TriClip G4 System for Treatment of Patients with Symptomatic, Severe Tricuspid Regurgitation

February 13, 2024

Circulatory System Devices Panel

Abbott

Introduction

Lars Sondergaard, MD, DMSc

Chief Medical Officer and Divisional Vice President, Medical Affairs

Abbott

Foundation of Development Program Built on Unmet Medical Need of Patients with Tricuspid Regurgitation (TR)

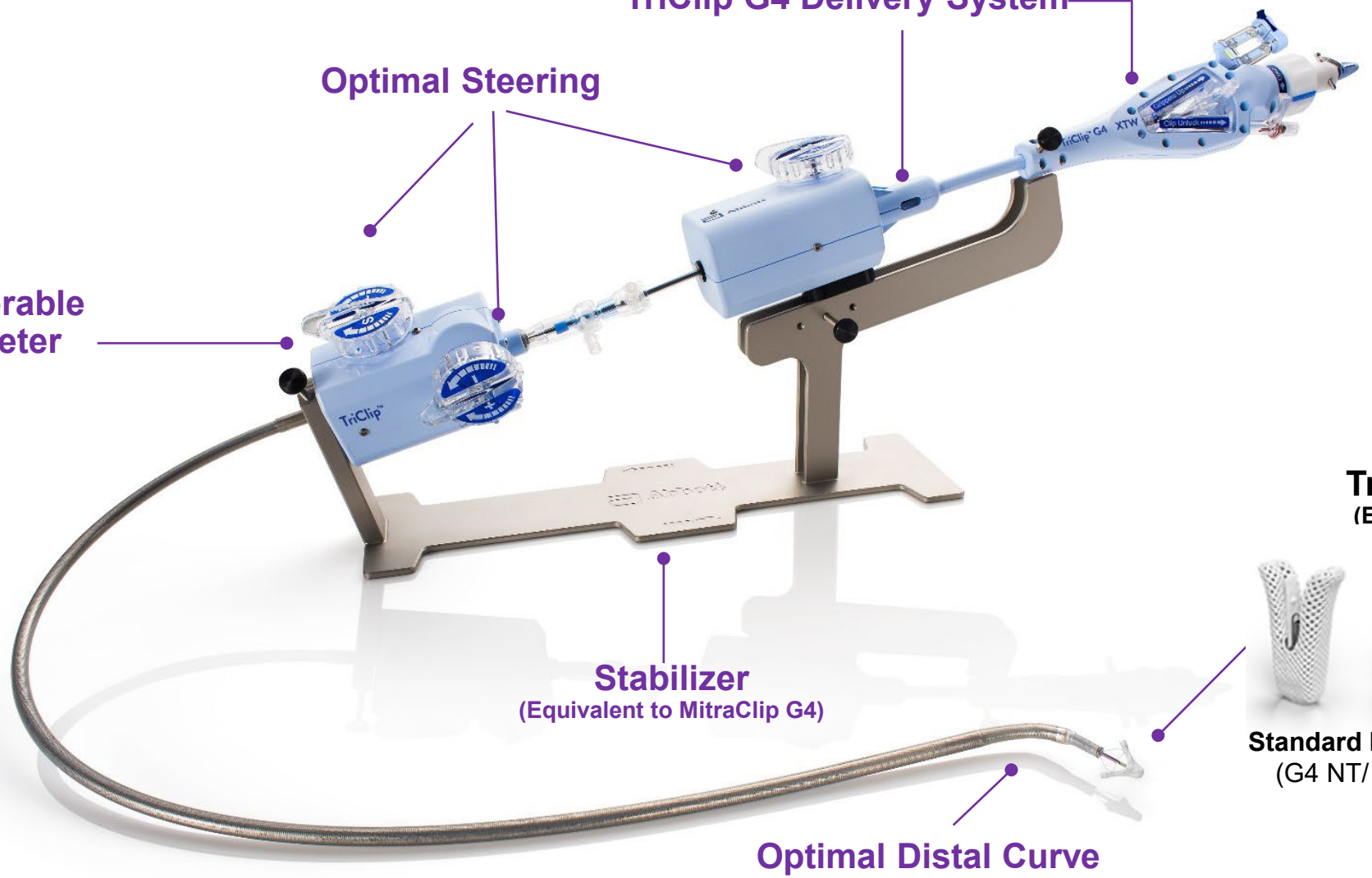
- Progressive disease
- Associated with debilitating symptoms that impact health status
- Limited treatment options for patients in US
  - High operative risk associated with surgery (8 – 10%)[1]
  - Medical therapy alone often ineffective
- Patients largely go untreated due to lack of treatment options

1. Chen, 2023

TriClip Design and Development Based on Well-Established MitraClip Clinical Experience

- MitraClip received CE mark in 2008, FDA approved in 2013
  - Transcatheter edge-to-edge repair technology for treatment of mitral regurgitation (left-sided heart valve)
  - > 200,000 patients treated with MitraClip
- Off-label use of MitraClip in TR highlights unmet need
- Dedicated clip delivery system needed to ensure easy, controlled, and precise delivery to tricuspid valve

TriClip G4 System

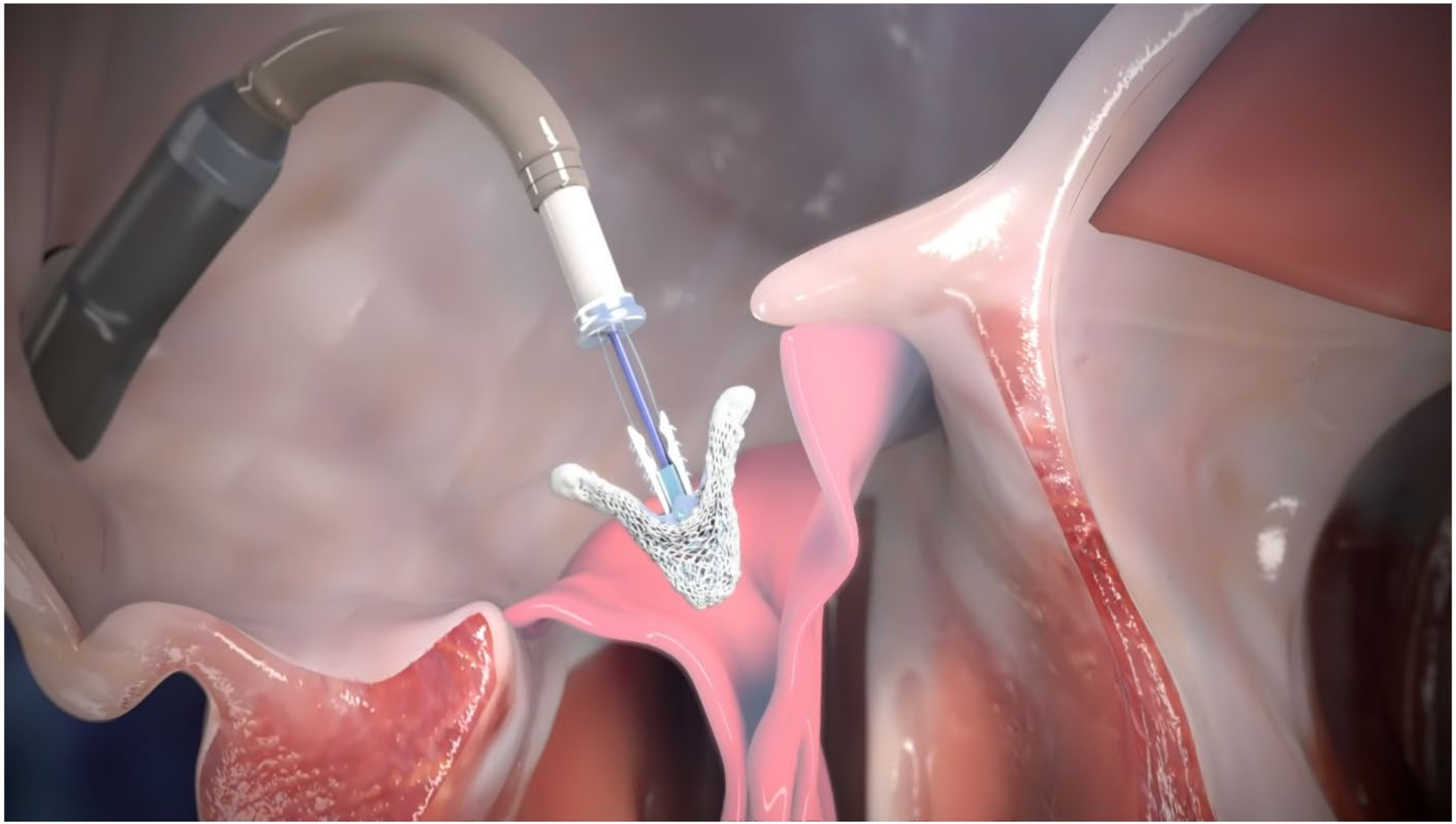


TriClip™ G4 Implant
(Equivalent to MitraClip G4)

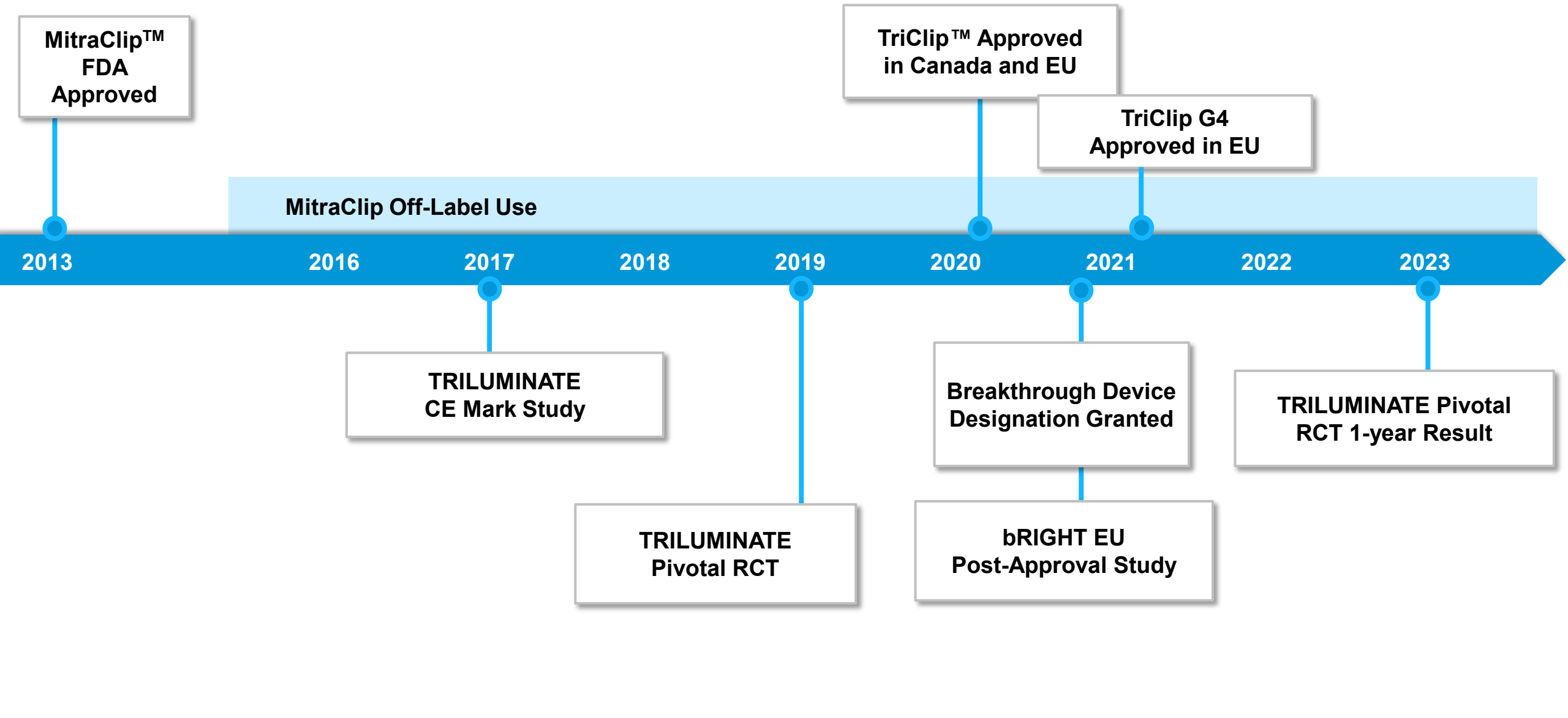
Standard Length Arm (G4 NT/ G4 NTW)

