PERCUTANEOUS DEVICES FOR TRICUSPID REGURGITATION

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DISCLOSURES

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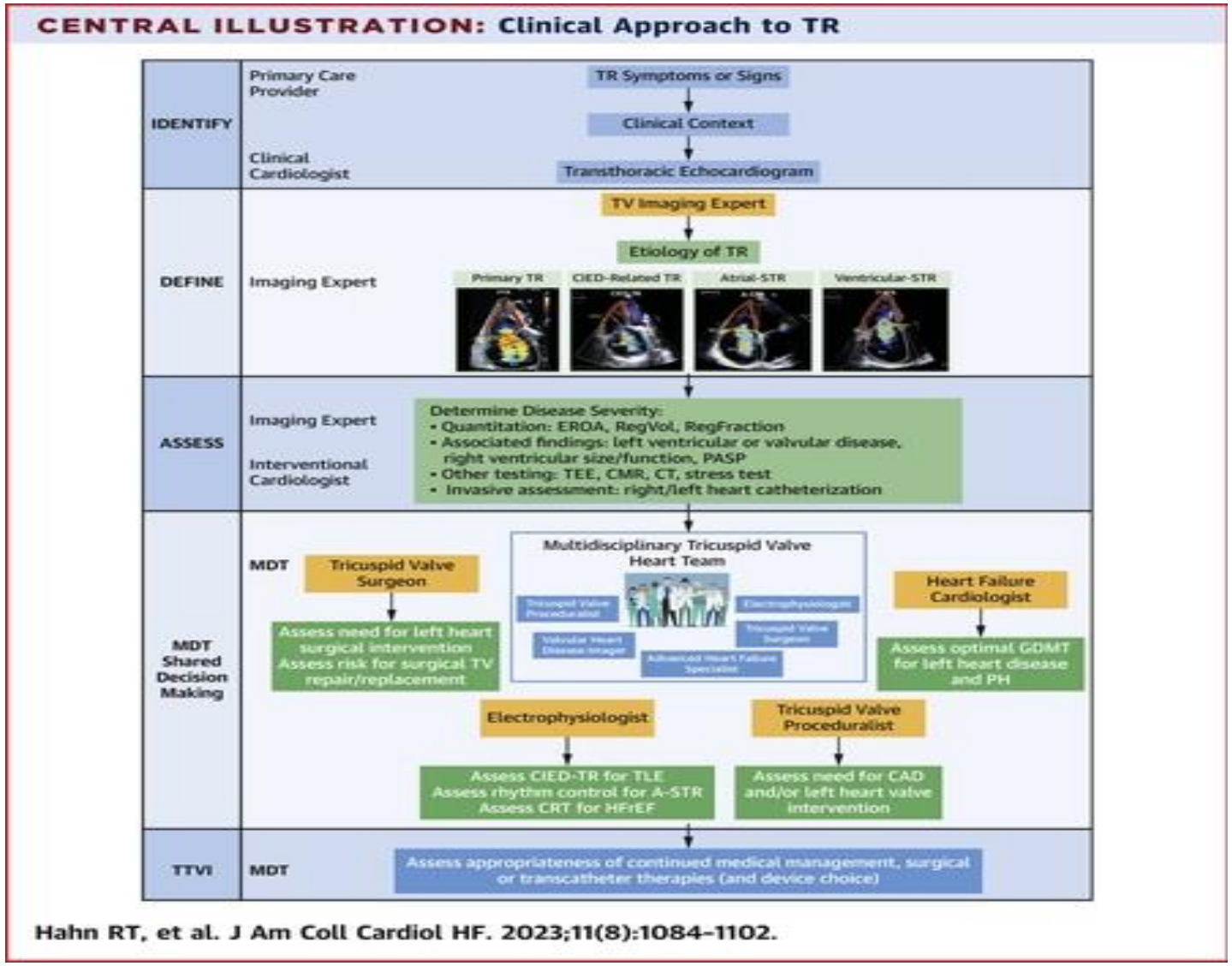
Proctor: Edwards Lifesciences, Medtronic, Boston Scientific

Medical Advisory Board: Boston Scientific, Recor Medical

Speakers Bureau: Edwards Lifesciences, Abbott Vascular, Boston Scientific

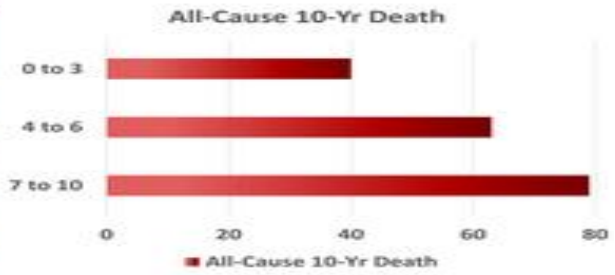


Rebecca T. Hahn et al. *J Am Coll Cardiol HF* 2023; 11:1084-1102.

JACC Heart Failure

A Risk Model for 10-Year All-Cause Mortality in patients with TR

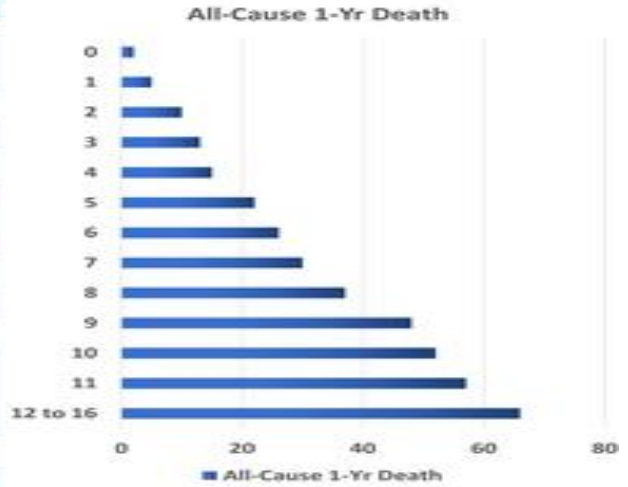
TRIO Score Parameters	Score
Age	
70-79 years	1
≥80 years	2
Male sex	1
Creatinine of ≥2 ml/dl	2
Congestive heart failure	2
Lung disease	1
Aspartate aminotransferase of ≥40 U/L	1
Heart rate 90 bpm or higher	1
Severe TR	1
Total	10



Lara-Breitinger KM. et al. Mayo Clin Proc. 2022 Aug;97(8):1449-1461

B Risk Model for 1-Year All-Cause Mortality in Isolated Secondary TR

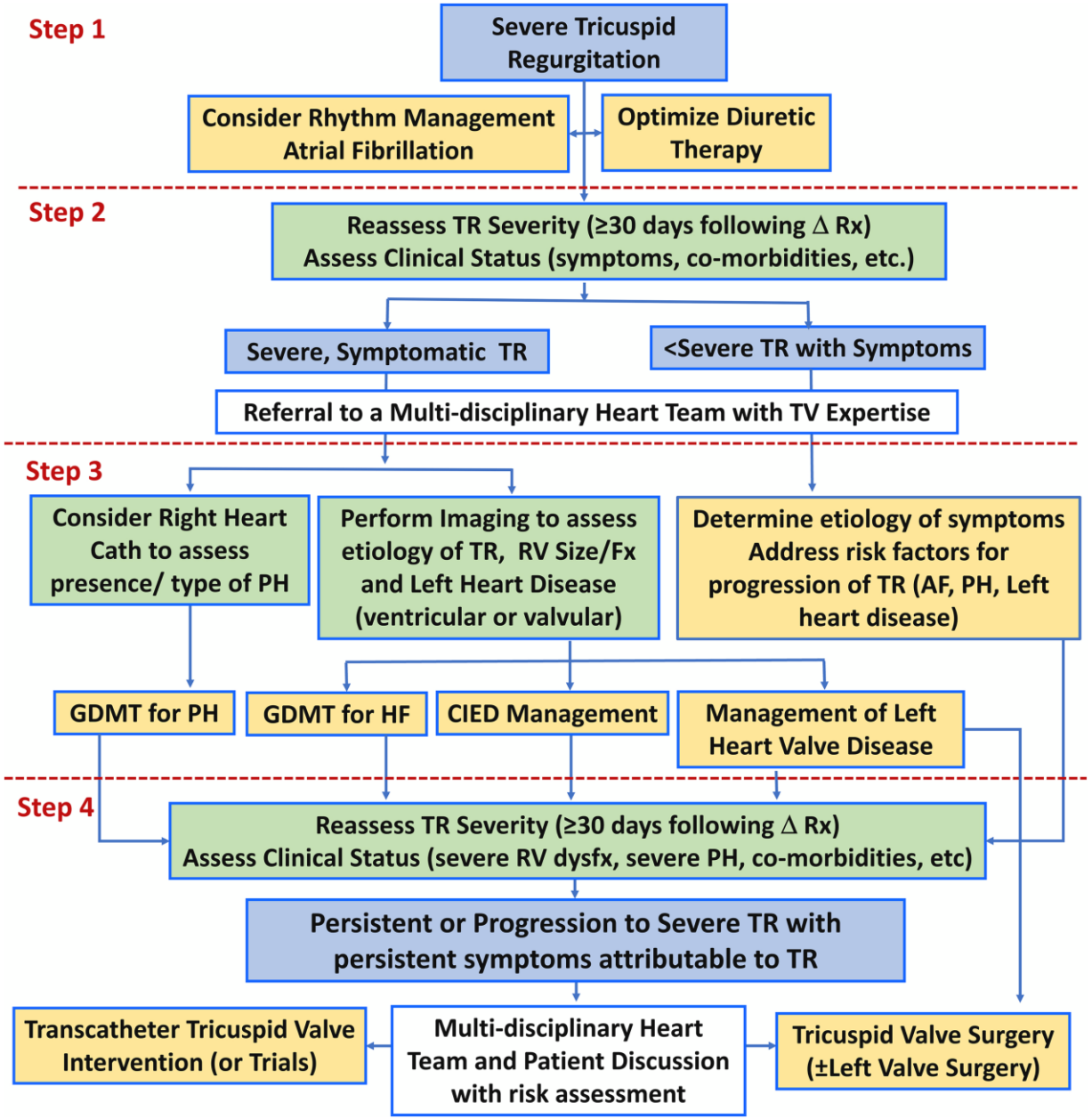
Parameter	Score
Age	
65-74 yrs	1
75+ yrs	2
Myocardial infarction	1
Peripheral vascular disease	1
Chronic lung disease	1
Chronic kidney disease (creatinine >1.4 mg/dL)	1
Loop diuretic use	1
Anemia (Hgb <10 g/dL)	1
Thromocytopenia (platelet <15 k/μL)	1
INR >1.5	1
Albumin <3.0 g/dL	2
RV Systolic Fx	
Mildly impaired	1
Moderately impaired	2
Severely impaired	3
Right ventricular systolic pressure >50 mmHg	1
TOTAL	16



Wang, TKM. et al. J Am Coll Cardiol Img. 2022:15(5):731-744

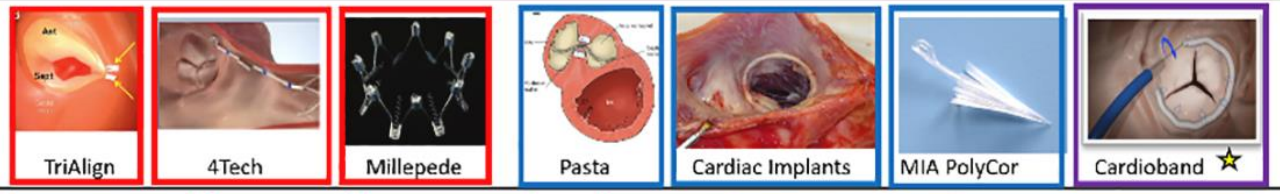
Rebecca T. Hahn et al. *J Am Coll Cardiol HF* 2023; 11:1084-1102.

