR remain untreated with surgery[3]
- Use of off-label TAVR devices for AR is associated with valve embolization (10%) and ≥moderate PVR (10%)[4] both of which increase mortality[5]



1. Dujardin K, et al. *Circulation*. 1999;99:1851-1857.
2. Otto CM, et al. *Circulation*. 2021;143:e72-e227.
3. Thourani VH, et al. *Structural Heart*. 2021;5:608-618.
4. Poletti E, et al. PURPOSE. *J Am Coll Cardiol Intv*. 2024;1597–1606
5. Poletti E, et al. PANTHEON. *J Am Coll Cardiol Intv* 2023;16:1974–1985

Trilogy Porcine Pericardial Valve

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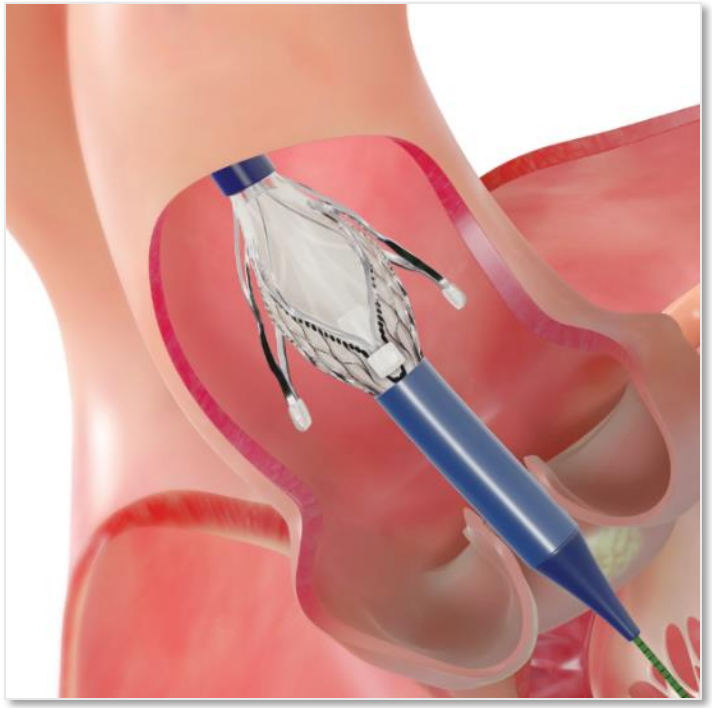
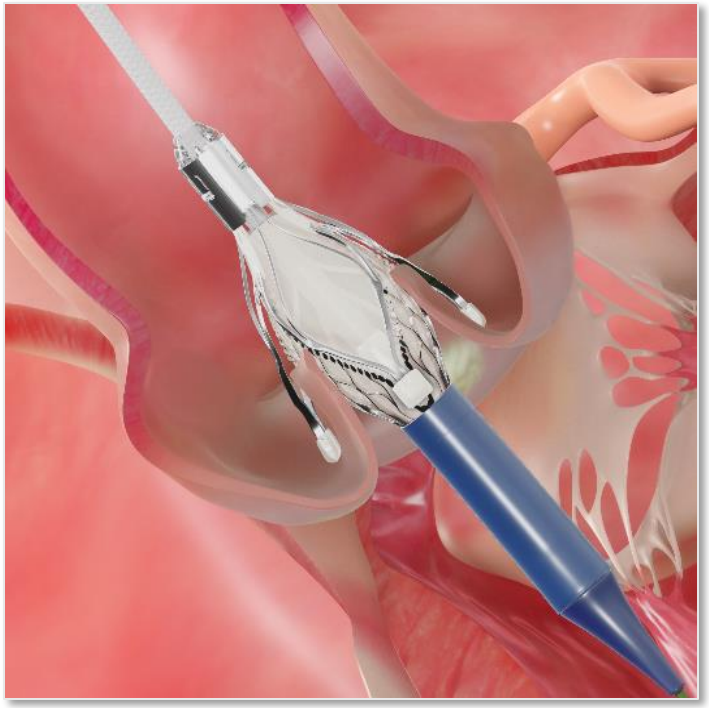
The Trilogy THV System is for <u>Investigational Use Only</u> in the United States and is Limited by Federal (or United States) law for this use.



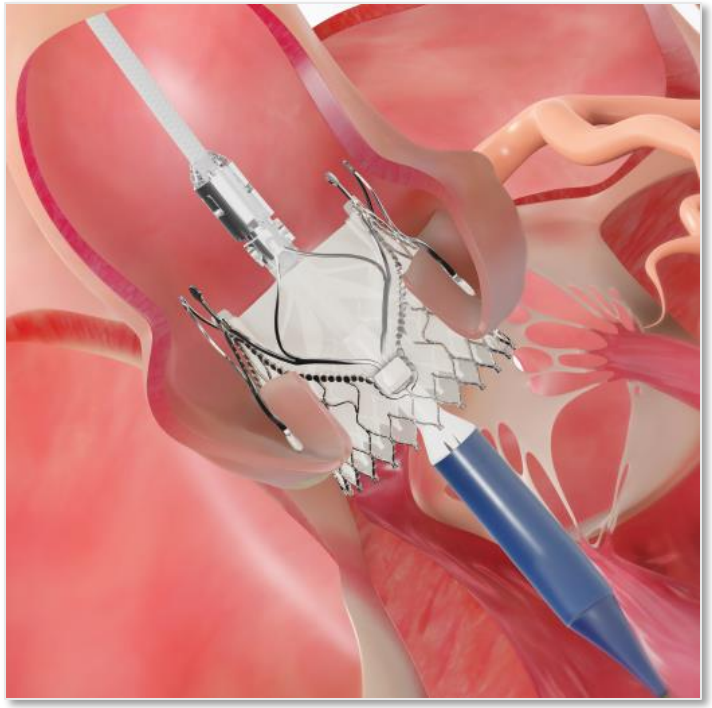
Alignment

Aligns THV with native cusps



Positioning/Anchoring

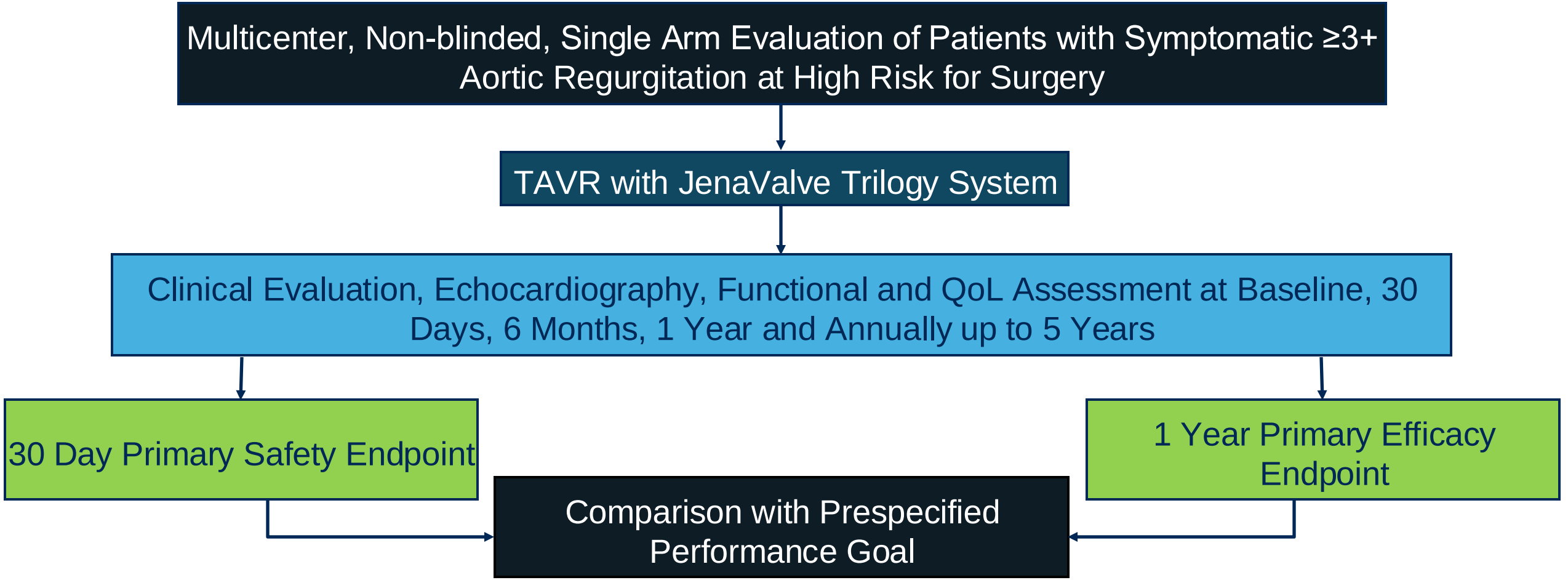
Locators “clip” onto native leaflets forming a natural seal and stable securement