Long Length Arm (G4 XT/ G4 XTW)

TriClip Delivery System Designed for Tricuspid Valve



Clinical Experience and Regulatory History



Proposed Indication

TriClip G4 System is indicated for the improvement of health status in patients with symptomatic severe tricuspid regurgitation despite being treated optimally with medical therapy, who are at intermediate or greater risk for surgery, and in whom tricuspid valve edge-to-edge repair is appropriate as determined by a heart team

Key Considerations

- TRILUMINATE trial met primary endpoint
  - No differences observed on mortality/surgery or HFH
  - Significant improvements in health status measured by KCCQ
- Open-label study may lend bias on patient-reported outcomes; however, totality of data substantiates treatment effectiveness
  - Consistent and sustained reductions in TR
  - Consistent and sustained reductions in symptoms
  - Improvements across KCCQ domains
  - Supported by full randomized cohort, single-arm cohort, physiological changes, and reverse remodeling

Benefit-Risk Supporting TriClip

Unmet Need

- Severe TR is a progressive disease
- Debilitating symptoms that impact QoL
- High operative risk with surgery
- Medical therapy alone ineffective
- Patients go untreated

Safety

- Favorable safety profile
- 98% free from MAEs
- Low procedural risk
  - No operative mortality
  - No embolization
  - No device thrombosis

Effectiveness

- TRILUMINATE Trial showed clinically meaningful reductions in TR
- Significant improvements in symptoms and health status sustained through 12 mo
- TR reduction correlates with KCCQ
- Supported by OUS experience

Agenda

Unmet Need, Trial Design Clinical Safety	**David Adams, MD** Chief Cardiac Surgeon Mount Sinai Health System
Clinical Effectiveness	**Paul Sorajja, MD** Interventional Cardiologist Minneapolis Heart Institute
Clinical Perspective	**Philipp Lurz, PhD, MD** Director Department of Cardiology Universitätsmedizin Mainz
Benefit / Risk	**Lars Sondergaard, MD, DMSc** Chief Medical Officer and Divisional Vice President, Medical Affairs Abbott
Moderator for Q&A	**Erin Spinner, PhD** Global Clinical Program Director Abbott

Additional Experts

Suzanne V. Arnold, MD, MHA
Saint Luke's Mid America Heart Institute/UMKC

Joao Cavalcante, MD, FACC
Director, Cardiac MR and Structural CT Labs
Minneapolis Heart Institute

Rebecca Hahn, MD
Chief Scientific Officer, Director of Interventional Echocardiography, Columbia Structural Heart & Valve Center

Raymond Benza, MD, FACC, FAHA, FACP
Professor and Network Director, Pulmonary Vascular Diseases
Icahn School of Medicine, Mount Sinai

David Cohen, MD, MSc
Director of Clinical and Outcomes Research
Cardiovascular Research Foundation