JACC Heart Failure



Rebecca T. Hahn et al. *J Am Coll Cardiol HF* 2023; 11:1084-1102.

JACC Heart Failure

Anchor/ Mechanism	Ideal Anatomy*	Historical and New Tricuspid Valve Technologies
Annuloplasty (Direct and Indirect) Device	• Atrial Secondary TR • Mild leaflet tethering • Central jet location • Sufficient landing zone and imaging for anchoring	
Leaflet Device/ Spacers	• Small septolateral gap ≤7 mm • Anteroseptal jet location • Small prolapse or flail region • Trileaflet morphology • Good multi-level imaging	
Heterotopic Valve (in IVC/SVC)	• Appropriate caval diameters • No other direct valve treatment option • Flow reversal into IVC • Preserved RV function	
Orthotopic Valve Replacement	• Annular size appropriate for device • Any leaflet morphology or jet location • Any primary or secondary etiology • CIED related or incidental • Preserved RV function	

= Not available for clinical use = Early human use = Early Feasibility Trial = Randomized Controlled Trial ☆= CE mark approval in Europe

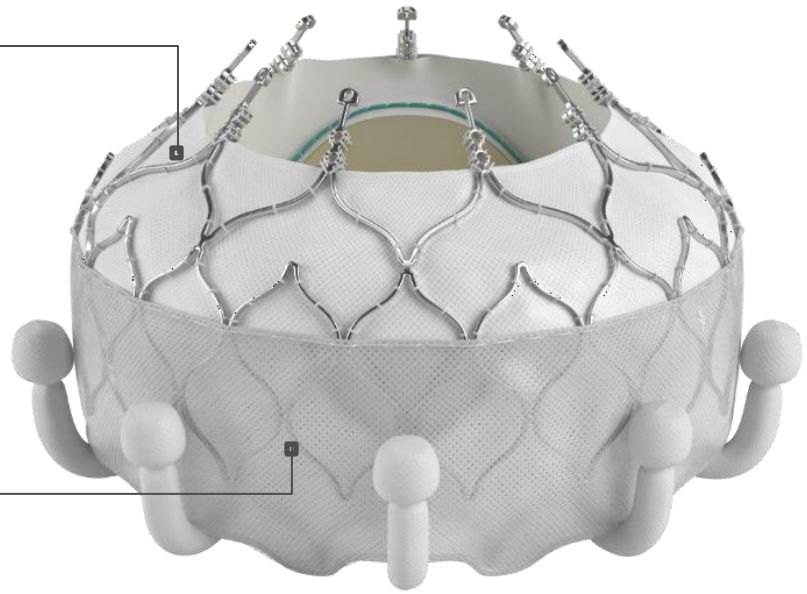
Rebecca T. Hahn et al. *J Am Coll Cardiol HF* 2023; 11:1084-1102.

JACC Heart Failure

EVOQUE TRANSCATHETER TRICUSPID VALVE REPLACEMENT SYSTEM

Designed for anatomical compatibility
Self-expanding shape-memory nitinol frame designed to conform to native valve anatomy

Designed to seal within native tricuspid annulus
Intra-annular sealing skirt and frame



4 sizes treat wide range of anatomies

44mm 48mm 52mm 56mm

Delivery System

Transfemoral **28 Fr** outer diameter **3 planes of movement**

SIMULTANEOUSLY PUBLISHED IN NEJM AND JACC

ORIGINAL ARTICLE

Transcatheter Valve Replacement in Severe Tricuspid Regurgitation

R.T. Hahn, R. Makkar, V.H. Thourani, M. Makar, R.P. Sharma, C. Haeffele, C.J. Davidson, A. Narang, B. O'Neill, J. Lee, P. Yadav, F. Zahr, S. Chadderdon, M. Eleid, S. Pislaru, R. Smith, M. Szerlip, B. Whisenant, N.K. Sekaran, S. Garcia, T. Stewart-Dehner, H. Thiele, R. Kipperman, K. Koulogiannis, D.S. Lim, D. Fowler, S. Kapadia, S. Harb, P.A. Grayburn, A. Sannino, M.J. Mack, M.B. Leon, P. Lurz, and S.K. Kodali, for the TRISCEND II Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

Quality of Life After Transcatheter Tricuspid Valve Replacement

1-Year Results From TRISCEND II Pivotal Trial

Suzanne V. Arnold, MD, MHA,[a] Rebecca T. Hahn, MD,[b] Vinod H. Thourani, MD,[c] Raj Makkar, MD,[d] Moody Makar, MD,[d] Rahul P. Sharma, MD,[e] Christiane Haeffele, MD,[e] Charles J. Davidson, MD,[f] Akhil Narang, MD,[f] Brian O'Neill, MD,[g] James Lee, MD,[g] Pradeep Yadav, MD,[c] Firas Zahr, MD,[h] Scott Chadderdon, MD,[h] Mackram Eleid, MD,[i] Sorin Pislaru, MD, PhD,[i] Robert Smith, MD,[j] Molly Szerlip, MD,[j] Brian Whisenant, MD,[k] Nishant Sekaran, MD,[k] Santiago Garcia, MD,[l] Terri Stewart-Dehner, MD,[l] Paul A. Grayburn, MD,[j,m] Anna Sannino, MD, PhD,[m] Clayton Snyder, MPH,[n] Yiran Zhang, MS,[n] Michael J. Mack, MD,[j] Martin B. Leon, MD,[b] Philipp Lurz, MD, PhD,[o] Susheel Kodali, MD,[b] David J. Cohen, MD, MSc,[n,p] the TRISCEND II Pivotal Trial Investigators

JACC

THE TRISCEND II PIVOTAL TRIAL

PURPOSE

Evaluate the safety and effectiveness of the EVOQUE tricuspid valve replacement system with optimal medical therapy compared with optimal medical therapy alone in patients with at least severe TR

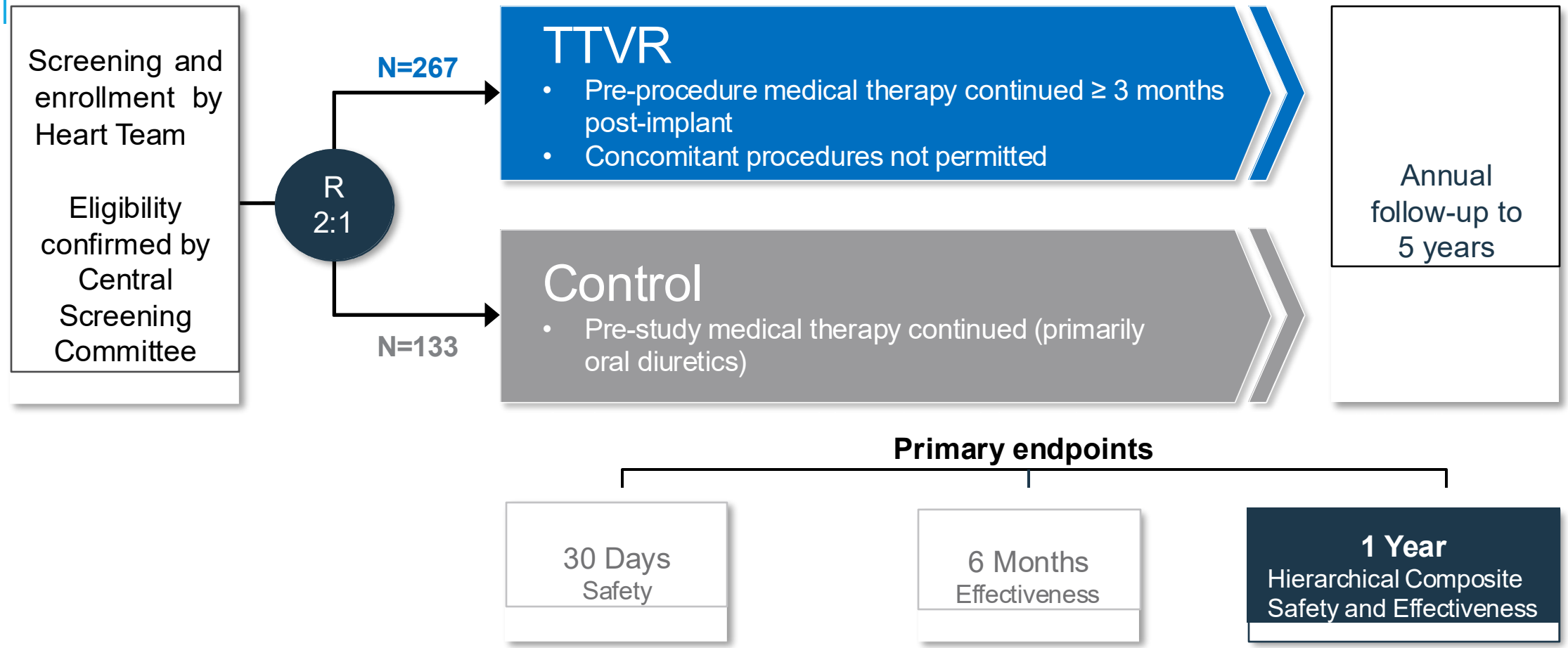
Key Inclusion Criteria

- Age ≥ 18 years
- Signs/symptoms of TR or prior heart failure hospitalization
- Medical therapy at the time of screening
- TR ≥ severe