Deployment

Large open cells provide access to low coronaries. Flared sealing ring conforms to annulus

ALIGN AR Study Design



Key Inclusion and Exclusion Criteria

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Inclusion

- Adult patients with moderate-to-severe or severe (Grade ≥3) AR assessed according to ASE criteria
- NYHA Class II or greater symptoms
- High-risk for surgery defined by the heart team

Exclusion

- Congenital unicuspid or bicuspid aortic valve
- Ascending aorta diameter >5.0 cm
- Previous prosthetic aortic valve
- Mitral regurgitation > moderate
- CAD requiring revascularization

Top 10 Enrolling Sites

	Principal Investigator	Number of Patients
Cedars-Sinai Medical Center	Raj Makkar	96
Columbia University Medical Center/NYP	Torsten Vahl	57
Piedmont Heart Institute	Vinod Thourani	30
Rutgers/Robert Wood Johnson	Mark Russo	27
University of Washington	Jamie McCabe	27
California Pacific Medical Center	David Daniels	25
University of Michigan	Stan Chetcuti	24
Medstar/Washington Hospital Center	Lowell Satler	22
Intermountain Health	Brian Whisenant	19
Oregon Health Sciences University	Firas Zahr	19
Scripps Health	Curtiss Stinis	17

500 patients were enrolled at 28 US sites

Baseline Characteristics (n=500)

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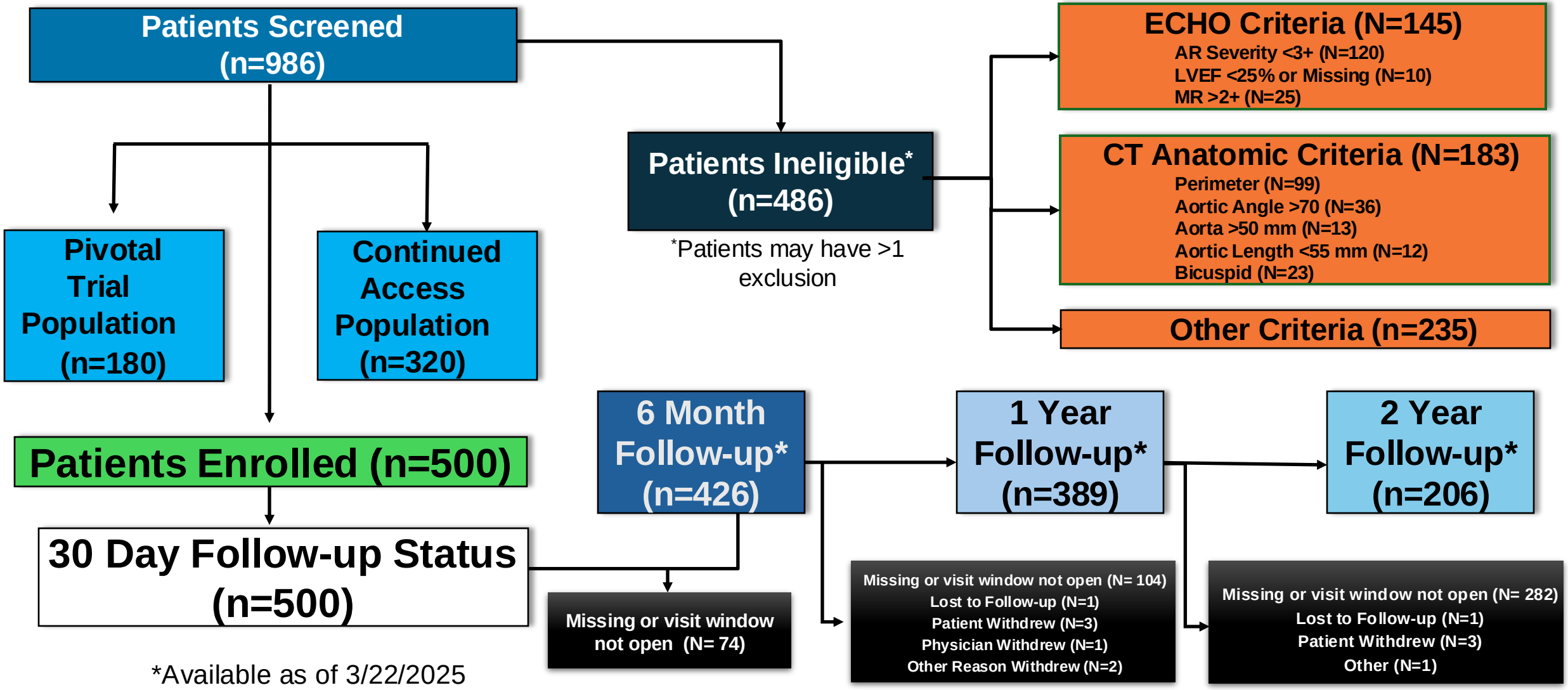
Demographics and Co-Morbidities		Vascular & Other Co-Morbidities	
Age (years)	76.6 ± 10.3	Atrial Fibrillation	39.0%
Female	46.2%	Pulmonary Hypertension	19.8%
BMI – kg/m^2	25.6 ± 5.7	Prior Permanent Pacemaker	15.2%
STS Score	3.9 ± 3.3	Left Bundle Branch Block	7.6%
NYHA Class III or IV	61.6%	RBBB/Bifascicular Block	12.2%
Hypertension	79.2%	Prior CABG	9.2%
Diabetes	16.0%	Prior PCI	19.0%
Renal Insufficiency	29.8%	Prior CVA	9.6%
Right Ventricular Dysfunction	5.2%	Carotid Disease	8.0%
Prior Endocarditis	5.8%	Peripheral Arterial Disease	10.0%

Screening and Patient Disposition



*Available as of 3/22/2025

Index Procedure

Procedural Factors	
Valve Size Implanted Small Medium Large	 24.8% 24.1% 51.0%
Post-Dilation	3.7%
Procedure Time (min)	69.5 ± 33.3
Sheath Time (min)	28.2 ± 27.1
Procedural Complications	
In-procedural Death	**0**
Annular Rupture	0
Ventricular Perforation	0
Coronary Obstruction	0
Valve Embolization	**1.6% (8)**
Aortic Dissection	0.6% (3)

Procedural Outcomes

Technical Success	**95.2%**
Procedural Death	0.0%
Surgery or intervention related to device/procedure	3.6%
THV deployment success	98.0%
Delivery system success	99.2%
Device Success	**96.4%**
Procedural Death	0.0%
THV deployment success	98.0%
Patient prosthesis mismatch (EOAi ≤0.85) at 30 days	0.4%
AOV gradient <20 mmHg at 30 days	100.0%
AOV peak velocity <3 m/s at 30 days	100.0%
Total AR Regurgitation: Moderate (n=3) or Severe (n=0) at 30 days	0.6%