Yu Shu, PhD
Director Global Biometrics
Abbott

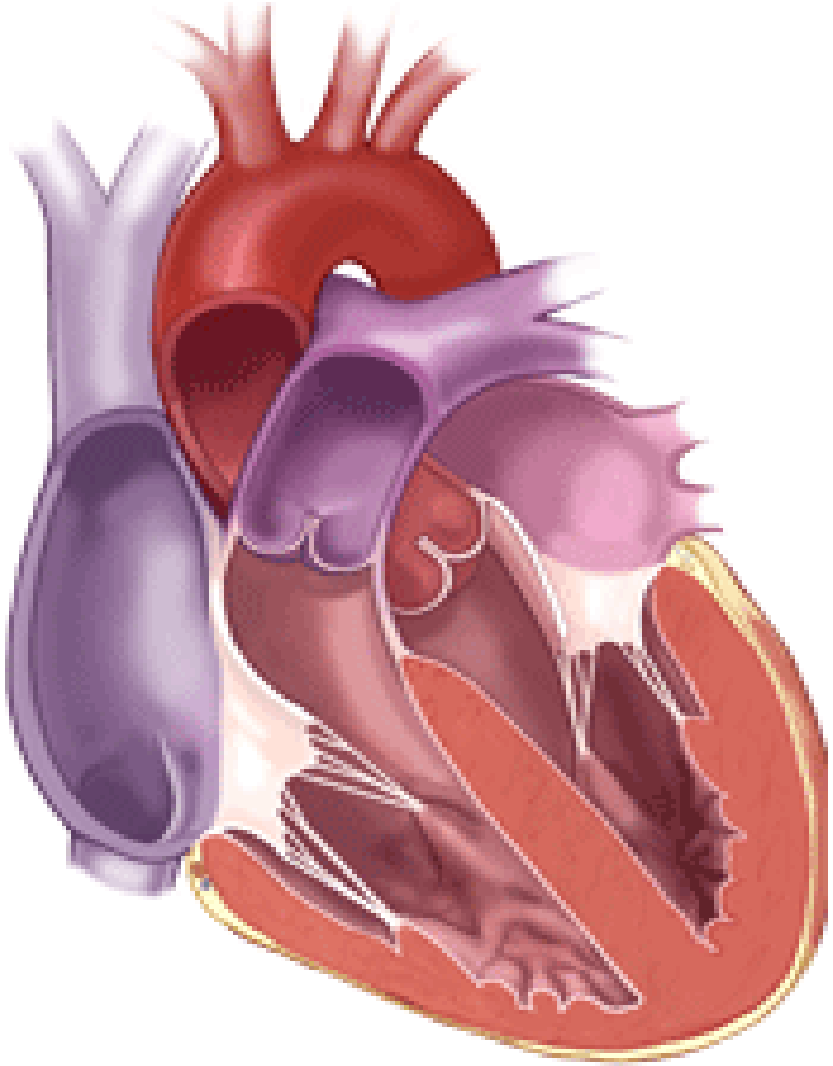
Unmet Need and Study Trial Design

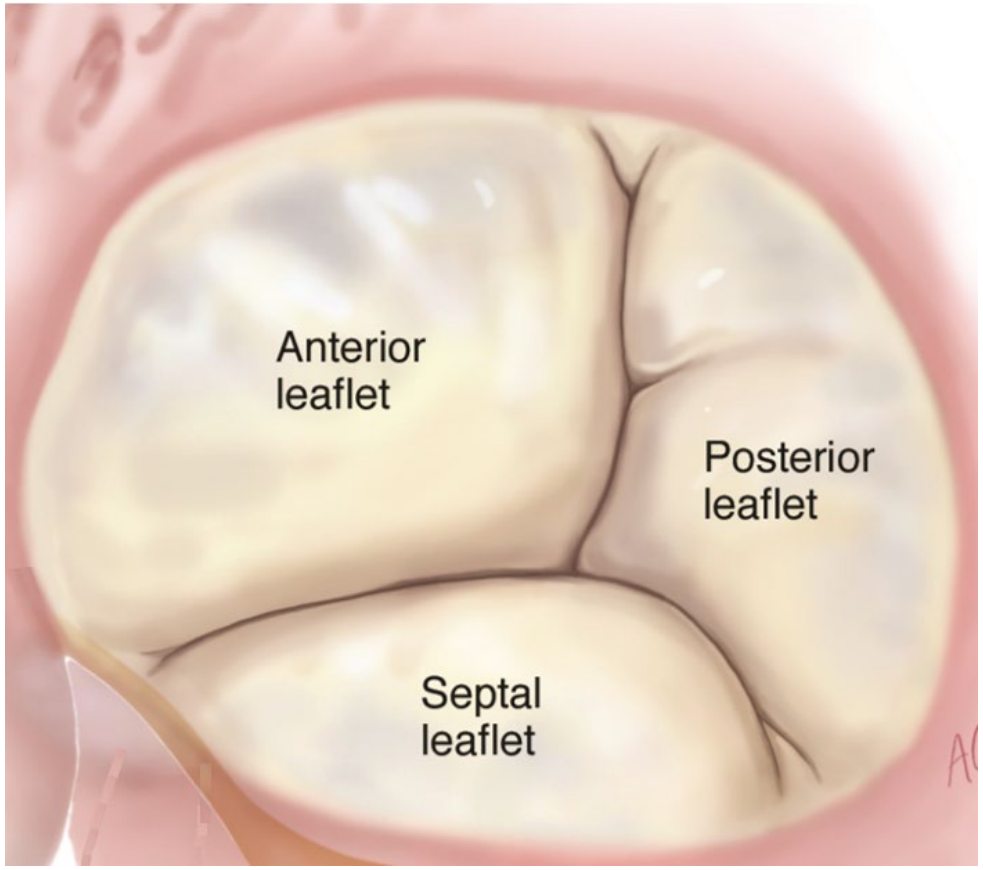
David Adams, MD

Chief Cardiac Surgeon

Mount Sinai Health System

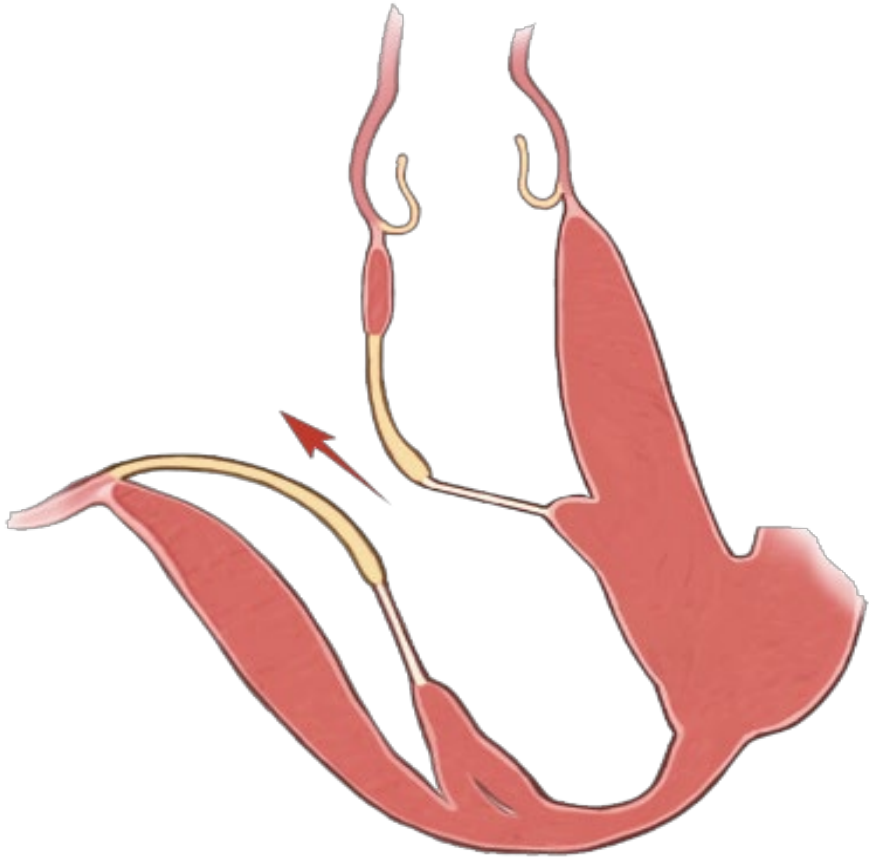
Normal Tricuspid Valve





Carpentier, 2010

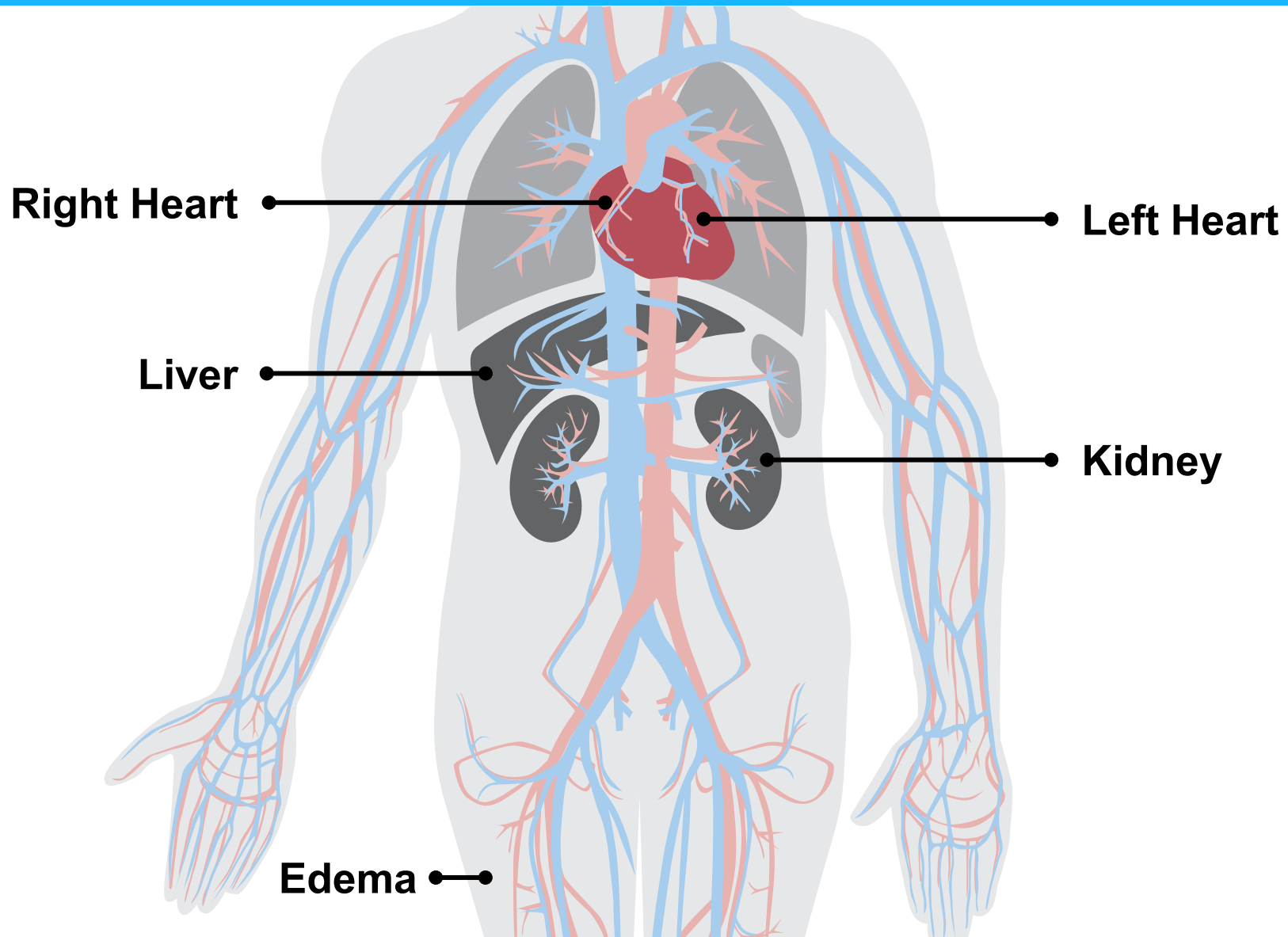
Functional Tricuspid Regurgitation



- Pulmonary Hypertension
- Atrial Fibrillation
- Left Sided Heart Disease

Carpentier, 2010

Severe TR has Cardiac and Systemic Consequences



Sequelae of Severe Tricuspid Regurgitation Over Time

Mild / Moderate → **Severe**

Earliest effects of TR

- Minimal symptoms

Common effects of TR

- Peripheral edema
- Fatigue
- Shortness of breath
- Loss of appetite
- Loss of mobility

Longer term effects

- Ascites and liver dysfunction
- Renal dysfunction
- Heart failure
- Heart rhythm disorder
- Mortality

ACC AHA Guidelines – Medical Therapy Alone Often Ineffective

COR	LOE	Recommendations
2a	C-EO	In patients with signs and symptoms of right-sided HF attributable to severe TR (Stages C and D), diuretics can be useful
2a	C-EO	In patients with signs and symptoms of right-sided HF attributable to severe secondary TR (Stages C and D), therapies to treat the primary causes of HF (e.g., pulmonary vasodilators to reduce elevated pulmonary artery pressures, GDMT for HF with reduced LVEF, or rhythm control of AF) can be useful (1,2)

Otto, 2021

ACC AHA Guidelines – Surgery Not a Viable Option for Many Due to Risk of Procedure

COR	LOE	Recommendations
1	B-NR	In patients with severe TR (Stages C and D) undergoing left-sided valve surgery, tricuspid valve surgery is recommended (1-8).
2a	B-NR	In patients with progressive TR (Stage B) undergoing left-sided valve surgery, tricuspid valve surgery can be beneficial in the context of either 1) tricuspid annular dilation (tricuspid annulus end diastolic diameter >4.0 cm) or 2) prior signs and symptoms of right-sided HF (3-10).
2a	**B-NR**	**In patients with signs and symptoms of right-sided HF and severe primary TR (Stage D), isolated tricuspid valve surgery can reduce symptoms and recurrent hospitalizations (11-14).**
2a	**B-NR**	**In patients with signs and symptoms of right-sided HF and severe isolated secondary TR attributable to annular dilation (in the absence of pulmonary hypertension or left-sided disease) who are poorly responsive to medical therapy (Stage D), isolated tricuspid valve surgery can be beneficial to reduce symptoms and recurrent hospitalizations (11,12,15-19).**
2b	C-LD	In asymptomatic patients with severe primary TR (Stage C) and progressive RV dilation or systolic dysfunction, isolated tricuspid valve surgery may be considered (12,20).
2b	**B-NR**	**In patients with signs and symptoms of right-sided HF and severe TR (Stage D) who have undergone previous left-sided valve surgery, reoperation with isolated tricuspid valve surgery may be considered in the absence of severe pulmonary hypertension or severe RV systolic dysfunction (1,2,11,18).**

Otto, 2021

Isolated Tricuspid Valve Surgery Remains a High-Risk Procedure

- Society of Thoracic Surgeons (STS) database: 6,507 patients undergoing isolated tricuspid surgery for functional TR
  - 2011 – 2020
  - Median age: 65 years
  - Operative mortality: 7.3%
  - Composite major complications: 32.0%
  - New dialysis required: 5.5%
  - Blood transfusions: 46.4%
  - Median length of hospital stay: 8 days

Chen, 2023

Symptomatic Severe TR Remains a Clinical Challenge

- Debilitating symptoms common
- Medical therapy has a role, but many patients unresponsive
- Surgery can effectively eliminate TR, but with high associated risks, including operative mortality
- Patients usually referred late in course of disease due to procedural risk
- New treatment strategies necessary to impact the course of patients in this disease process

Unmet Need of Severe TR

The Journal of Thoracic and Cardiovascular Surgery JTCVS

Commentary: Tricuspid: The frustrating and unloved valve

"The tricuspid valve was ignored for years, but this has changed. It is the hardest valve to treat successfully, however, with many anatomic and physiologic challenges for evolving therapies"

Patrick M. McCarthy, MD

McCarthy, 2020

TRILUMINATE Pivotal Trial Design

Trial Includes a Randomized Cohort and a Single-Arm Cohort with an Imaging Sub-study

Patients with severe TR who remain symptomatic despite medical therapy

	Randomized	Single-Arm	Imaging Sub-study
Patient Population	Ability to reduce TR to Moderate or less	Low likelihood of achieving moderate or less, with ability to reduce TR by 1 grade	Enrolled subjects at select sites willing to undergo additional study related imaging (CT and MRI)
Randomization	1:1 TriClip: Control (Medical Therapy)	TriClip Only	
Endpoint	Hierarchical composite of all-cause mortality or tricuspid valve surgery, HFH, and KCCQ improvement ≥ 15 points at 12 months	Survival through 12 months with KCCQ improvement ≥ 10 points compared to baseline	Cardiac reverse remodeling and quantitative “gold standard” measurements

Key Enrollment Criteria

- Inclusion Criteria
  - Severe, symptomatic TR
  - Stable medical therapy and/or device therapy for heart failure for ≥ 30 days
  - ≥ intermediate risk of mortality / morbidity with tricuspid valve surgery
- Exclusion Criteria
  - Indication for other valve disease intervention
  - Severe pulmonary HTN
  - Left ventricular ejection fraction ≤ 20%
  - Anatomy not suitable for TriClip therapy

Independent Review Committees

Core Labs

Echo

- Determination of TR Severity (baseline and 12 months)
- Gap measurement
- SLDA

CT/MRI

- Quantitative assessments of TR
- Right heart anatomical measurements

Anatomical Eligibility

- Structural interventionalists and echocardiographers
- Determines clippability: reviews site clipping strategy and Echo Core Lab feedback
- Determined patients in Randomized or Single Arm
  - Severity of TR
  - Coaptation gap size
  - Presence / location of pacing lead

Patient Management

- Heart Failure Specialists
- Reviews right heart catheterization data
- Confirms optimal guideline directed medical therapy