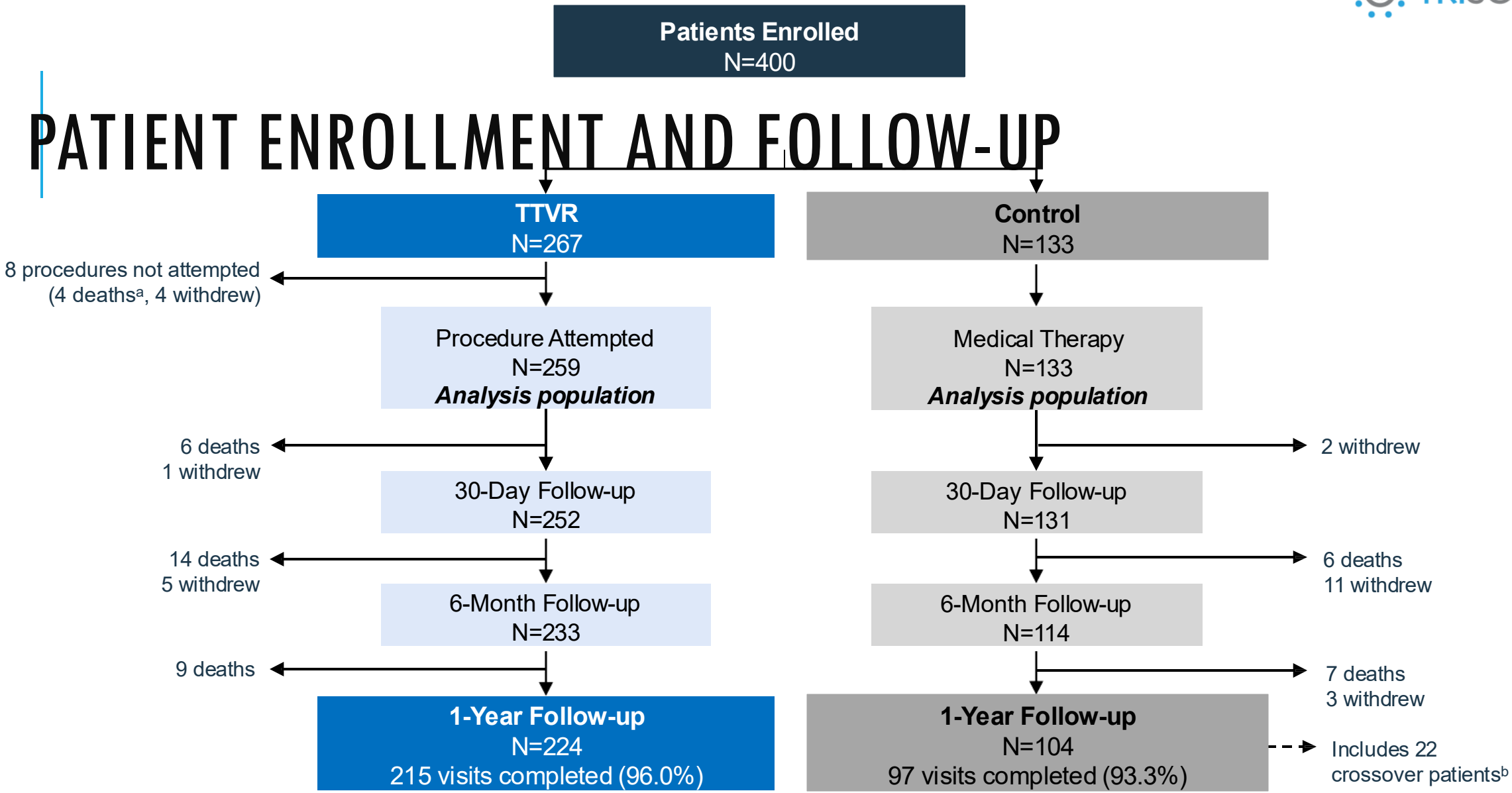
Key Exclusion Criteria

- Anatomy precluding proper implant
- Life expectancy < 12 months
- LVEF < 25%
- Evidence of severe RV dysfunction[a]
- Severe renal insufficiency[b]
- Severe pulmonary hypertension[c]

THE TRISCEND II PIVOTAL TRIAL



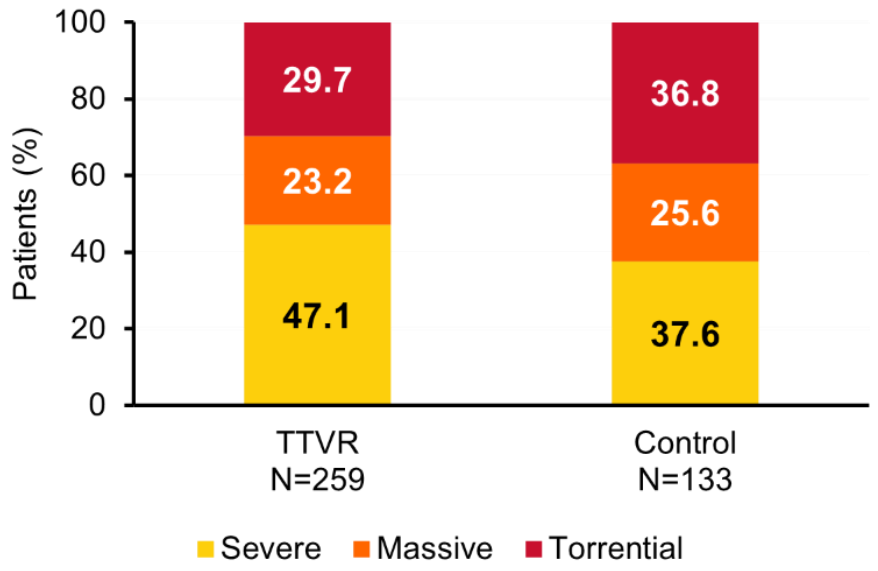
PATIENT ENROLLMENT AND FOLLOW-UP



	TTVR N=259 Mean ± SD or %	Control N=133 Mean ± SD or %
Age, years	79.3 ± 7.4	79.1 ± 7.8
Female	74.9%	76.7%
NYHA class III-IV	73.0%	69.2%
KCCQ overall score, points	52.8 ± 22.0	50.6 ± 21.4
STS score, mitral valve replacement, %	9.6 ± 5.1	10.0 ± 5.2
Left ventricular ejection fraction, %	54.4 ± 9.9	54.3 ± 11.1
TAPSE, mm	16.3 ± 4.5	15.6 ± 4.2
Pulmonary artery systolic pressure, mmHg	38.6 ± 10.9	37.6 ± 11.3
Atrial fibrillation	96.1%	92.5%
Stroke	15.1%	9.0%
Chronic kidney disease	54.1%	59.4%
Ascites	18.5%	21.8%
HF hospitalization in past 12 months	34.0%	36.1%
History of pacemaker/CIED	38.2%	39.8%
Prior valve surgery/intervention	33.6%	30.8%

TR Etiology	TTVR N=259	Control N=133
Primary[a]	14.7%	14.3%
Secondary[b]	74.1%	71.4%
Mixed	9.7%	9.0%
Indeterminate	1.5%	5.3%

TR Severity by Core Lab



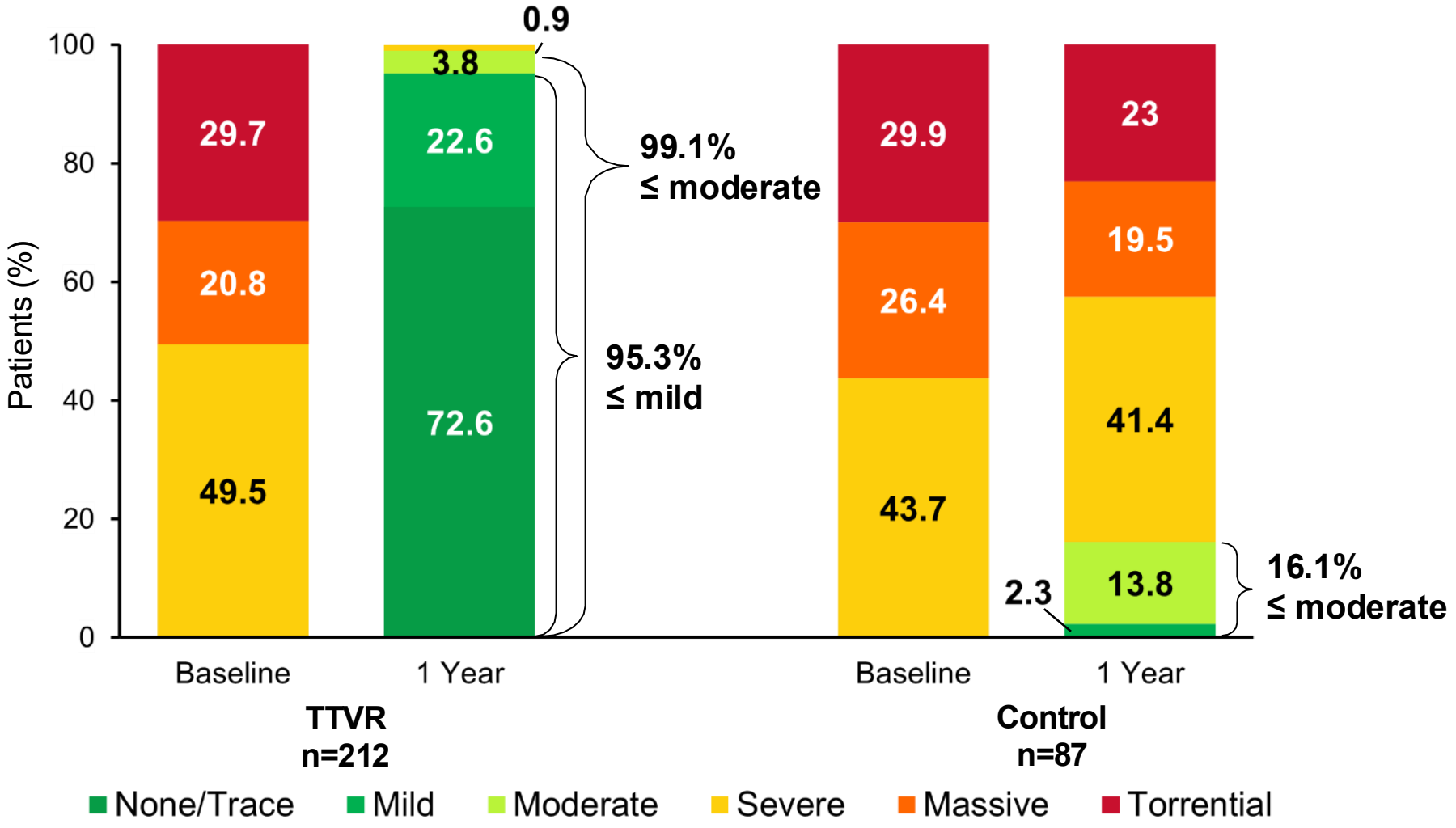
EVOQUE SYSTEM PROCEDURAL CHARACTERISTICS