Primary Safety Endpoint at 30 Days

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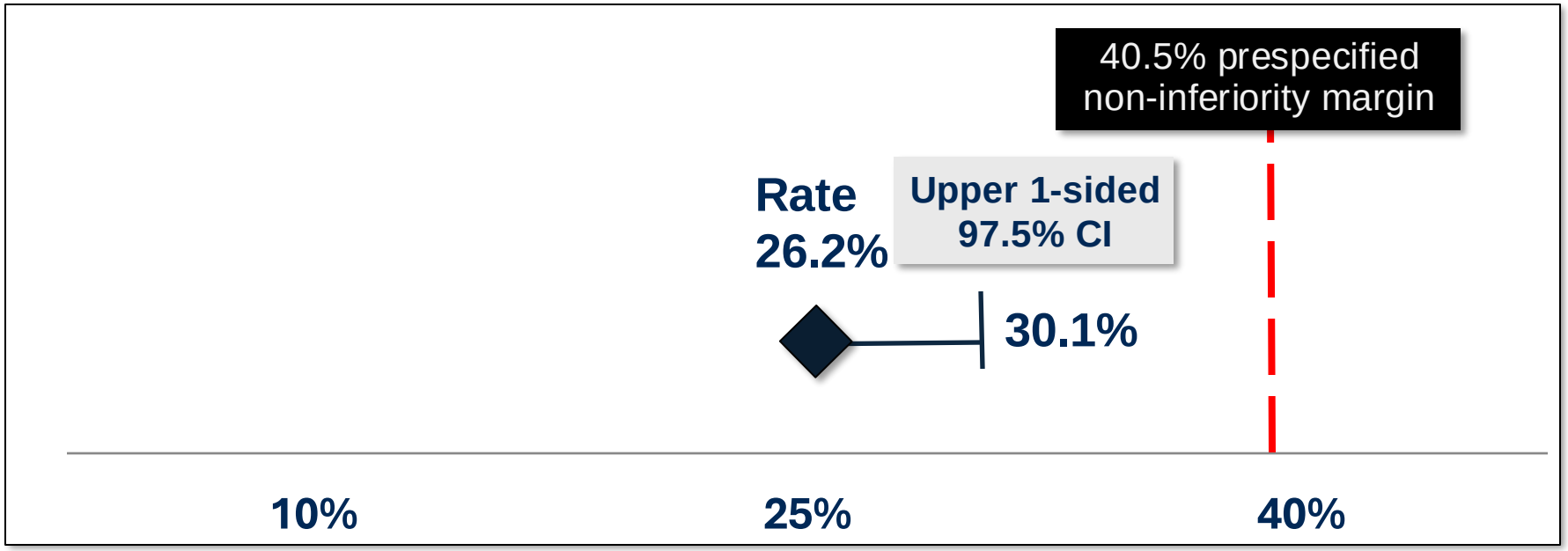
	ALIGN-AR (n=500)
Primary Safety Composite Endpoint	**26.2% (131)**
All Cause Mortality	1.4% (7)
Cardiovascular Mortality	1.2% (6)
Any Stroke	2.0% (10)
Disabling Stroke	0.8% (4)
Non-disabling Stroke	1.2% (6)
Major/Life Threatening Bleeding	3.2% (16)
Major Vascular Complication	2.8% (14)
Acute Kidney Injury Stage 2,3 or Dialysis (7 Days)	0.6% (3)
Surgery/Intervention Related to the Device	4.4% (22)
New Pacemaker Implantation	23.3% (99)
Pre-existing Pacemaker	15.2% (76)
≥ Moderate Total Regurgitation	0.6% (3)

Primary Safety Endpoint at 30 Days

THE ALIGN AR TRIAL

	ALIGN-AR (n=180)	ALIGN-AR CAP (n=320)
Primary Safety Composite Endpoint	**26.7% (48)**	**25.9% (83)**
All Cause Mortality	2.2% (4)	0.9% (3)
Cardiovascular Mortality	1.7% (3)	0.9% (3)
Any Stroke	2.2% (4)	1.9% (6)
Disabling Stroke	1.1% (2)	0.6% (2)
Non-disabling Stroke	1.1% (2)	1.3% (4)
Major/Life Threatening Bleeding	4.4% (8)	2.5% (8)
Major Vascular Complication	3.9% (7)	2.2% (7)
Acute Kidney Injury Stage 2,3 or Dialysis (7 Days)	1.1% (2)	0.3% (1)
Surgery/Intervention Related to the Device	5.0% (9)	4.1% (13)
New Pacemaker Implantation	24.0% (36)	23.0% (63)
Pre-existing Pacemaker	16.7% (30)	14.4% (46)
≥ Moderate Total Regurgitation	0.6% (1)	0.7% (2)

Primary Safety Endpoint at 30 Days*

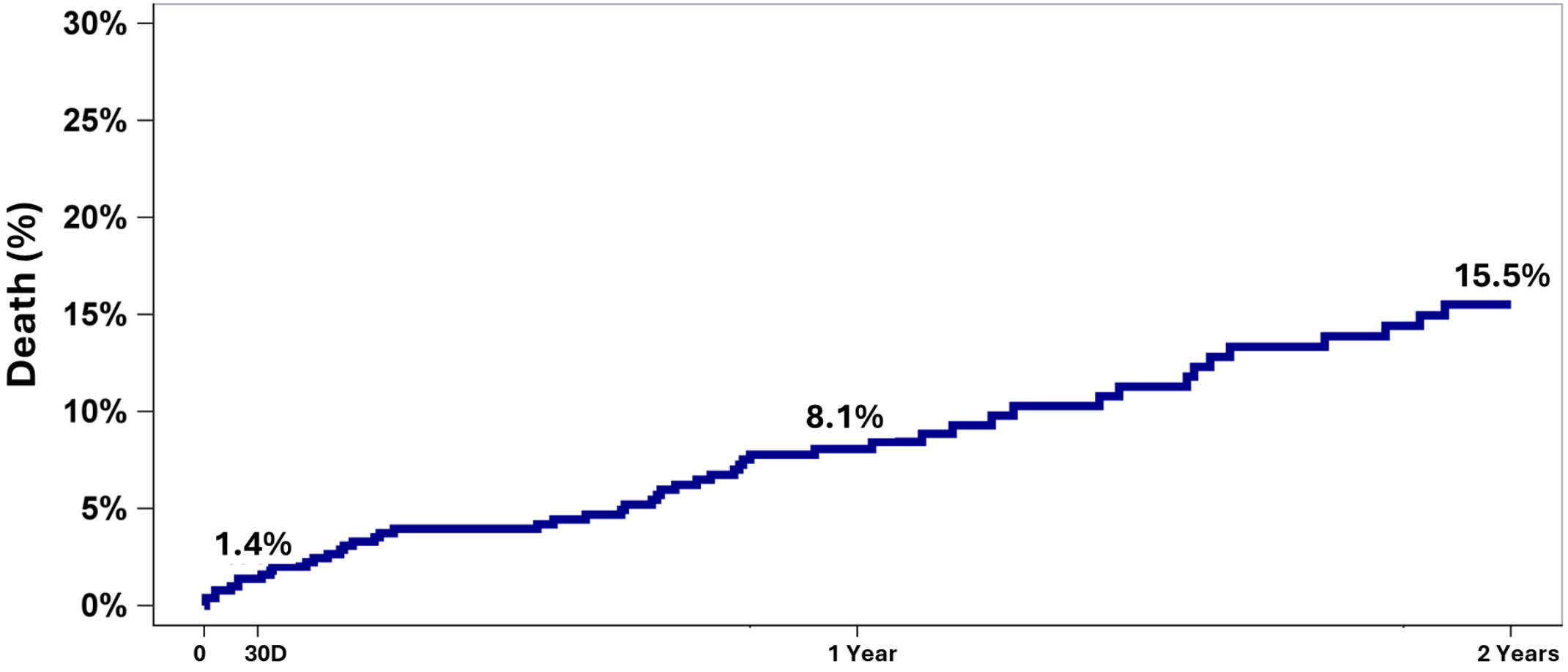


p<0.0001

***Composite of 30-day all-cause mortality, any stroke, life-threatening/major bleeding, major vascular complication, AKI ≥2 or dialysis, valve intervention, new permanent pacemaker, ≥ moderate valvular regurgitation**