CEC Adjudication

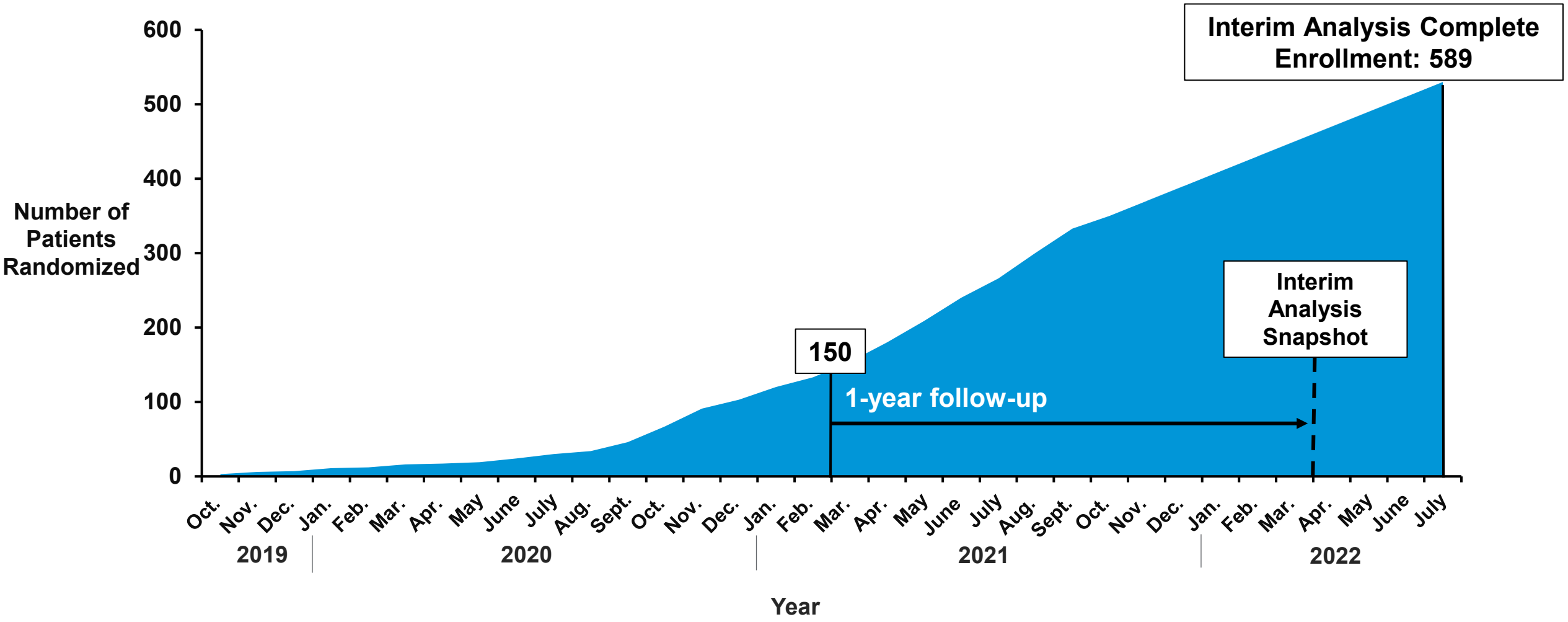
Through 30 days

- Myocardial infarction
- Major bleeding
- New onset renal failure
- Non-elective cardiovascular surgery for device-related adverse event
- Endocarditis requiring surgery

Through 1 year

- All-cause mortality
- Hospitalization
- Stroke

Randomized Patient Enrollment



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Primary Analysis	350	100	Up to 100
Total Enrolled (Randomized/Treated)	589 (572)	200 (188)	On-going (82)

Primary Endpoint – Randomized Cohort

- Evaluated at 12 months in a hierarchical order
  - Time to all-cause death or tricuspid valve surgery
  - Number of Heart Failure Hospitalizations (HFH)
  - Improvement of ≥ 15 points in Kansas City Cardiomyopathy Questionnaire Overall Summary (KCCQ-OS) from baseline
- Order determined by clinical importance (i.e., death more important than HFH)

Kansas City Cardiomyopathy Questionnaire (KCCQ)

- 100-point scale, includes 23 questions regarding
  - Symptom stability, frequency, and burden (leg swelling, fatigue and shortness of breath)
  - Limitations of physical and social activities
  - Mental health due to heart failure symptoms

Scale	Symptom Severity
0 – 24	Very poor – Poor
25 – 49	Poor – Fair
50 – 74	Fair – Good
75 – 100	Good – Excellent

- 5-point change in KCCQ-OS considered small but clinically meaningful[1]
  - 15-point change is moderate to large clinical benefit

1. Spertus, 2020

Primary Analysis Used Finkelstein-Schoenfeld Method

- Finkelstein-Schoenfeld: Provides a p-value to assess statistical significance
  - Nonparametric statistical test combines endpoints in a hierarchical order
  - Assign score: +1 (win), -1 (loss), 0 (tie)

- Win ratio: Provides estimate of treatment effect
  - Win ratio: # wins in device / # wins in control

Example of Win Ratio

Hierarchical Endpoint	TriClip Patient 1	Control Patient 1	Winner
Mortality / TV Surgery	Alive	Alive	-
HFH	No HFH	No HFH	-
≥ 15 points on KCCQ	≥ 15 points on KCCQ	< 15 points	1 Win TriClip

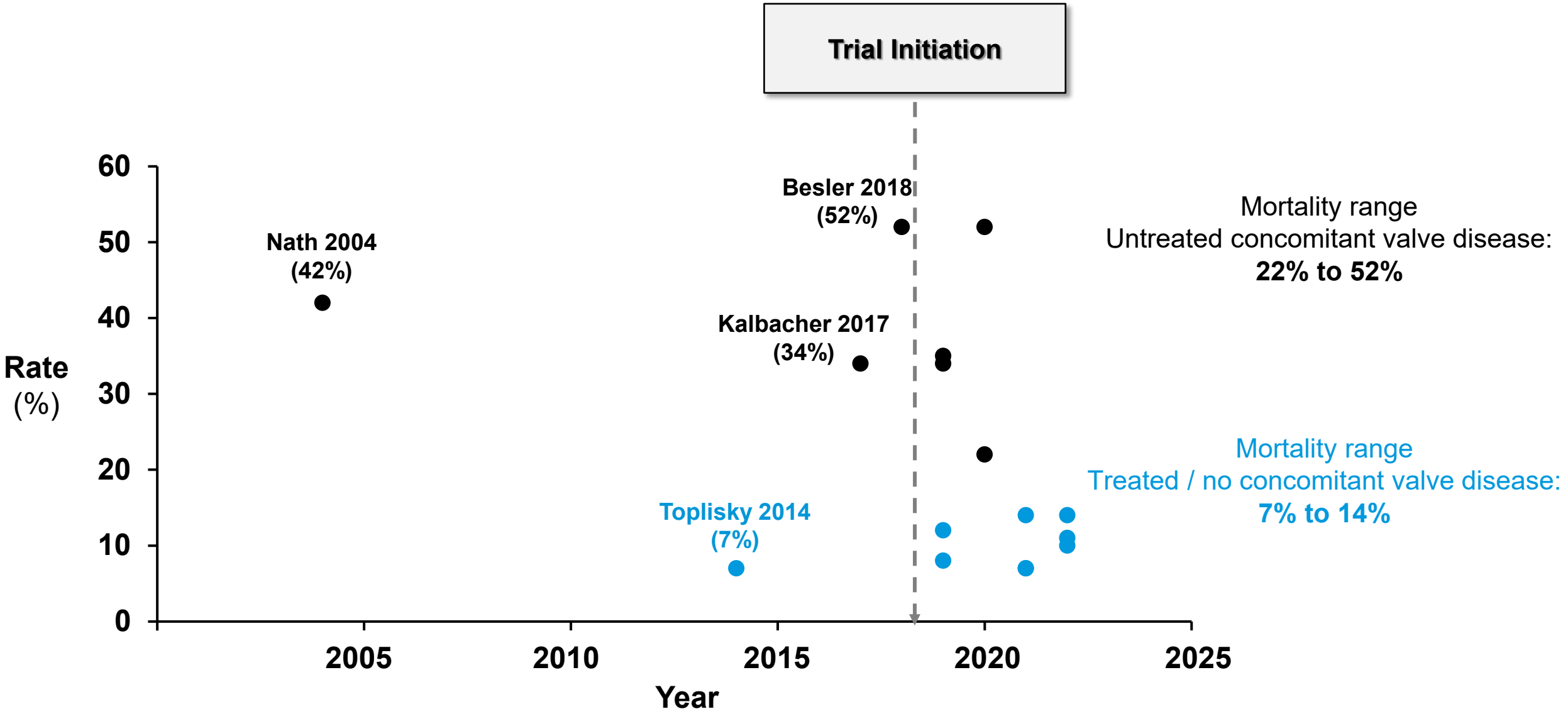
Hierarchical Endpoint	TriClip Patient 1	Control Patient 2	Winner
Mortality / TV Surgery	Alive	Died	1 Win TriClip
HFH			
≥ 15 points on KCCQ			

- Analysis yields a total of 30,625 comparisons
- Win ratio = total winners on TriClip vs total winners on Control

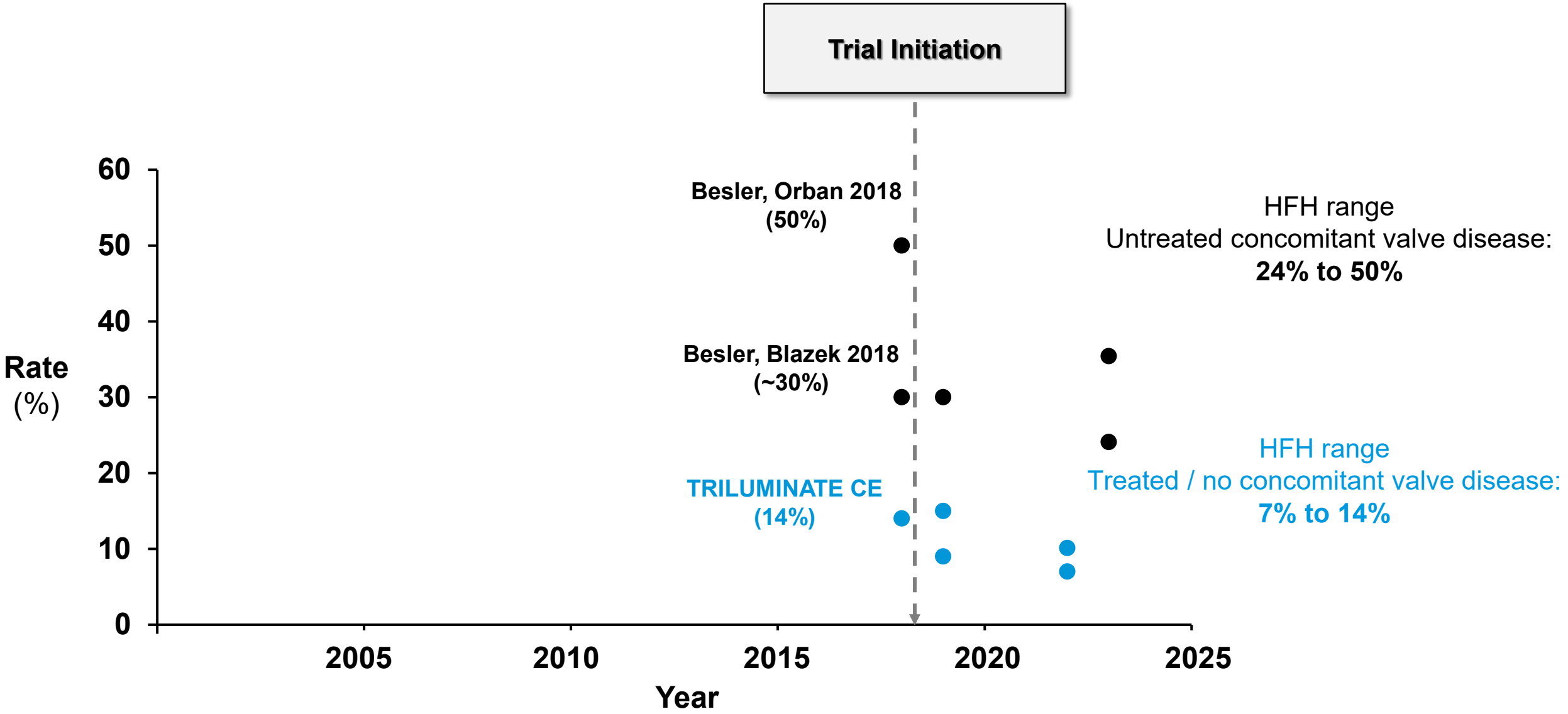
SAP Assumptions Based on Information Available at Time of Study Design