	TTVR N=259
Patients with study valve implanted	95.4%[a]
Procedure time, minutes[b]	98.0 (76.0, 127.0)
Device time, minutes[c]	56.5 (41.0, 75.0)
Percutaneous access Right femoral vein Left femoral vein	100.0% 89.1% 10.9%
Conversion to surgery	1.2%
Length of hospital stay (post procedure), days	3.0 (2.0, 6.0)
Discharged to home	93.0%

SAFETY OUTCOMES

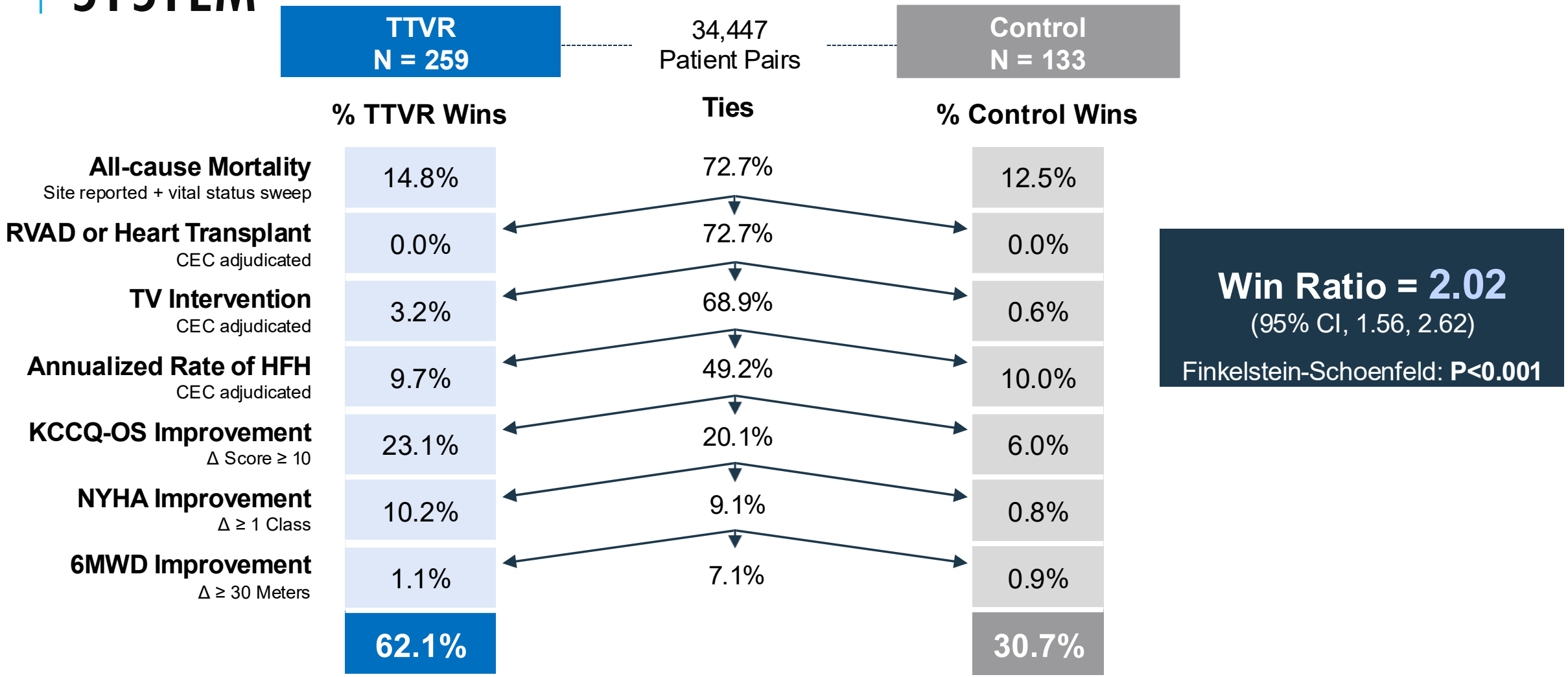
CEC-adjudicated Event	Early Events (≤ 30 Days)		Late Events (31 to 365 Days)[a]	
	TTVR N=259 % (n)	Control N=133 % (n)	TTVR N=247 % (n)	Control N=128 % (n)
Cardiovascular mortality	3.1% (8)	0.0% (0)	5.7% (14)	7.8% (10)
Myocardial infarction	0.8% (2)	0.0% (0)	1.2% (3)	0.8% (1)
Stroke	0.4% (1)	0.0% (0)	1.2% (3)	0.0% (0)
Severe bleeding[b]	10.4% (27)	1.5% (2)	5.3% (13)	4.7% (6)
Nonelective TV reintervention	0.8% (2)	0.8% (1)	0.0% (0)	2.3% (3)
New Pacemaker/CIED Implantation				
CIED implant in pacemaker-naïve patients[c]	24.7% (40/162)	0.0% (0/80)	4.2% (5/118)[d]	3.9% (3/76)[d]

TR GRADE REDUCTION AT 1 YEAR WITH EVOQUE SYSTEM



PRIMARY SAFETY AND EFFECTIVENESS ENDPOINT – PERCENT WINS

SUPERIOR CLINICAL BENEFITS WITH EVOQUE SYSTEM



Win Ratio = 2.02
(95% CI, 1.56, 2.62)
Finkelstein-Schoenfeld: **P<0.001**

6MWD, 6-minute walk distance; *CEC*, clinical events committee; *HFH*, heart failure hospitalization, *KCCQ-OS*, Kansas City Cardiomyopathy Questionnaire Overall Summary score; *NYHA*, New York Heart Association; *RVAD*, right ventricular assist device; *TTVR*, transcatheter tricuspid valve replacement; *TV*, tricuspid valve