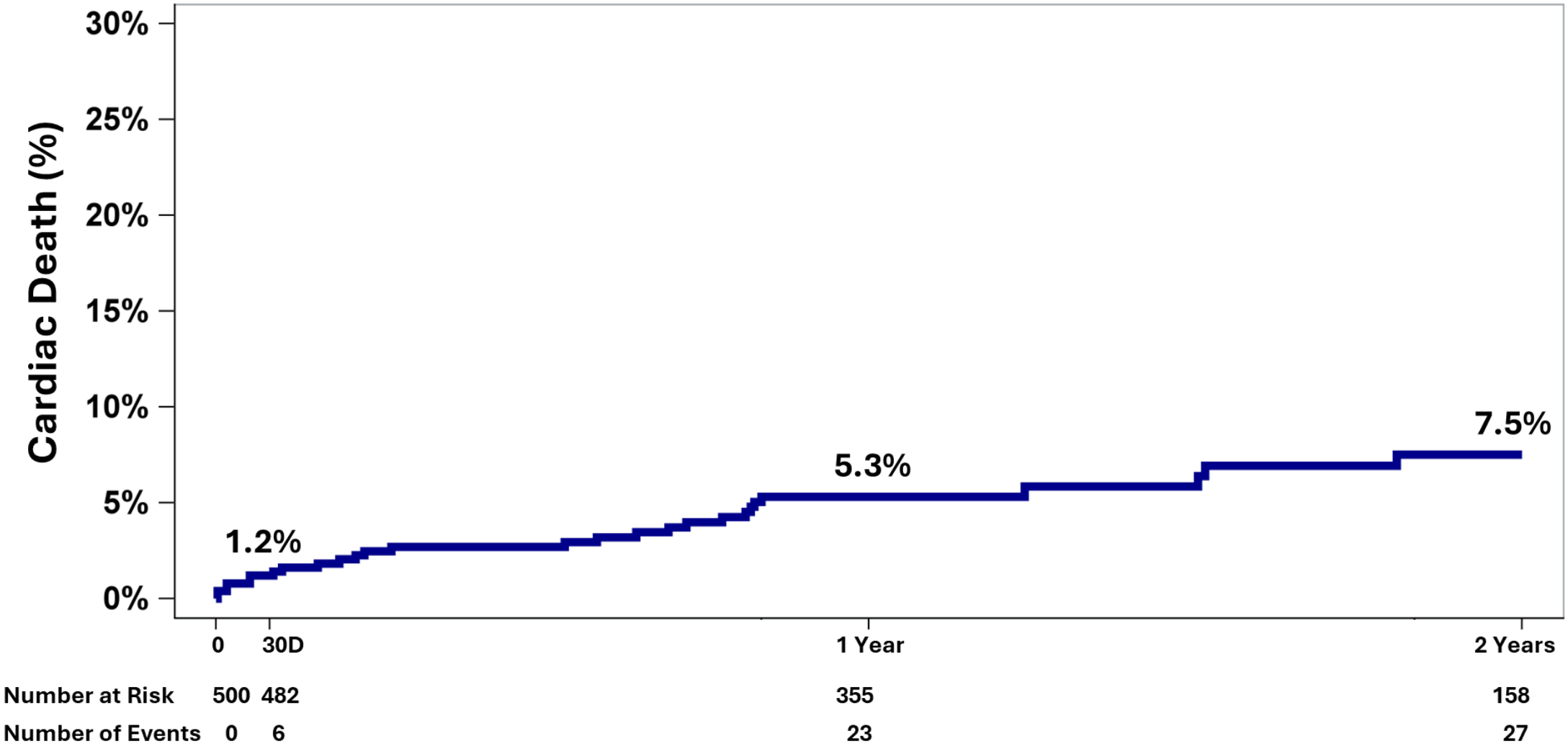
1. Feldman TE, Reardon MJ, Rajagopal V, et al. The REPRISE III Randomized Clinical Trial. *JAMA.* 2018; 319: 27-37.
2. Makkar RR, Cheng W, Waksman R, et al. Self-expanding intra-annular versus commercially available transcatheter heart valves in high and extreme risk patients with severe aortic stenosis (PORTICO IDE): a randomised, controlled, non- inferiority trial. *Lancet.* 2020; 369: 669-683.
3. Thiele H, Kurz T, Feistritzer H-J, et al. Comparison of newer generation self-expandable vs. balloon-expandable valves in transcatheter aortic valve implantation: the randomized SOLVE-TAVI trial. *Eur Heart J.* 2020; 41:1890-1899.