Assumptions at 12 months	TriClip	Control
All-cause mortality or tricuspid valve surgery rate	15%	20%
Annualized HF hospitalization rate (event/patient-year)	0.35	0.5
% of KCCQ-OS improvement (≥ 15 pt)	45%	20%

Understanding of 1-Year Mortality Rates for TR has Evolved with Time



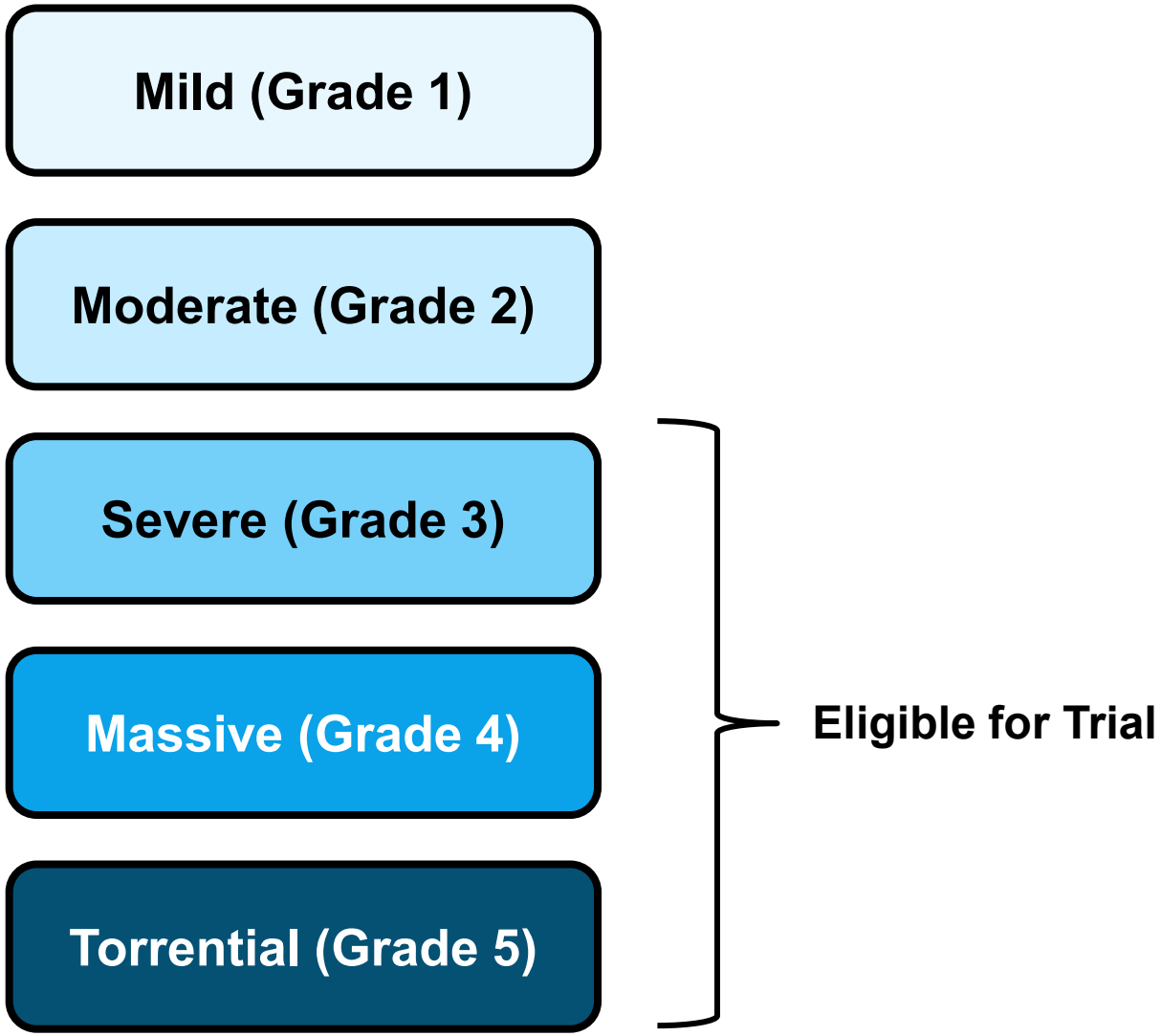
Understanding of 1-Year HFH Rates for TR has Evolved with Time



Secondary Endpoints – Randomized Cohort

- Assessed after first 350 randomized complete 12 months
  1. Freedom from major adverse events (MAE) after procedure attempt at 30 days
  2. Change in KCCQ-OS at 12 months
  3. TR Reduction to moderate or less at 30-day post procedure
  4. Change in 6MWD at 12 months

TR Grading Scale Expanded to Allow Further Gradation of Severity



Hahn, 2017

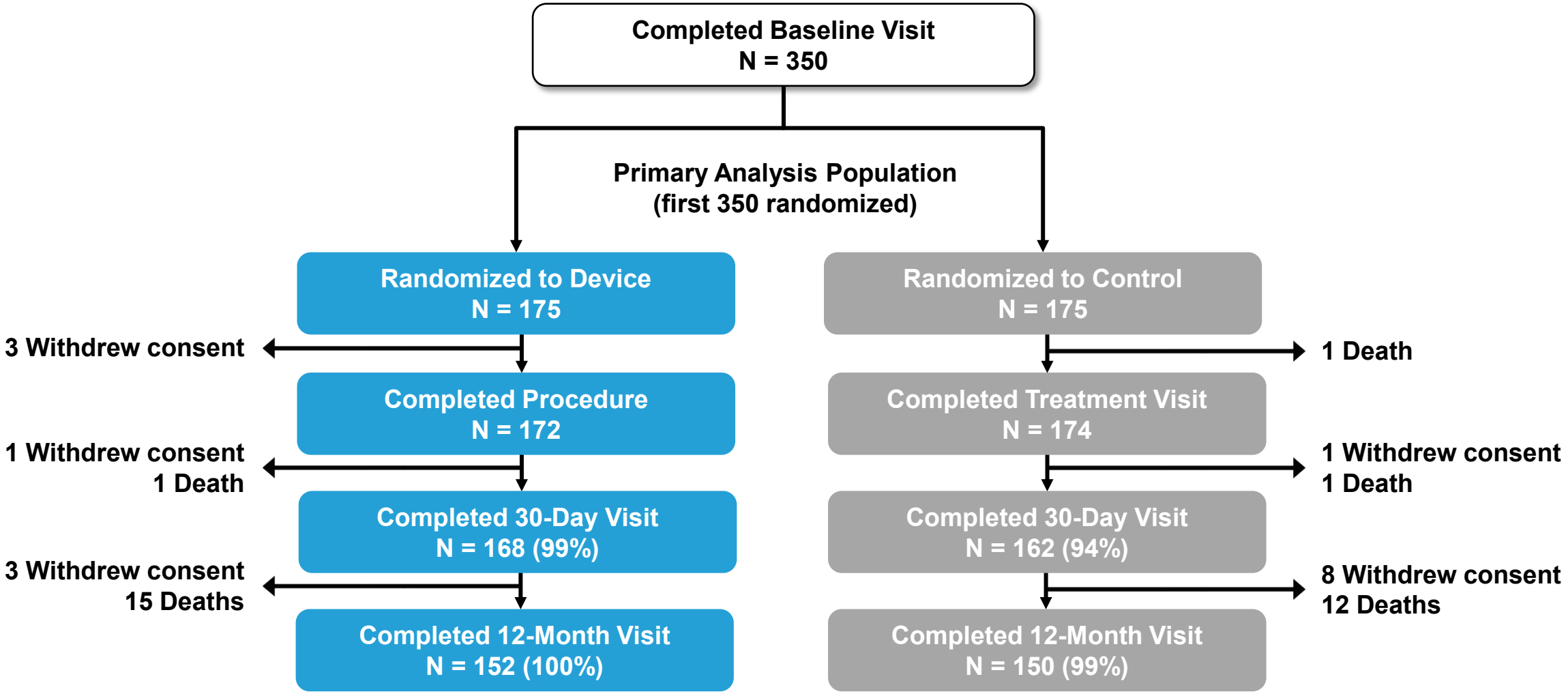
Randomized Cohort: Baseline Characteristics Represent a Sick Population

	TriClip N = 175	Control N = 175
Age, mean ± SD (years)	78.0 ± 7.4	77.8 ± 7.2
Sex (female)	56%	54%
Race (white)	85%	82%
NYHA class III or IV	59%	55%
KCCQ-OS Score, mean ± SD	56.0 ± 23.4	54.1 ± 24.2
Renal disease	35%	35%
Hypertension	81%	81%
Atrial fibrillation	87%	93%
COPD	11%	14%
HFH within 12 months prior to enrollment	25%	25%
CRT / CRT-D / ICD / PPM	16%	14%
Prior aortic and / or mitral valve intervention	39%	35%

Randomized Cohort: Baseline Echo Characteristics

	TriClip N = 175	Control N = 175
TR severity grading		
Moderate (Grade 2)	2%	1%
Severe (Grade 3)	25%	30%
Massive (Grade 4)	21%	18%
Torrential (Grade 5)	51%	51%
Etiology (functional)	95%	93%
Coaptation gap, mean ± SD (mm)	5.5 ± 1.8	5.2 ± 1.7
Heart size / function, mean ± SD		
RVEDD (base, cm)	5.0 ± 0.8	5.2 ± 0.8
TV annulus diameter (cm)	4.3 ± 0.7	4.5 ± 0.8
RV TAPSE (cm)	1.7 ± 0.4	1.6 ± 0.4
LVEF (%)	59.3 ± 9.3	58.7 ± 10.5
CO (L/min)	4.1 ± 1.2	4.2 ± 1.1

Randomized Cohort: Disposition



N represents completed visits

Randomized Cohort: Implant Characteristics

	TriClip N = 172
Technical success at exit from procedure room	99%
Number of clips implanted, mean ± SD	2.2 ± 0.7
Device used	
TriClip (first generation)	47%
TriClip G4	53%
Device time (min), mean (SD)	89.7 (66.4)
Length of stay in hospital (days), median (IQR)	1 (1, 2)
Discharge status	
Home	98%
Nursing home	2%
Death	0

Safety

Secondary Safety Endpoint Met: Low MAE Rate in Treated Device Patients

	Estimate (SE)	Lower Limit for 95% CI	Performance Goal	p-value
Freedom from MAE through 30 Days	98.3% (1.0%)	96.3%	90%	< 0.0001

Major Adverse Events (MAE) through 30-Days Post-Procedure	TriClip N = 172
Any MAE	3 (1.7%)
New-onset renal failure	2 (1.2%)
Cardiovascular mortality	1 (0.6%)
Endocarditis requiring surgery	0
Non-elective CV Surgery, TriClip-related AE	0