THE TRISCEND II PIVOTAL TRIAL

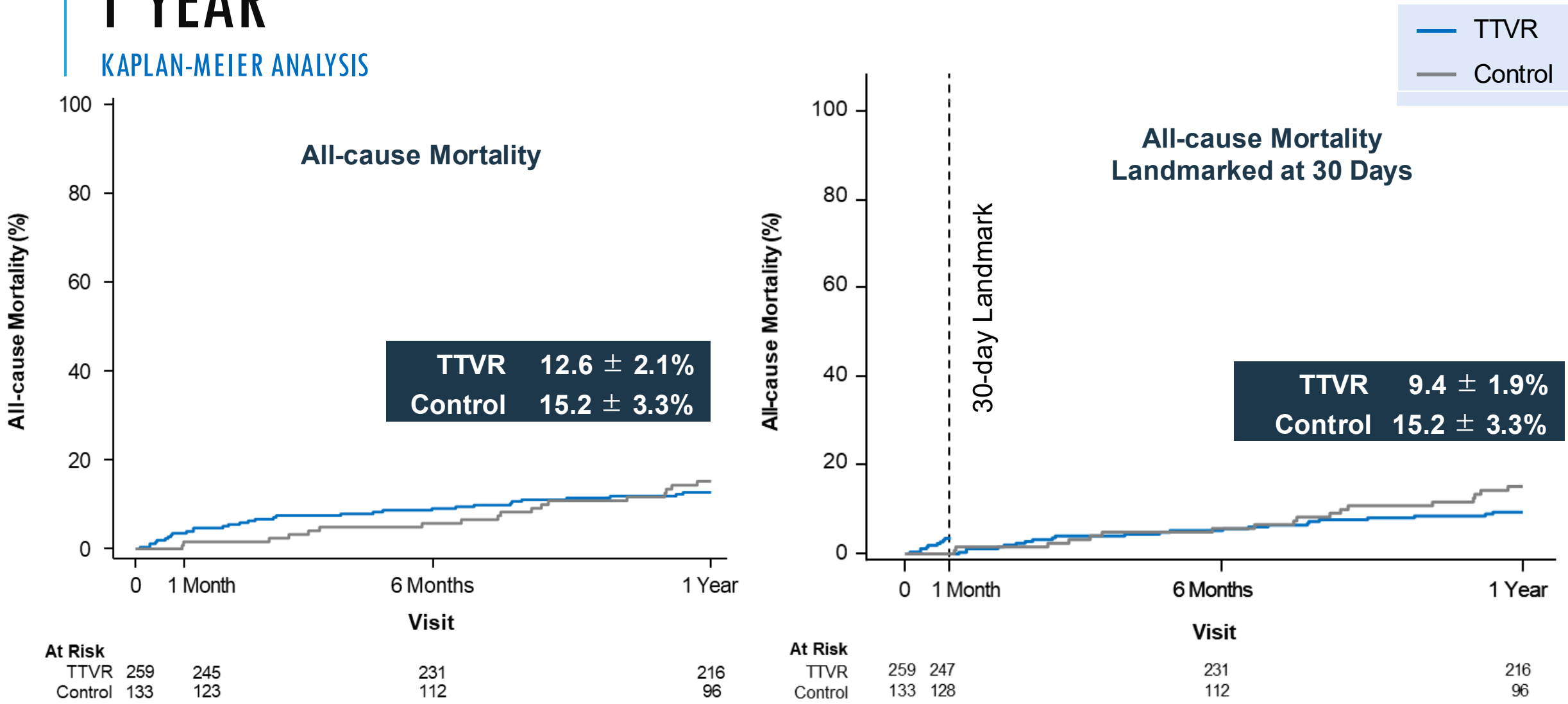
CLINICAL BENEFITS MAINTAINED IN SUBGROUPS TO 1 YEAR

Subgroup (Baseline)		No. of Patients	Number of Wins (%) TTVR	Number of Wins (%) Control	Win Ratio (95% CI)
All Patients		392	**21397** (62.1)	**10591** (30.7)	**2.02** (1.56 - 2.62)
Age	< 80 Years	175	**4369** (65.0)	**2078** (30.9)	**2.10** (1.41 - 3.13)
	≥ 80 Years	217	**6388** (59.6)	**3294** (30.7)	**1.94** (1.37 - 2.75)
Sex	Male	96	**1149** (57.0)	**710** (35.2)	**1.62** (0.98 - 2.67)
	Female	296	**12620** (63.8)	**5802** (29.3)	**2.18** (1.60 - 2.96)
NYHA Class	I or II	111	**1941** (67.6)	**660** (23.0)	**2.94** (1.71 - 5.05)
	III or IV	281	**10500** (60.4)	**5716** (32.9)	**1.84** (1.36 - 2.48)
STS MV Replacement	< 8%	167	**3900** (65.2)	**1620** (27.1)	**2.41** (1.57 - 3.70)
	≥ 8%	225	**6980** (59.8)	**3930** (33.7)	**1.78** (1.27 - 2.48)
EuroSCORE II	< 5%	234	**7761** (63.8)	**3352** (27.5)	**2.32** (1.62 - 3.30)
	≥ 5%	158	**3383** (59.7)	**2010** (35.5)	**1.68** (1.14 - 2.49)
KCCQ-OS Score	< 50 Points	187	**4775** (60.2)	**2582** (32.6)	**1.85** (1.28 - 2.66)
	≥ 50 Points	204	**6058** (65.5)	**2543** (27.5)	**2.38** (1.61 - 3.52)
6MWD	< 240 m	196	**4778** (57.0)	**3202** (38.2)	**1.49** (1.06 - 2.10)
	≥ 240 m	196	**5979** (67.8)	**2015** (22.8)	**2.97** (1.95 - 4.52)
Atrial Fibrillation	Yes	372	**19078** (62.3)	**9594** (31.3)	**1.99** (1.52 - 2.61)
	No	20	**61** (61.0)	**15** (15.0)	**4.07** (0.99 - 16.79)
Coronary Artery Disease	Yes	107	**1433** (53.5)	**1011** (37.7)	**1.42** (0.90 - 2.24)
	No	285	**11626** (65.1)	**5074** (28.4)	**2.29** (1.66 - 3.16)
Diabetes	Yes	90	**982** (52.2)	**716** (38.1)	**1.37** (0.83 - 2.26)
	No	302	**13159** (65.1)	**5802** (28.7)	**2.27** (1.67 - 3.09)
History of Ascites	Yes	77	**771** (55.4)	**576** (41.4)	**1.34** (0.79 - 2.25)
	No	315	**14019** (63.9)	**6133** (27.9)	**2.29** (1.69 - 3.10)
HFH Past 12 Months	Yes	136	**2769** (65.6)	**1077** (25.5)	**2.57** (1.59 - 4.16)
	No	256	**8824** (60.7)	**4864** (33.5)	**1.81** (1.33 - 2.48)
Pacemaker or ICD	Yes	152	**3047** (58.1)	**1804** (34.4)	**1.69** (1.13 - 2.52)
	No	240	**8298** (64.8)	**3634** (28.4)	**2.28** (1.61 - 3.24)

Subgroup (Baseline)		No. of Patients	Number of Wins (%) TTVR	Number of Wins (%) Control	Win Ratio (95% CI)
Prior Valve Intervention	Yes	128	**2440** (68.4)	**984** (27.6)	**2.48** (1.53 - 4.01)
	No	264	**9397** (59.4)	**5104** (32.3)	**1.84** (1.35 - 2.52)
Baseline TR Severity	Severe	172	**3497** (57.3)	**2126** (34.9)	**1.64** (1.11 - 2.43)
	Massive	94	**1267** (62.1)	**662** (32.5)	**1.91** (1.15 - 3.18)
	Torrential	126	**2473** (65.5)	**1001** (26.5)	**2.47** (1.52 - 4.01)
TR Etiology	Primary	57	**352** (48.8)	**261** (36.1)	**1.35** (0.71 - 2.56)
	Secondary	287	**11823** (64.8)	**5346** (29.3)	**2.21** (1.62 - 3.02)
	Mixed/ Indeterm.	48	**336** (61.0)	**179** (32.5)	**1.88** (0.92 - 3.84)
RV End-Diastolic Mid Diameter	<40 mm	192	**5027** (60.4)	**2816** (33.9)	**1.79** (1.24 - 2.56)
	≥ 40 mm	189	**4947** (62.3)	**2252** (28.4)	**2.20** (1.48 - 3.25)
TAPSE	< 17 mm	197	**5831** (66.9)	**2533** (29.1)	**2.30** (1.58 - 3.36)
	≥ 17 mm	151	**2870** (56.8)	**1696** (33.6)	**1.69** (1.12 - 2.56)
PASP	< 40 mmHg	229	**7489** (61.5)	**3591** (29.5)	**2.09** (1.48 - 2.95)
	≥ 40 mmHg	153	**3317** (65.1)	**1578** (31.0)	**2.10** (1.37 - 3.22)
Region	US	362	**17981** (61.2)	**9373** (31.9)	**1.92** (1.46 - 2.51)
	Germany	30	**150** (75.0)	**30** (15.0)	**5.00** (1.55 - 16.14)
Site Volume	<10 Patients	157	**3399** (61.7)	**1667** (30.2)	**2.04** (1.33 - 3.12)
	≥10 Patients	235	**7774** (62.7)	**3779** (30.6)	**2.05** (1.46 - 2.87)
Subgroup (Events up to 1 year)					
Severe bleeding[a]	Yes	47	**203** (72.5)	**76** (27.1)	**2.67** (1.10 - 6.51)
	No	345	**17223** (62.4)	**8219** (29.8)	**2.10** (1.58 - 2.78)
New PPM/ICD implant[b]	Yes	48	**91** (61.4)	**41** (30.4)	**2.22** (0.69 - 7.11)
	No	194	**6007** (66.7)	**2333** (25.9)	**2.57** (1.74 - 3.82)