All Cause Mortality

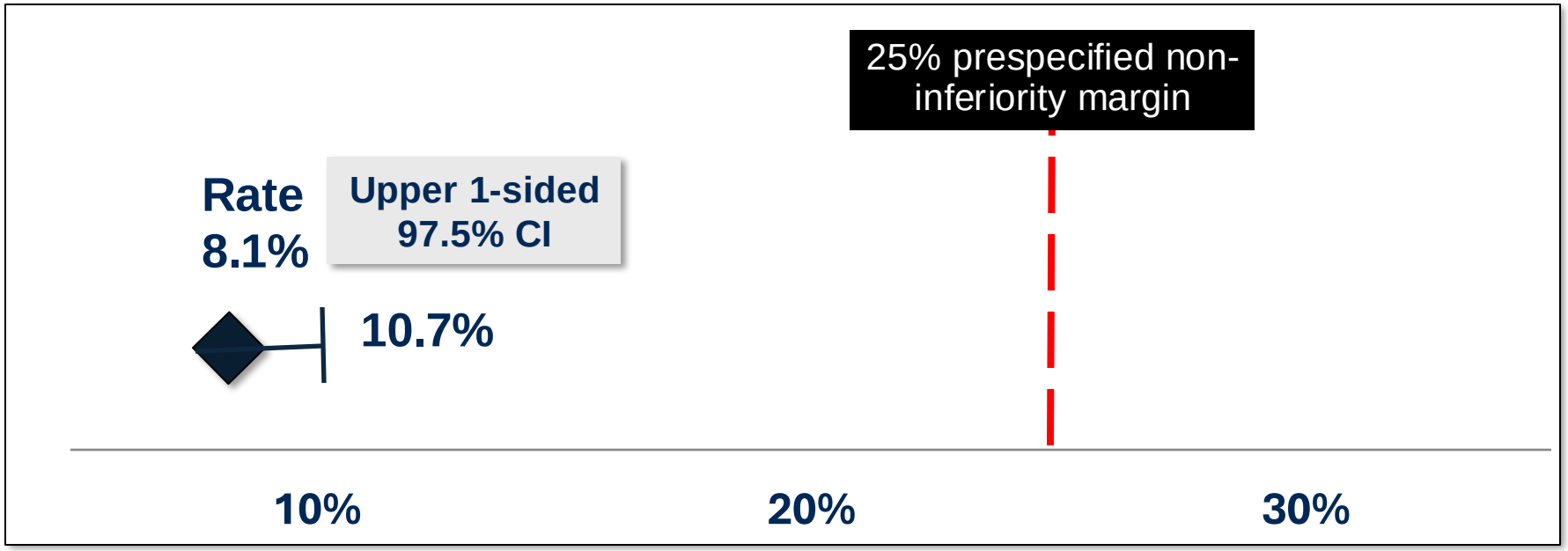


Number at Risk	500	482	354	156
Number of Events	0	7	35	50

Cardiac Mortality



Primary Efficacy Endpoint at 1 Year*

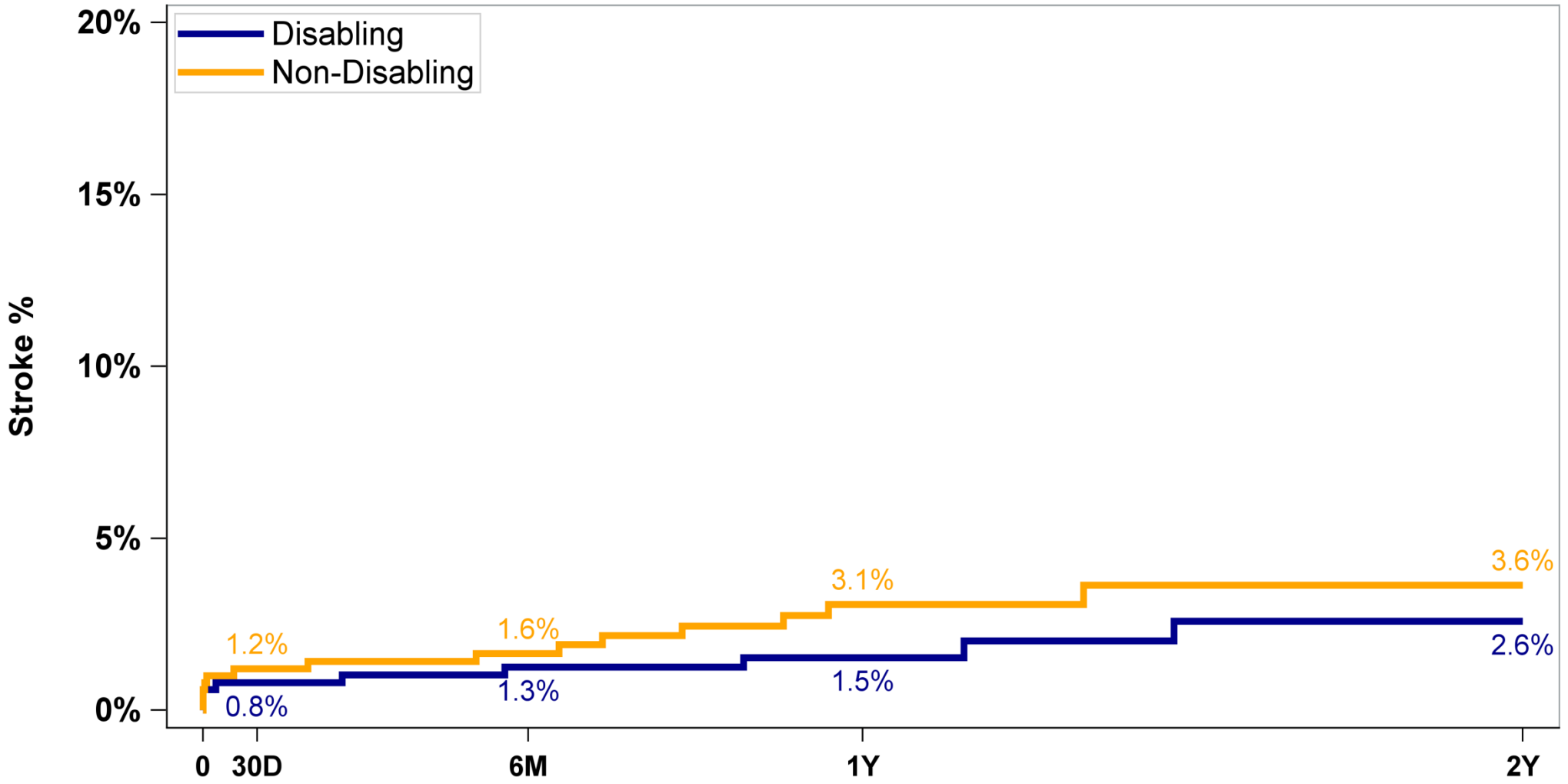


p<0.0001

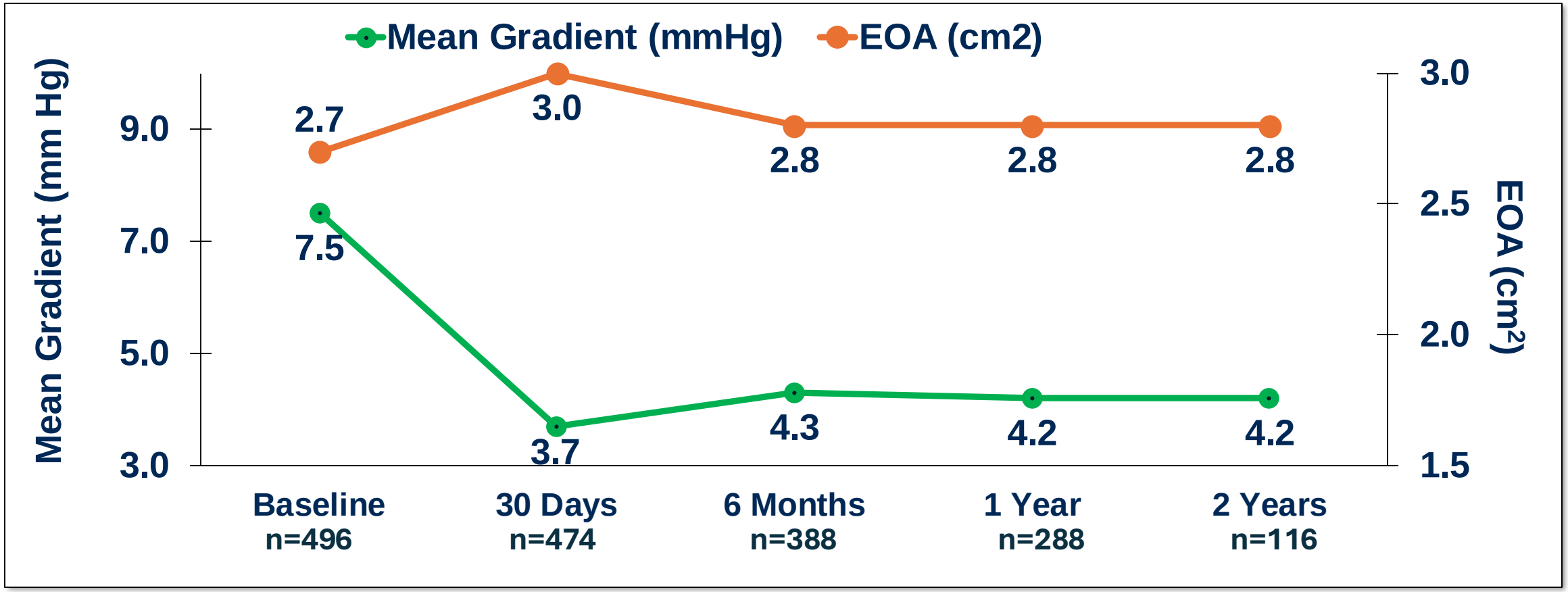
***All Cause Mortality at 1 Year**

1. Fiedler AG, Bhambhani V, Laikhter E, et al. *Heart. 2018;* 104:835-840.
2. Kamath AR, Varadarajan P, Turk R, et al. *Circulation. 2009:* 120:S134-8.
3. Turk R, Varadarajan P, Kamath A, et al. *Ann Thorac Surg.* 2010; 89: 731-737.
4. Sampat U, Varadarajan P, Turk R, Kamath A, Khandhar S, Pai RG. *J Am Coll Cardiol. 2009;* 54:452-457.