Secondary endpoint # 1 : Safety Endpoint met, p < 0.0001

Randomized Cohort: Other Adjudicated Clinical Safety Endpoints

	TriClip N = 172	Control N = 174
From Treatment Visit through 30-Days		
Death (All-cause)	0.6%	0.6%
Major bleeding (≥ BARC 3)	5.2%	1.7%
New-onset renal failure	1.2%	0.6%
Cardiogenic shock	0.0%	0.6%
New pacemaker implantation*	0.7%	1.3%

BARC = Bleeding Academic Research Consortium determined bleeding classifications
*Not adjudicated, site reported

Major Bleeding

- 9 events[1] in TriClip group, with no fatal bleeding events and all resolved without serious sequalae
  - 3 access site bleeds, attributable to procedural requirement for large-bore venous access
  - Gastrointestinal (4), urologic bleed (1), and intracranial bleed (1), not device/procedure related

1. BARC Type 3

Randomized Cohort: Other Adjudicated Clinical Safety Endpoints

	TriClip N = 175	Control N = 175
From Randomization Through 12 Months		
All-Cause mortality	8.6%	7.4%
Stroke	1.7%	1.7%
Tricuspid valve surgery	1.7%	3.4%
Cardiogenic shock	0.0%	0.6%
Device embolization	0.0%	n/a
Device thrombosis	0.0%	n/a
New pacemaker implantation*	3.4%	3.3%

*Not adjudicated, site reported

Safety Summary: Favorable Safety Profile for TriClip

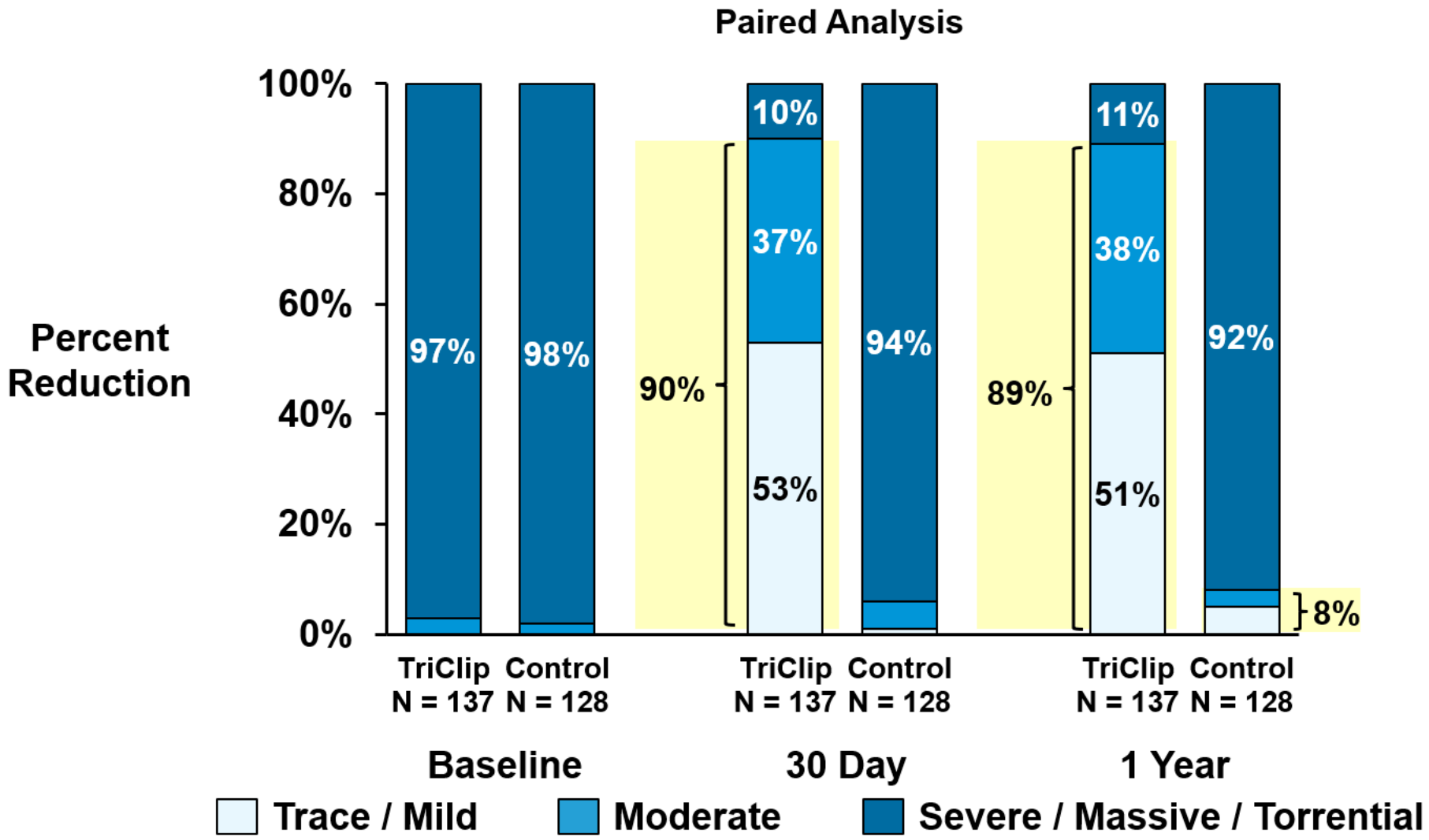
- Secondary Safety Endpoint Met: 98.3% freedom from MAEs occurring after procedure through 30 days
- Low procedural risk
  - No procedural mortality
  - No embolization
  - No device thrombosis
- Safety profile of device comparable to control
- Average length of hospital stay for TriClip is 1 day

Efficacy

Paul Sorajja, MD

Interventional Cardiologist
Minneapolis Heart Institute

Randomized Cohort: Significant and Sustained Reduction in TR Severity with Device



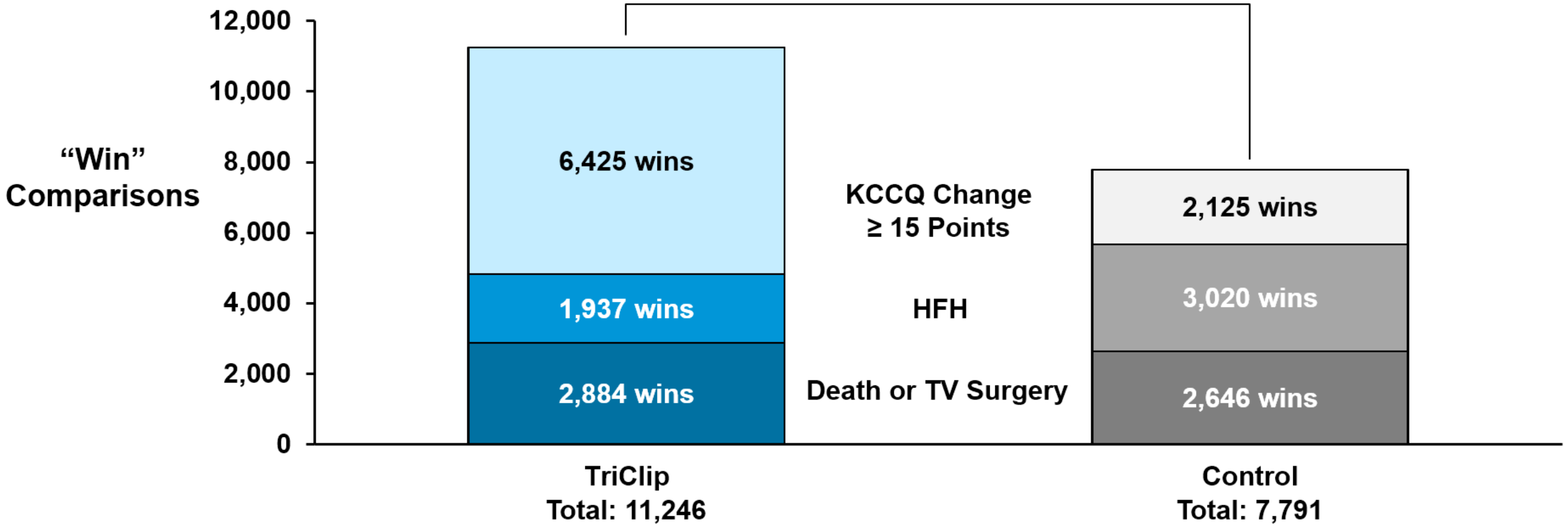
Secondary endpoint # 3 : TR Reduction to moderate or less at 30-day post procedure met, p < 0.0001

Primary Endpoint: TriClip Demonstrated Superiority to Medical Therapy Driven by Improvement in KCCQ

Device patients 44% more likely to have better outcome

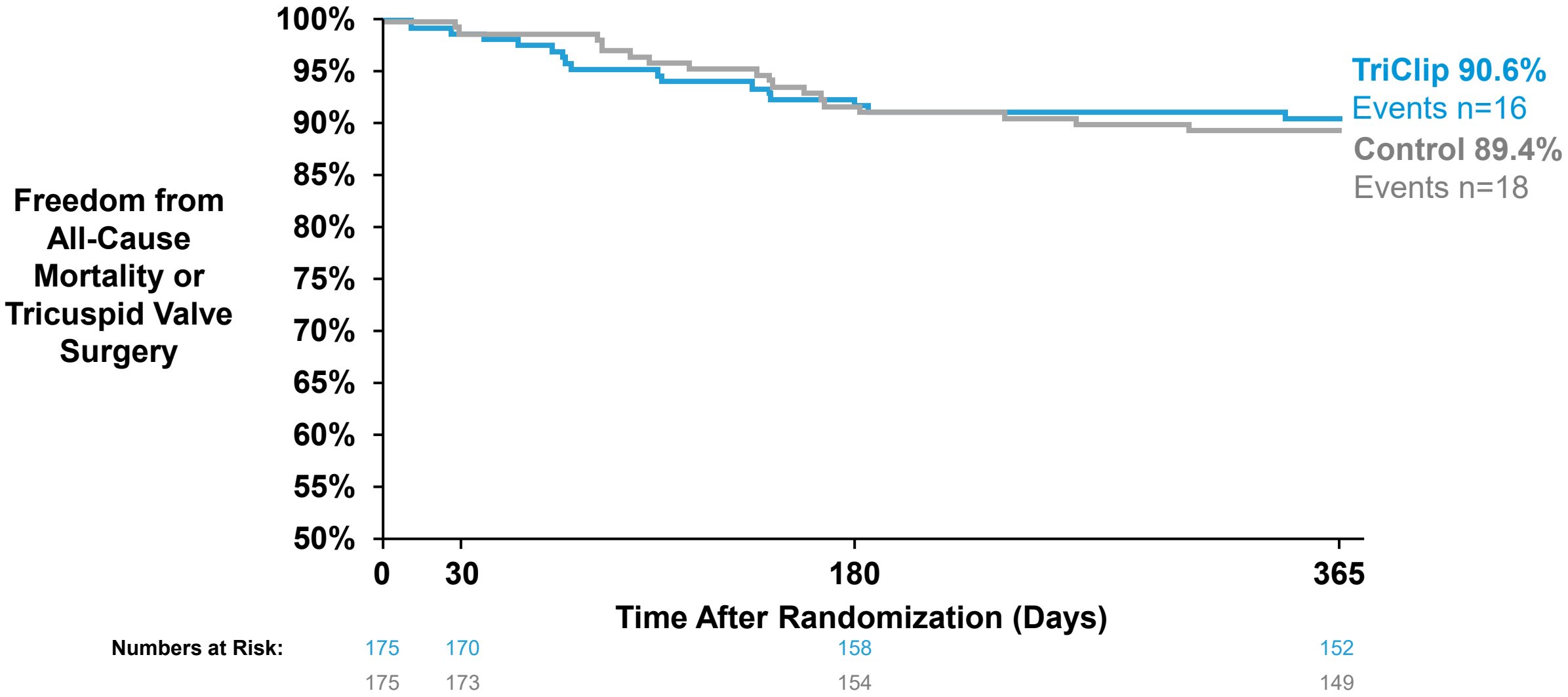
Primary Analysis, F-S p = 0.03

Win ratio [95% CI]: **1.44** [1.03, 2.08]