CEC-ADJUDICATED ALL-CAUSE MORTALITY TO 1 YEAR

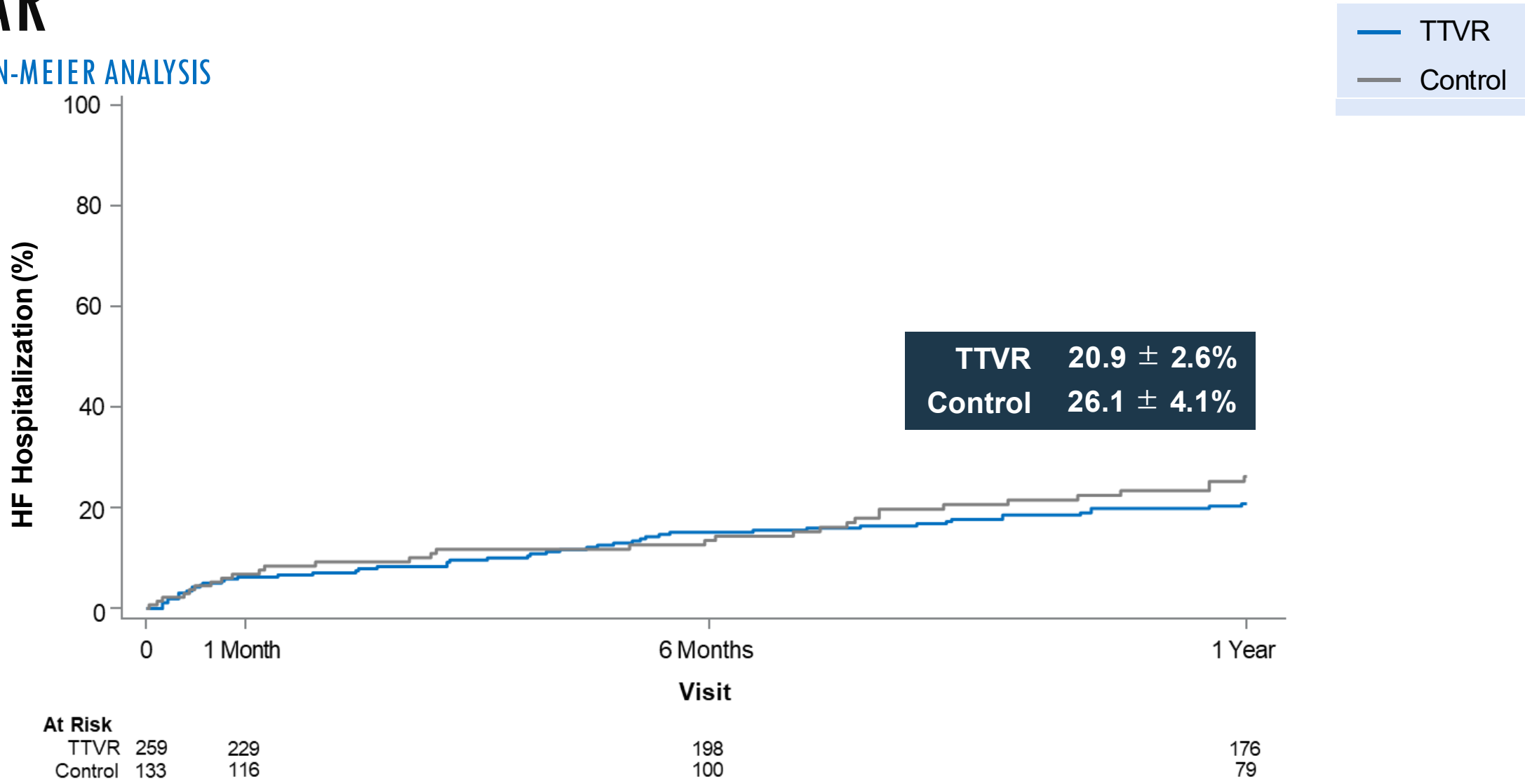
KAPLAN-MEIER ANALYSIS



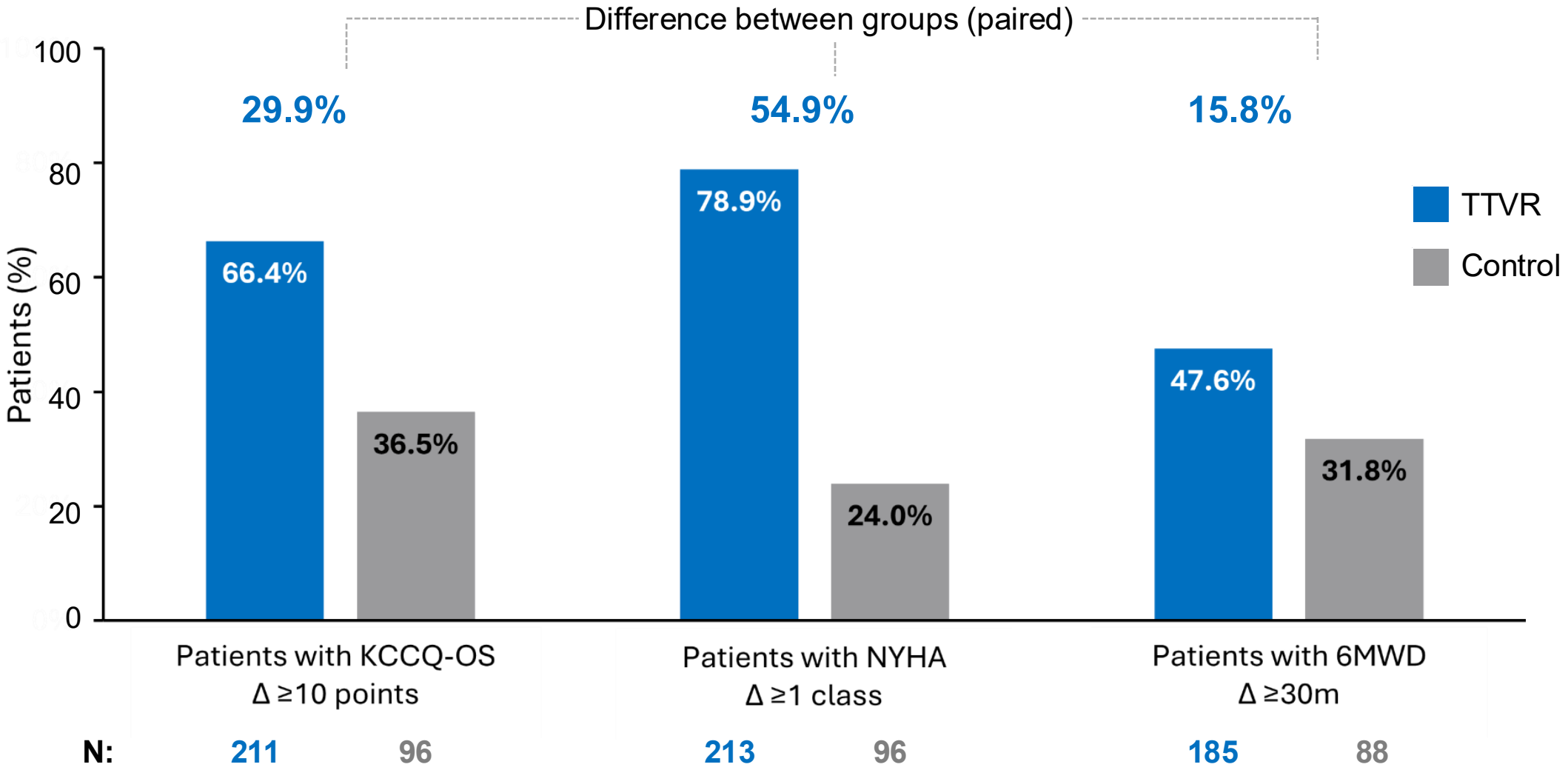
Kaplan-Meier estimates include standard error. *CEC*, clinical events committee; *TTVR,* transcatheter tricuspid valve replacement