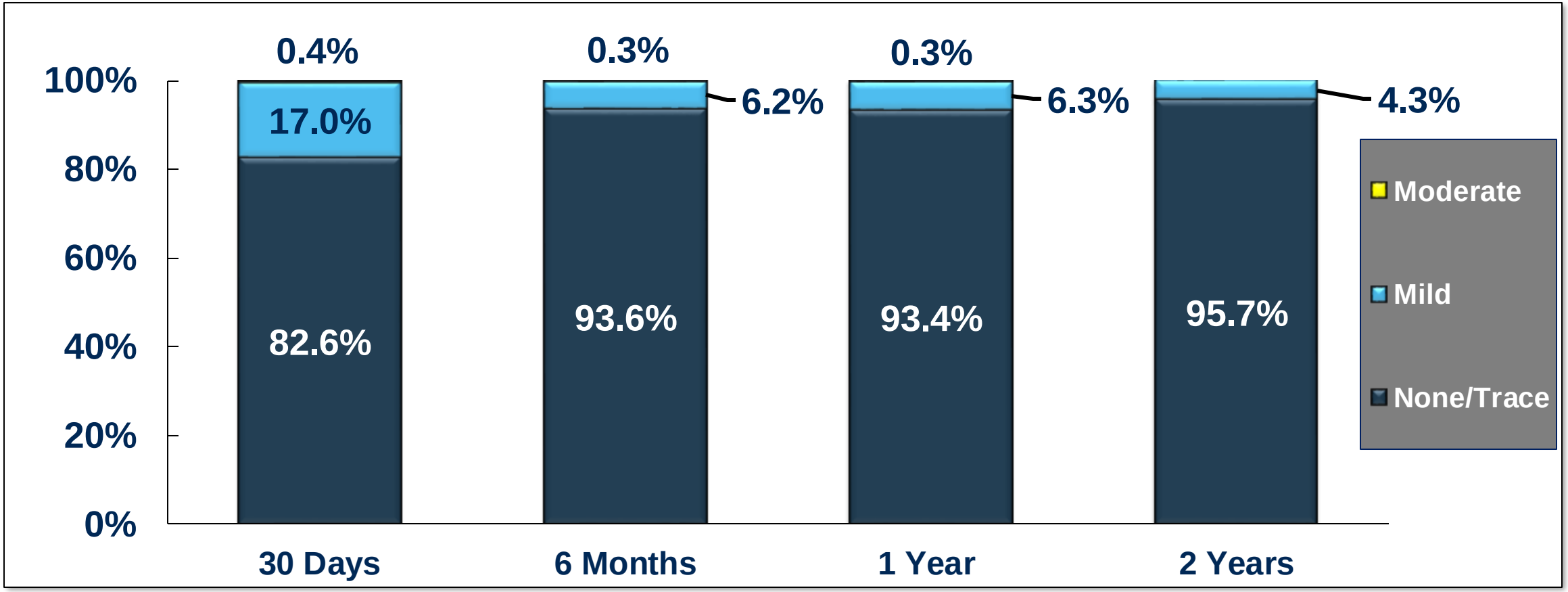
All Stroke


Disabling
Non-Disabling
Stroke %
20%
15%
10%
5%
0%
0
30D
6M
1Y
2Y
1.2%
1.6%
3.1%
3.6%
0.8%
1.3%
1.5%
2.6%