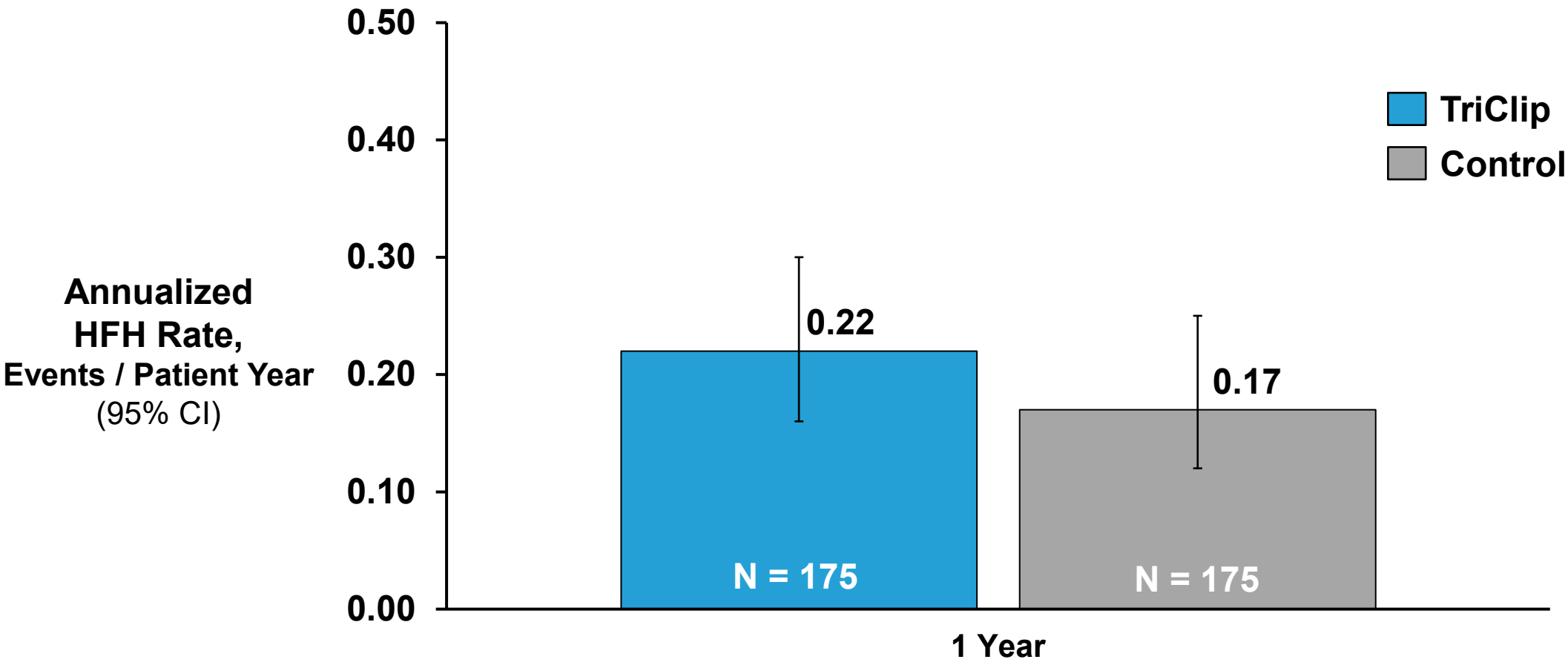


F-S = Finkelstein-Schoenfeld

Primary Endpoint Component: All-Cause Mortality or Tricuspid Valve Surgery

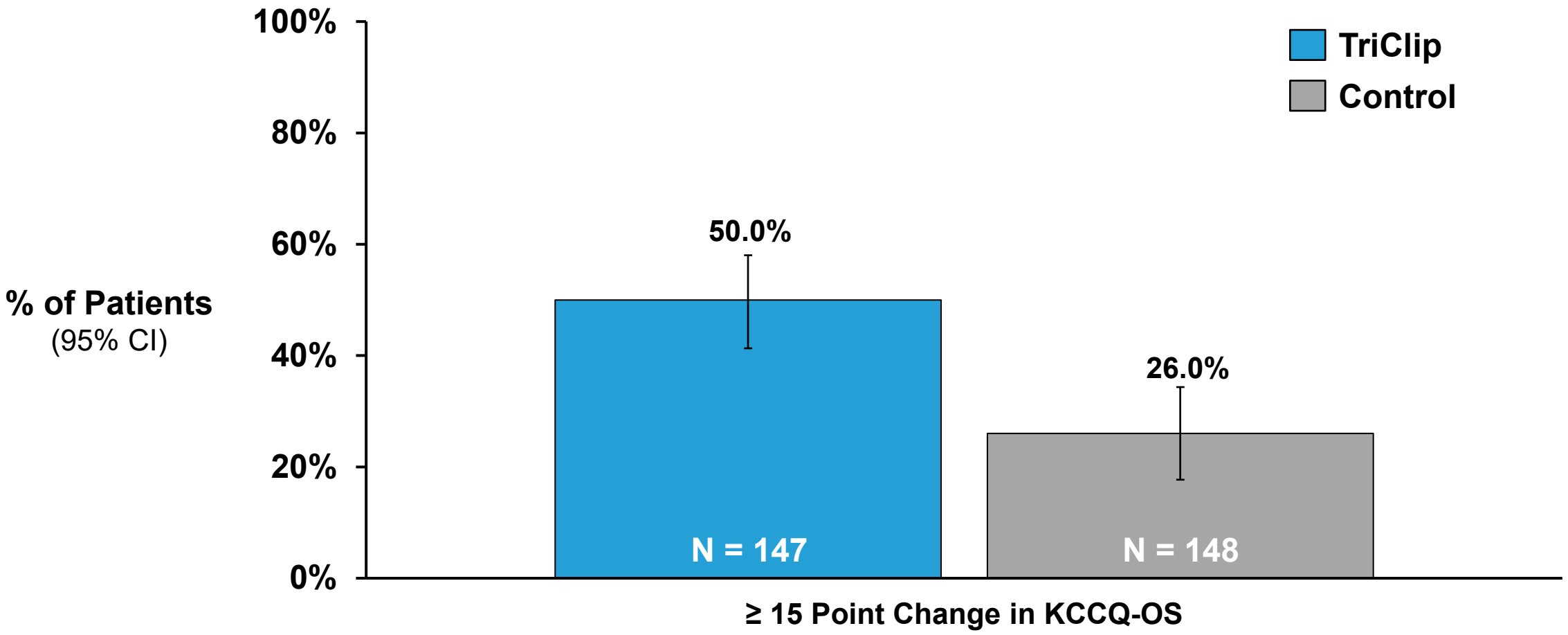


Primary Endpoint Component: Heart Failure Hospitalization (HFH)



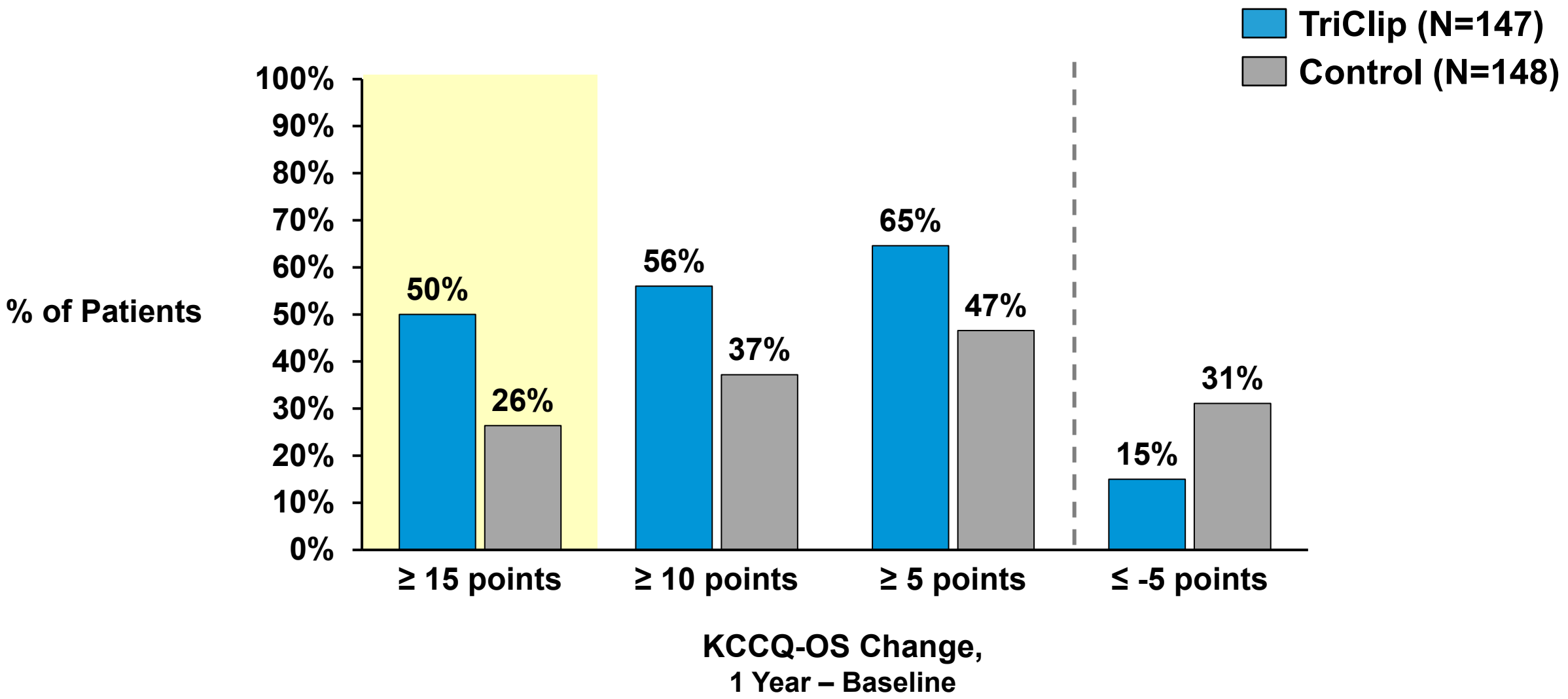
Number of HFH Events	**35**	**28**
Number of Patients	**26**	**20**
Patient-Years	**160**	**162**