CEC-ADJUDICATED HF HOSPITALIZATION TO 1 YEAR

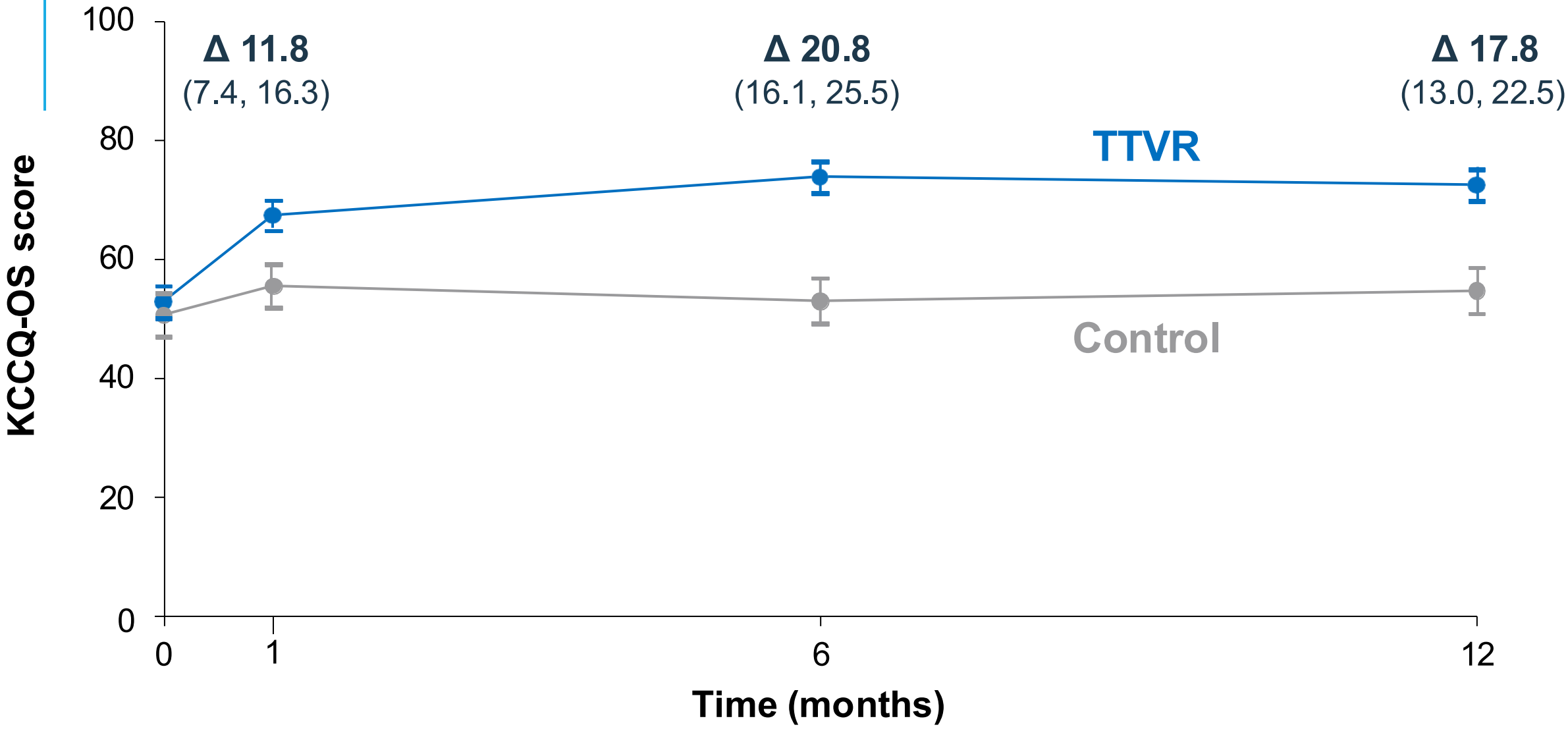
KAPLAN-MEIER ANALYSIS



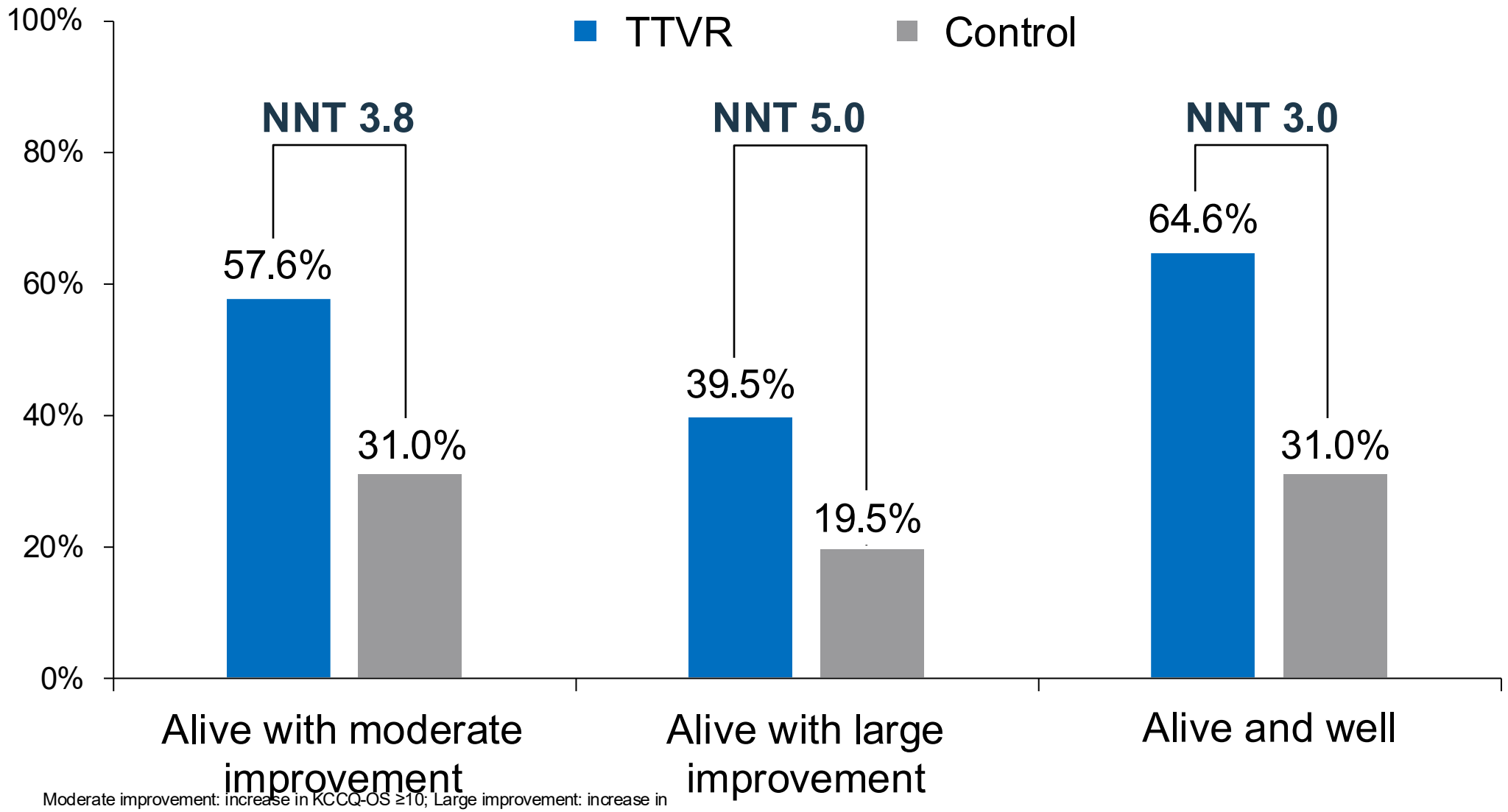
FUNCTIONAL AND QUALITY-OF-LIFE IMPROVEMENTS AT 1 YEAR



KEY HEALTH STATUS OUTCOME: KCCQ-OS



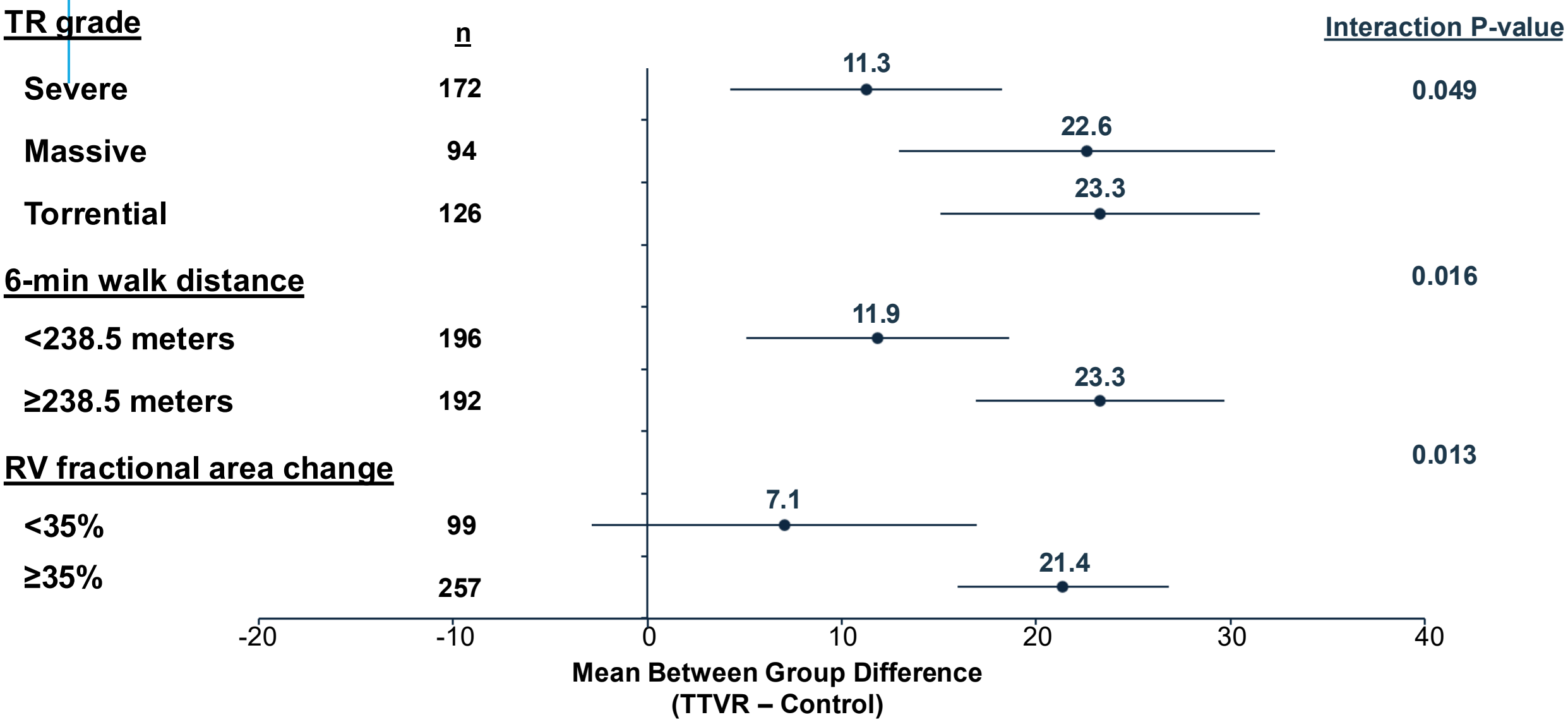
SURVIVAL AND HEALTH STATUS BY KCCQ-OS AT 1 YEAR



Moderate improvement: increase in KCCQ-OS ≥10; Large improvement: increase in KCCQ-OS ≥20; Alive and well: KCCQ-OS at 1 year of ≥60 and no decline from baseline of ≥10 points. *KCCQ-OS,* Kansas City Cardiomyopathy Questionnaire Overall Summary score*; NNT*, number needed to treat; *TTVR,* transcatheter tricuspid valve replacement

All treatment comparisons P<0.001

BASELINE SUBGROUP ANALYSES AT 1 YEAR BY KCCQ-OS



SUMMARY AND CONCLUSIONS

- At 1 year, TRISCEND II primary endpoint demonstrated superiority of EVOQUE TTVR for a patient population with limited treatment options
- TTVR with the EVOQUE system led to sustained TR reduction to ≤ mild in nearly all patients
- These TR reductions were associated with significant and marked improvement in symptoms, function, and quality of life at 1 year with favorable numerical trends in mortality and HF hospitalization
- These quality-of-life and symptomatic benefits should be balanced against periprocedural risks

The TRISCEND II trial confirms the clinical and quality-of-life benefits of the EVOQUE system for patients with ≥ severe TR

TRILUMINATE PIVOTAL STUDY DESIGN

- TRILUMINATE Pivotal is the first randomized, controlled trial to evaluate TEER in subjects with severe tricuspid regurgitation (TR).
- TRILUMINATE Pivotal included 2 arms based on expected TR reduction, and an imaging sub-study:
  - **Randomized**: Subjects expected to achieve TR of moderate or less were randomized 1:1 to TriClip™ device vs. medical therapy alone.
  - **Single-arm**: Subjects with expected TR reduction by at least 1 grade (but not to moderate or less) were treated with the TriClip device.

The TriClip device is available under investigational use only in the United States.

KEY ENROLLMENT CRITERIA

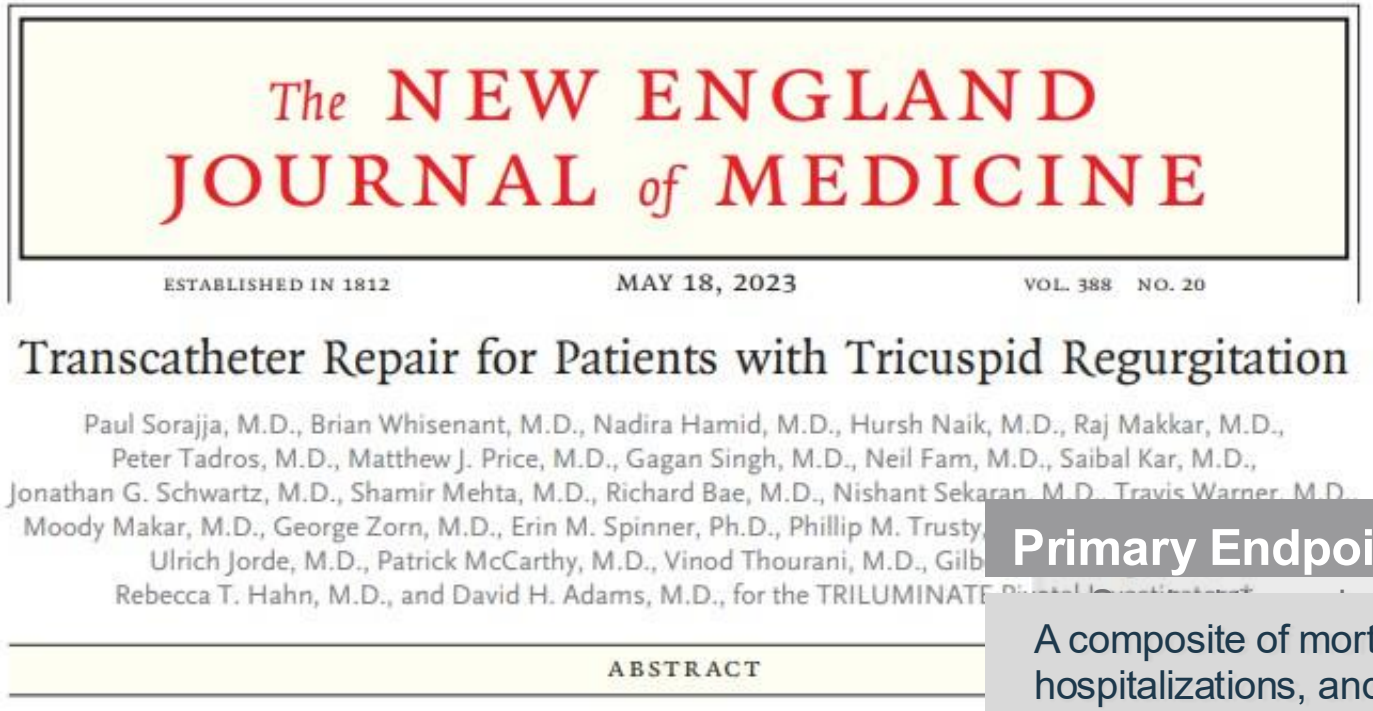
Key Inclusion Criteria

- Severe, symptomatic TR
- Stable GDMT and/or device therapy for heart failure ≥ 30 days
- ≥Intermediate risk of mortality or morbidity with tricuspid valve surgery

Key Exclusion Criteria

- Indication for other valve disease intervention
- Severe pulmonary hypertension
- Left ventricular ejection fraction ≤20%
- Anatomy not suitable for TriClip therapy

PRIMARY ENDPOINT WAS MET FOR RANDOMIZED COHORT



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Transcatheter Repair for Patients with Tricuspid Regurgitation