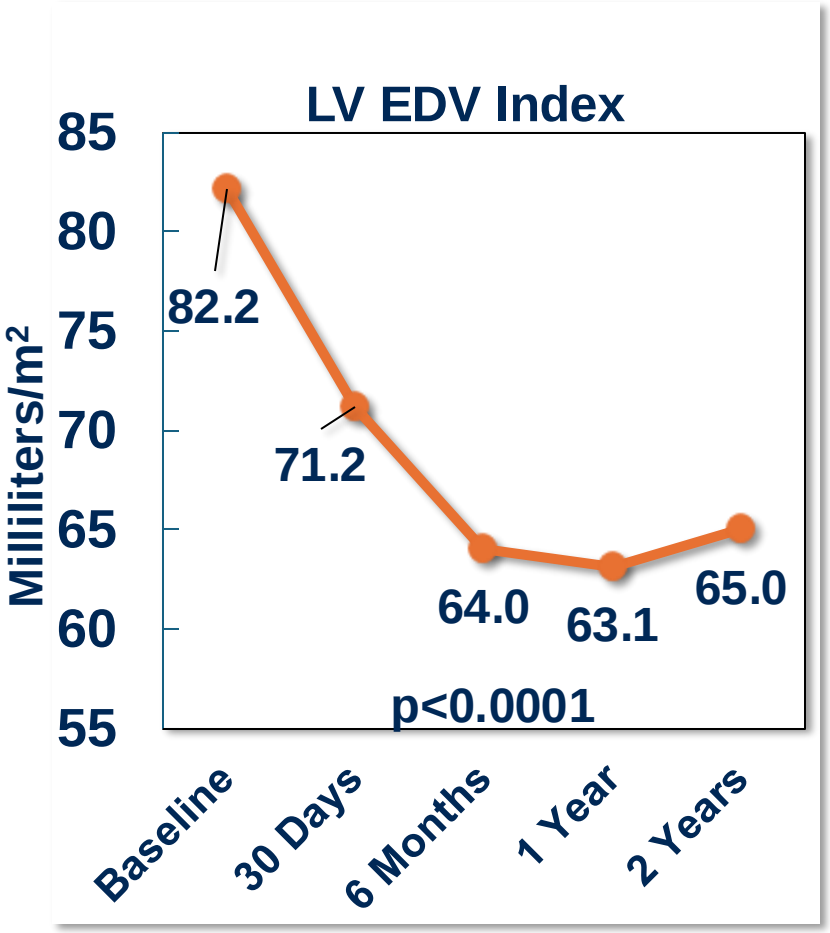
Hemodynamic Valve Performance

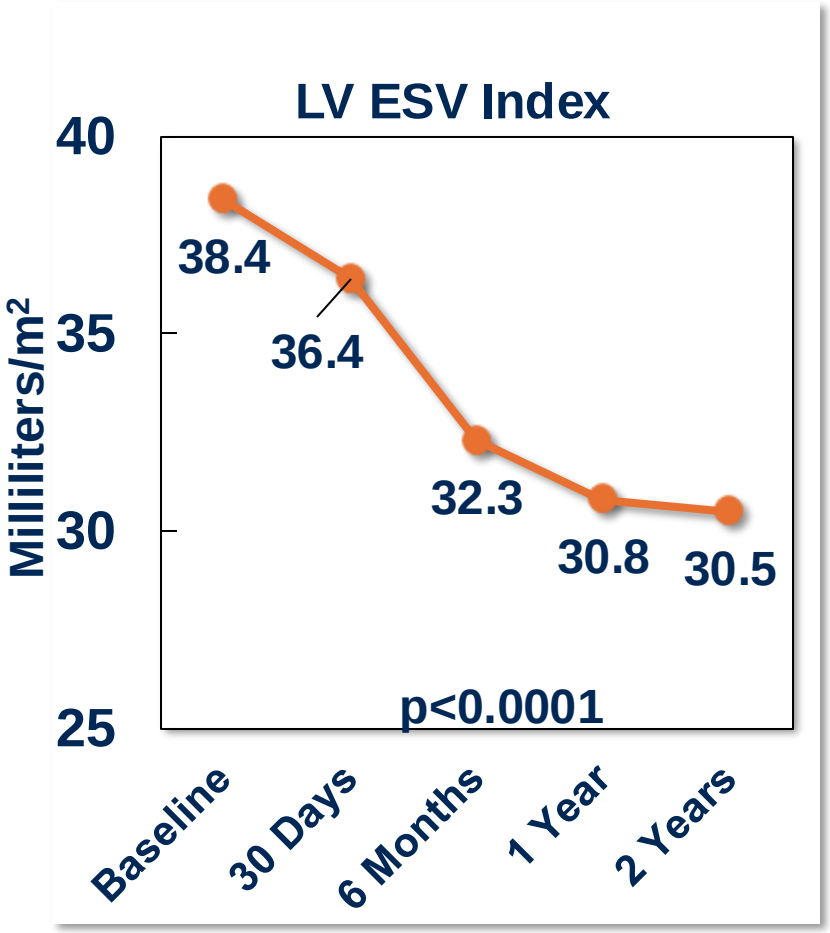


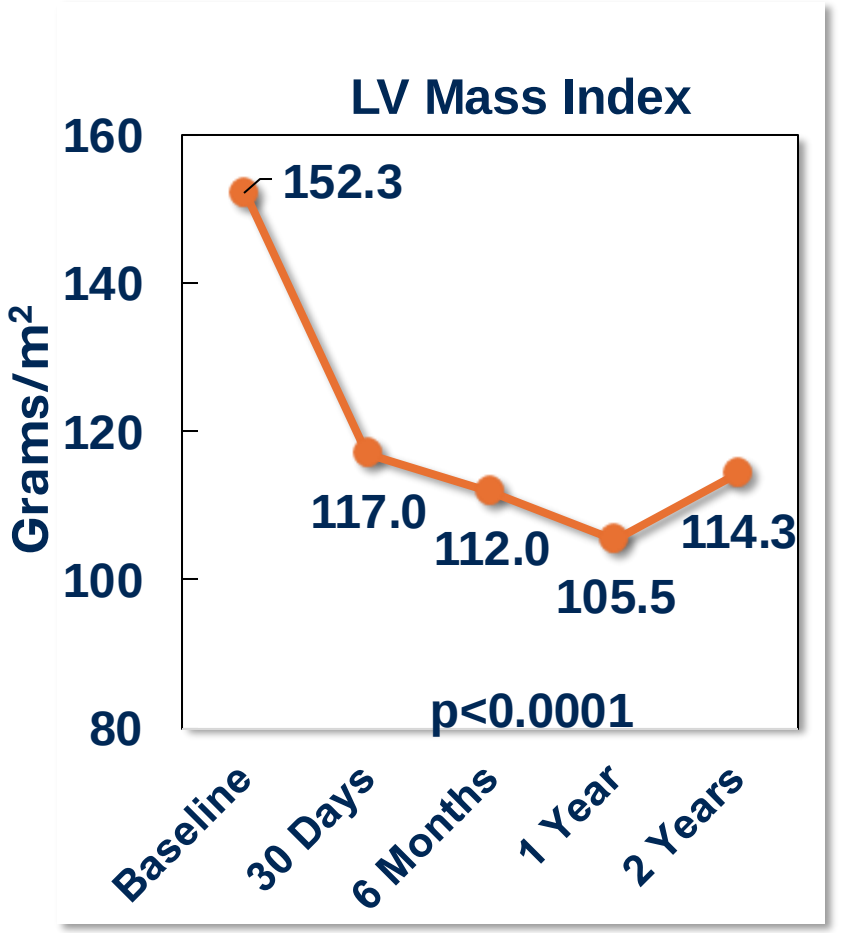
Paravalvular Regurgitation



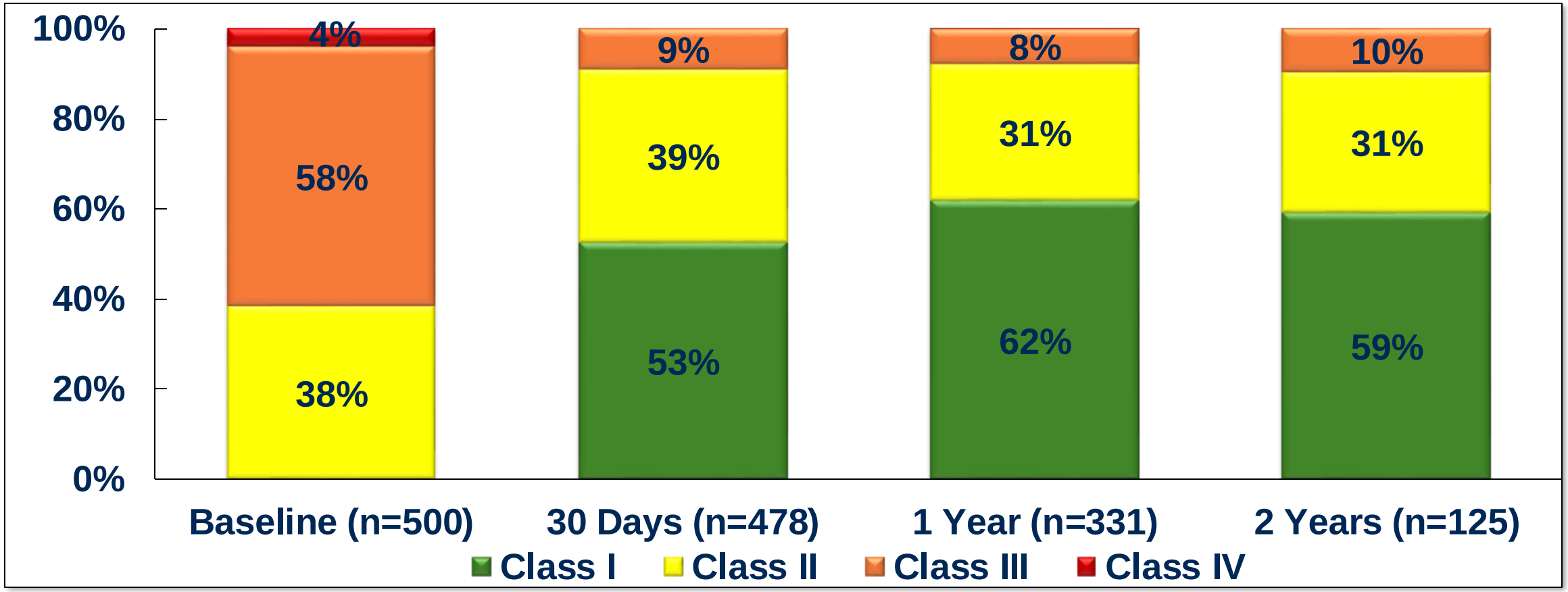
Left Ventricular Remodeling



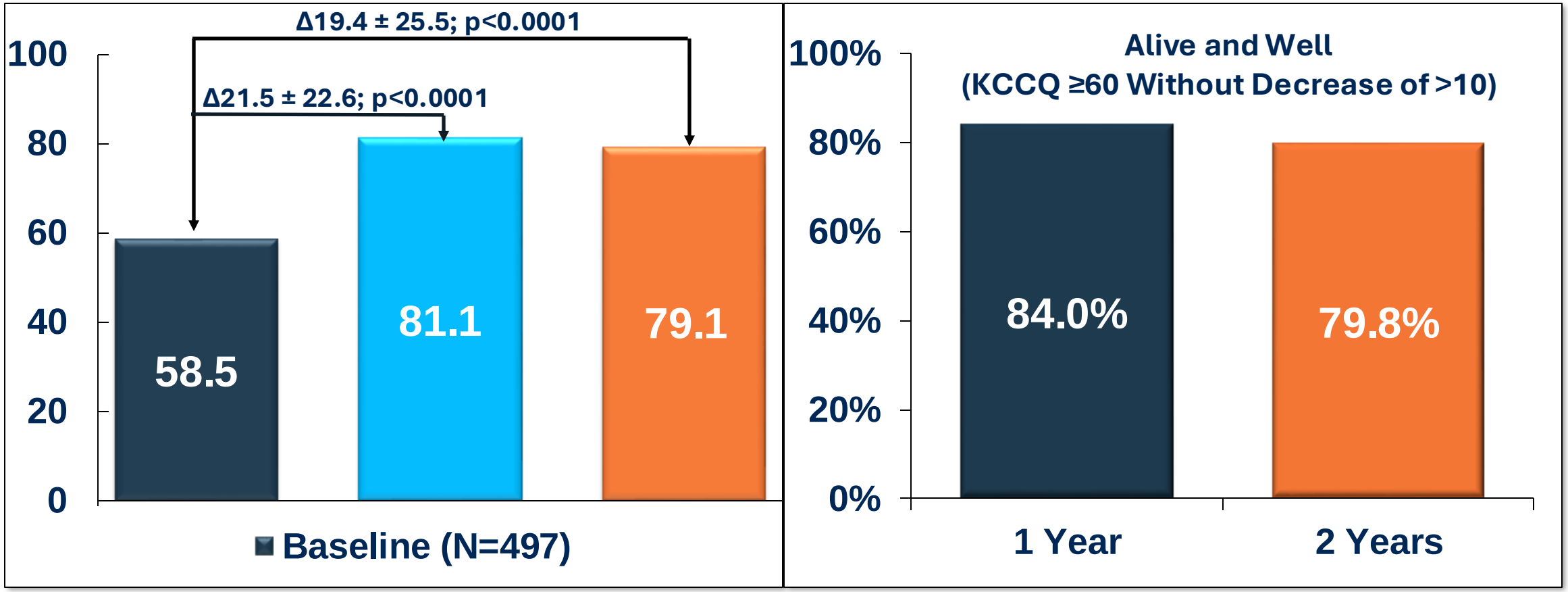




NYHA Functional Class

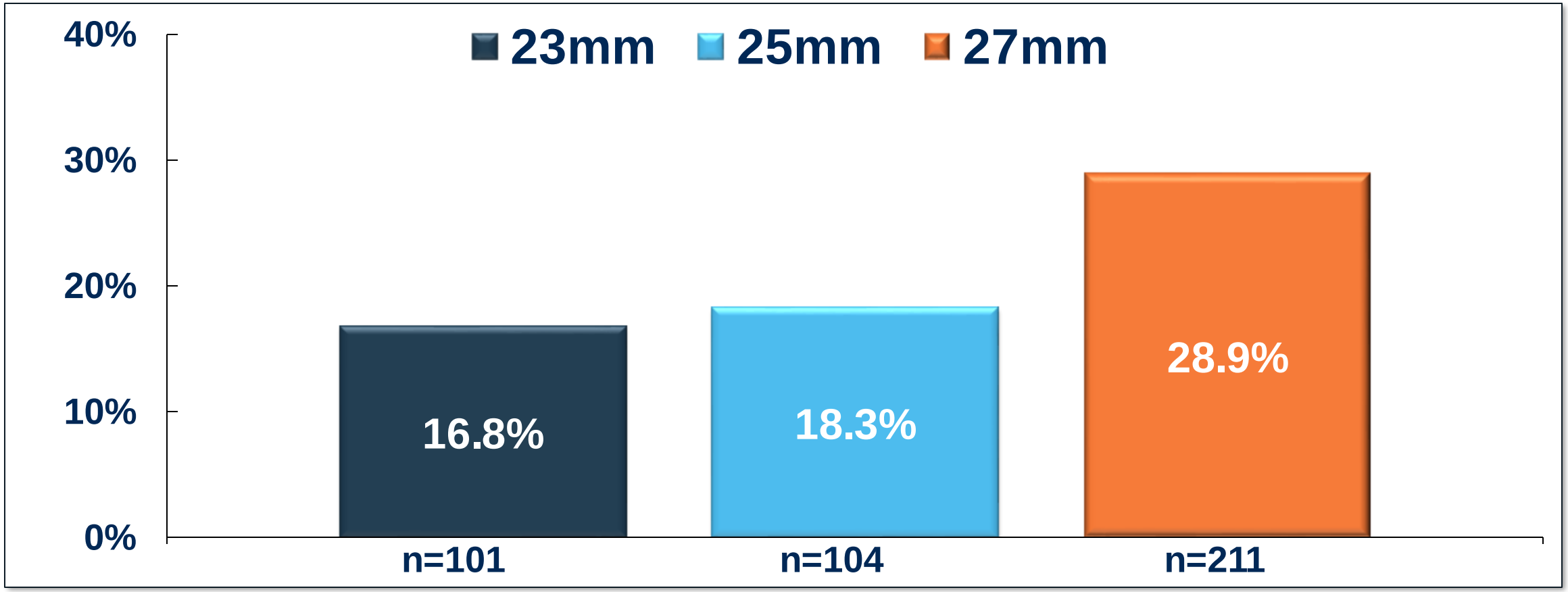


KCCQ-Overall Summary



KCCQ-OS scores range from 0 to 100, with higher scores indicating better health status. A large change is defined as ≥20 points compared with baseline.

Pacemaker by Valve Size*



*Excludes 76 patients with prior pacemaker and 8 patients who did not receive the Trilogy THV

Predictors of New Pacemaker

	Odds Ratio	95% Wald Confidence Limits		p-value
History of Congestive Heart Failure	1.92	1.15	3.21	0.01
Baseline Severe AR vs. Moderate to Severe	1.88	1.10	3.19	0.02
Annular Perimeter ≥85mm	2.08	1.24	3.46	0.005
Baseline RBBB	6.66	3.48	12.75	<0.0001

Variables not associated with new pacemaker included NYHA classification, STS score, LBBB, Oversizing, Depth by echocardiography, LVEF, LV Dimensions, LV Volume, LV Mass, Site Experience, Enrollment Tercile, Baseline KCCQ

Conclusions

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In the largest cohort of high-risk patients with symptomatic native aortic regurgitation undergoing TAVR with the JenaValve:

- **The primary safety and efficacy outcomes achieved prespecified performance goals**
  - Safety - 26.2% vs. 40.5%, p<0.0001
  - Efficacy (all-cause mortality) - 8.1% vs. 25%, p<0.0001
- **High device success rates (96.4%) and acceptable rates of complications highlight a favorable risk-benefit profile**