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ABSTRACT

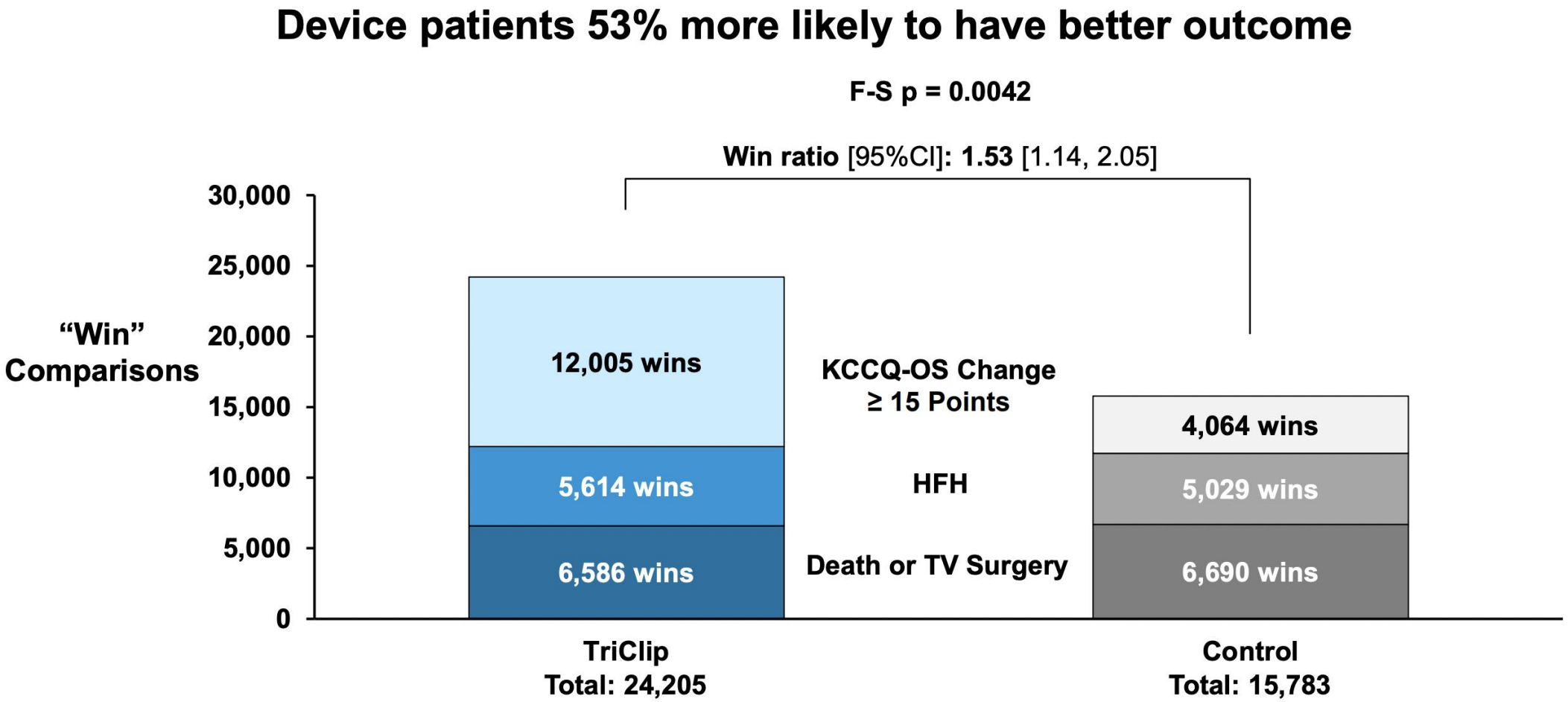
Primary Endpoint

A composite of mortality or tricuspid valve surgery, heart failure hospitalizations, and quality of life improvement ≥15 points assessed using the Kansas City Cardiomyopathy Questionnaire (KCCQ), evaluated at 12 months in a hierarchical fashion using the Finkelstein-Schoenfeld methodology.

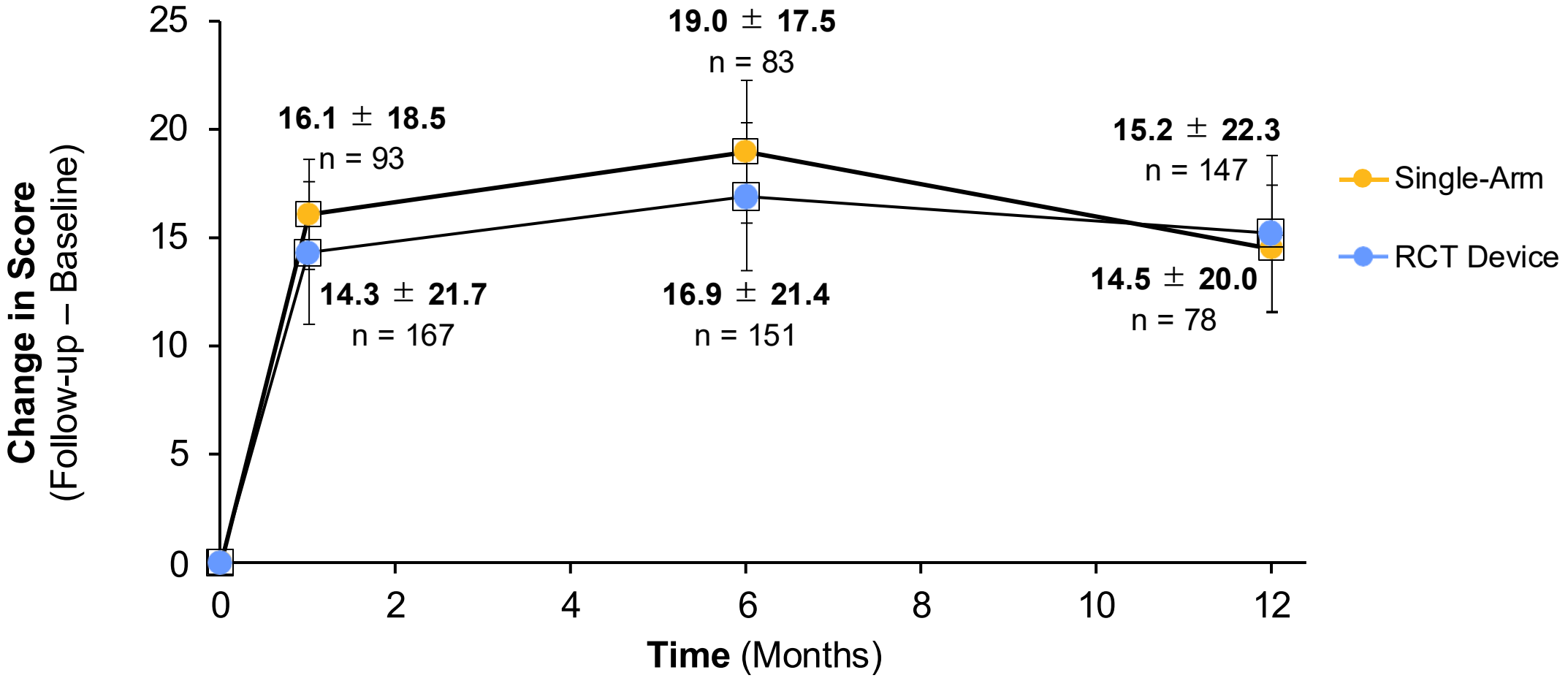
✓ **Met for primary endpoint analysis population (first 350 randomized subjects).**

Sorajja P, et al. *N Engl J Med.* 2023;388(20):1833-1842

PRIMARY ENDPOINT IN ALL RANDOMIZED SUBJECTS



KCCQ-OS IMPROVEMENT

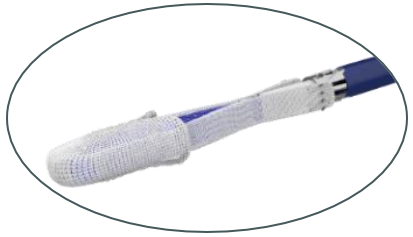


PASCAL Implant

Paddles

Nitinol construction

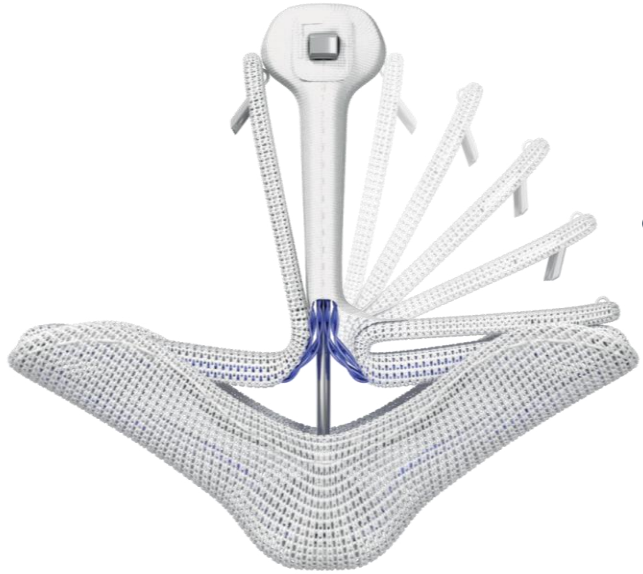
Passive closure,
acute implant flexing



Elongation

Navigate in dense chordae

PASCAL Ace Implant



Clasps

Two Implants

PASCAL with a wider spacer and broad contoured paddles and Ace with a narrower profile and spacer provide options for varied clinical needs

Roll-in cohort:

Conclusions

THE CLASP II TR TRIAL

- The PASCAL transcatheter valve repair system demonstrated favorable 30-day outcomes in 73 roll-in patients with symptomatic ≥ severe TR
- Low MAE rate, no mortality, and no heart failure hospitalization
- Core lab adjudicated significant TR reduction
  - 73.6% of patients reached ≤ moderate TR
  - 83% of patients had ≥ 1 TR grade reduction
- Significant improvements in ventricular performance and RV remodeling
- Significant improvements in KCCQ score (+17.9 points) and NYHA class (86.0% class I/II)
- The randomized CLASP II TR trial is ongoing (NCT04097145)

CONCLUSIONS

Tricuspid Regurgitation in patients with CHF carries a poor prognosis

In patients who have severe TR or worse despite optimal medical therapy percutaneous options are feasible and safe.

The approved devices thus far show improvements in QoL but not survival or CHF hospitalizations.