  - Procedural death 0%, 30-day death 1.4%, valve embolization 1.6%, 30-day disabling stroke 0.8%
- **Favorable valve performance was evidenced by consistently low valve gradients, large valve areas, and low rates of valvular regurgitation**
  - EOA ~ 2.8 cm^2 and mean gradient 4.2 mm Hg, ≥ moderate total AR 0.9% at 2 years

Conclusions (continued)

THE ALIGN AR TRIAL

- **Sustained improvement in functional status (NYHA class improvement) and patient-reported quality-of-life measures (KCCQ score improvement)**
  - NYHA class I/II: 90% at 2 years
  - KCCQ-OS score 58.5 at baseline to 79.1 at 2 years
- **Significant reductions in LV end systolic and diastolic volumes and regression of LV mass**
  - LVESVI 38.4 ml/m^2 at baseline decreased to 30.5 ml/m^2 at 2 years
  - LV mass index decreased from 152.3 g/m^2 to 114.3 g/m^2
- **New pacemaker implantation rates are 23% reflecting underlying pathology**
  - Risk factors include larger annular sizes, heart failure, severity of AR, and RBBB

The ALIGN AR Trial
Clinical Implications

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The TRILOGY THV is a unique TAVR device for symptomatic patients with ≥3+ AR. Upon FDA approval, such patients at high-risk for surgery will have a new and much-needed therapeutic option.

The technical success, reassuring safety profile and positive clinical outcomes in ALIGN-AR support a randomized trial comparing this device to SAVR in a patient population not at high-risk for surgery.

The ARTIST Trial

Aortic Regurgitation Trial Investigating Surgery and Trilogy

MRtist TRIAL

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Stephan Baldus, University Cologne
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