Primary Endpoint Component: KCCQ-OS Score Change

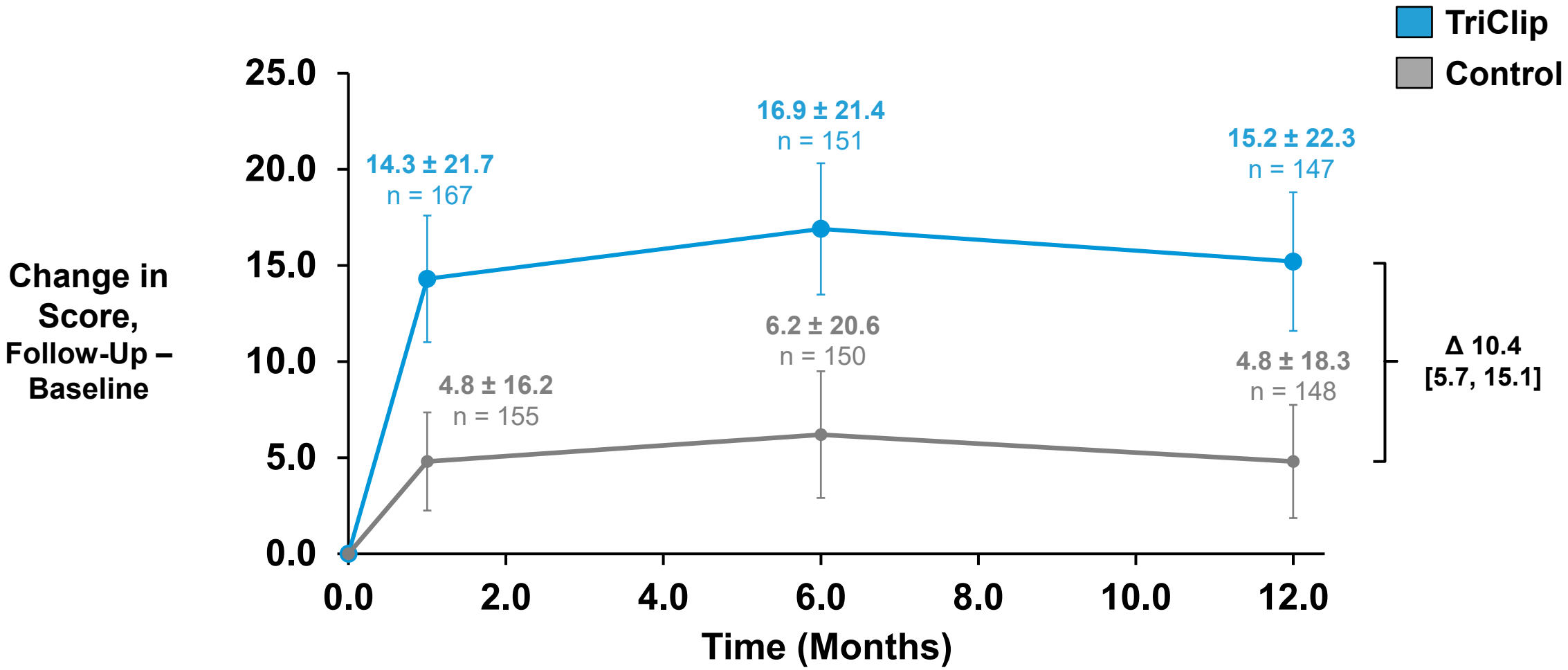


Health Status Improvements Supported by Additional Metrics

More TriClip Patients Improved KCCQ-OS Across Thresholds



Sustained Improvement in KCCQ-OS



Secondary endpoint # 2 change in KCCQ-OS at 12 months met, p<0.001

95% CI, not adjusted for multiple testing

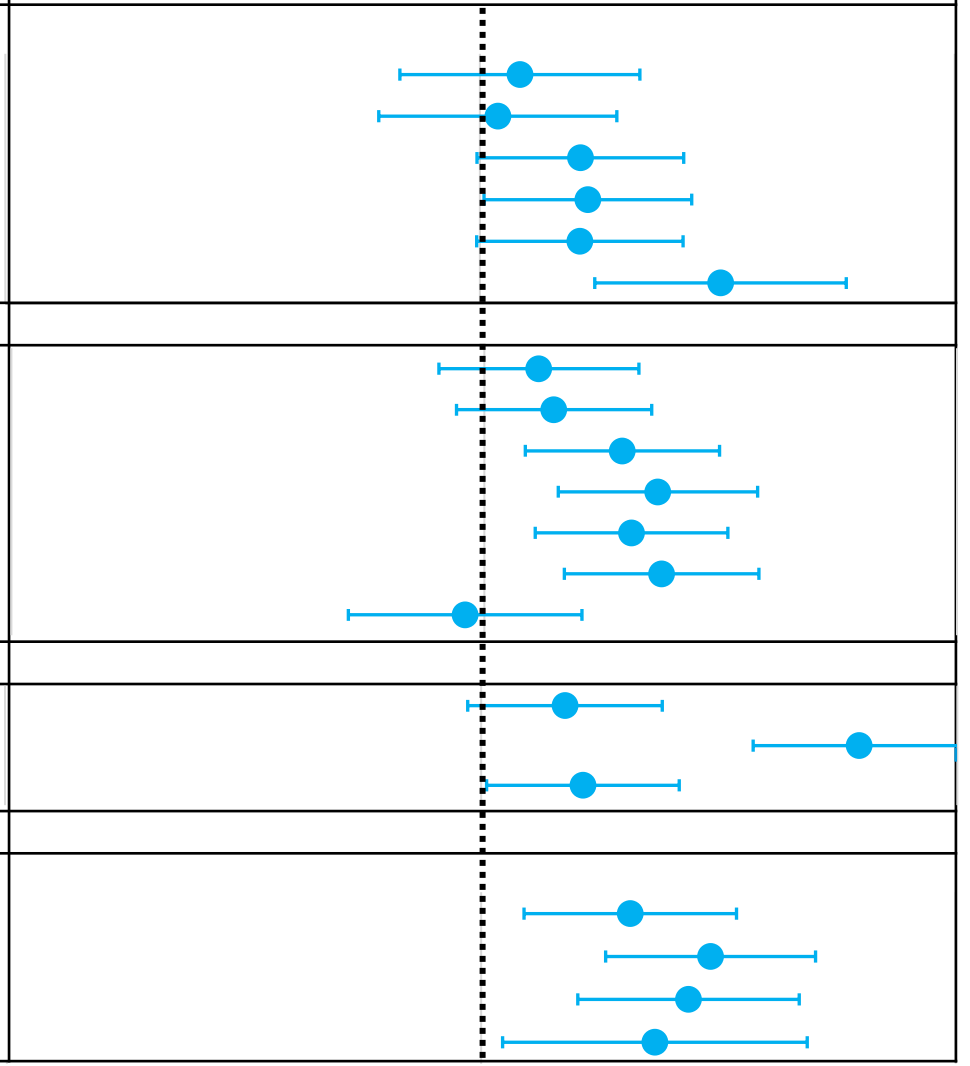
KCCQ-OS – Significant Improvements Observed in TriClip as Compared to Control Across All Domains

KCCQ	Paired Difference (12 months – Baseline) Mean ± SD	
	TriClip	Control
Overall Summary Score	15.2 ± 22.5	4.0 ± 17.7
Physical Limitation Domain	9.2 ± 22.9	1.6 ± 21.6
Total Symptom Domain	12.0 ± 23.2	4.2 ± 20.9
Quality of Life Domain	21.4 ± 26.3	6.4 ± 20.8
Social Limitation Domain	19.1 ± 28.4	3.6 ± 28.1

Patients who underwent TV surgery before 12-month follow-up were excluded from this analysis

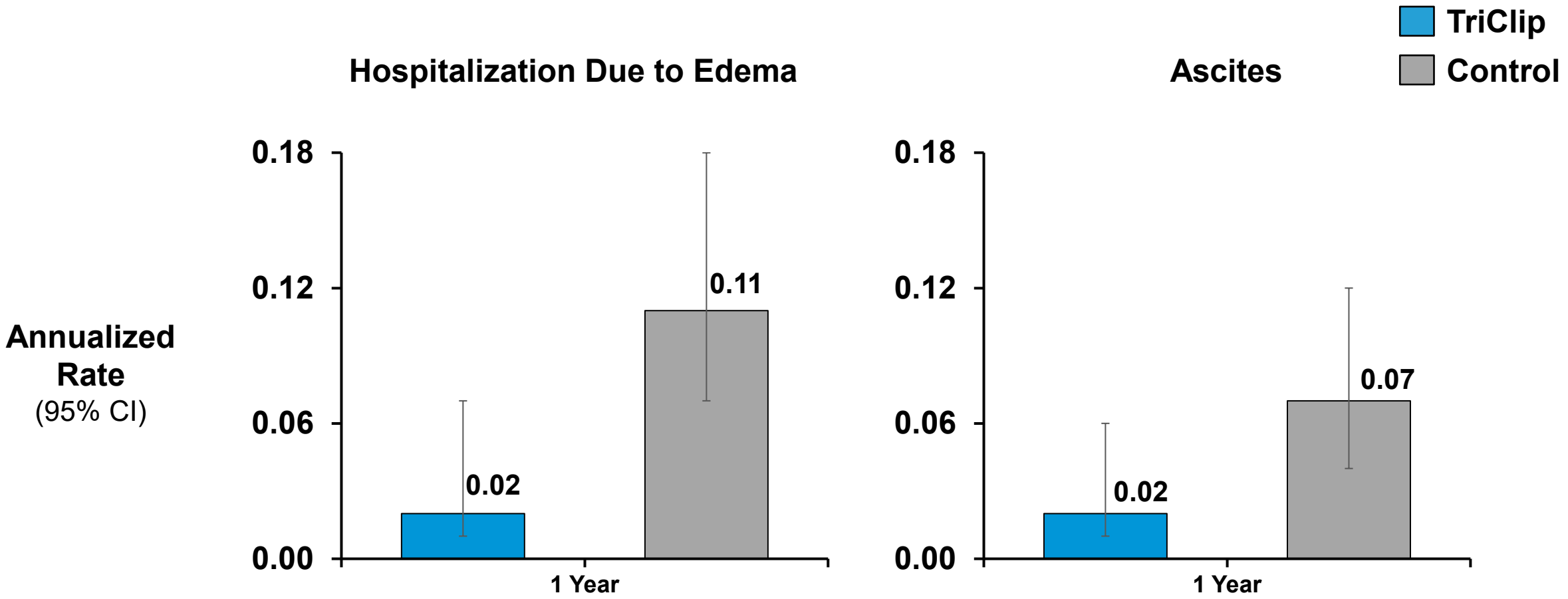
Odds of Subject Response Improvement for Individual Questions in KCCQ

	Odds Ratio (# of patients who improved) [95% CI]
Physical Limitation Domain	
How much were you limited by heart failure in your ability to do the following:	
Dressing Yourself	
Showering/Bathing	
Walking one block on level ground	
Doing yardwork, housework, or carrying groceries	
Climbing a flight of stairs without stopping	
Hurrying or jogging	
Total Symptom Domain	
How often are you waking up with swelling in your legs, ankles, or feet?	
How bothered are you by swelling in your legs, ankles, or feet?	
How often does fatigue limit your ability to do what you want?	
How bothered are you by fatigue?	
How often does shortness of breath limit your ability to do what you want?	
How bothered are you by shortness of breath?	
How often have you slept elevated due to shortness of breath?	
Quality of life Domain	
How much has your heart failure limited your enjoyment of life?	
If you had to live with your heart failure symptoms as they are now, how satisfied would you be?	
How often have you felt discouraged or down in the dumps because of heart failure?	
Social Limitation Domain	
How much were you limited by heart failure in your ability to participate in the following activities:	
Hobbies, recreational activities	
Working or doing household chores	
Visiting family or friends outside your home	
Intimate relationships with loved ones	



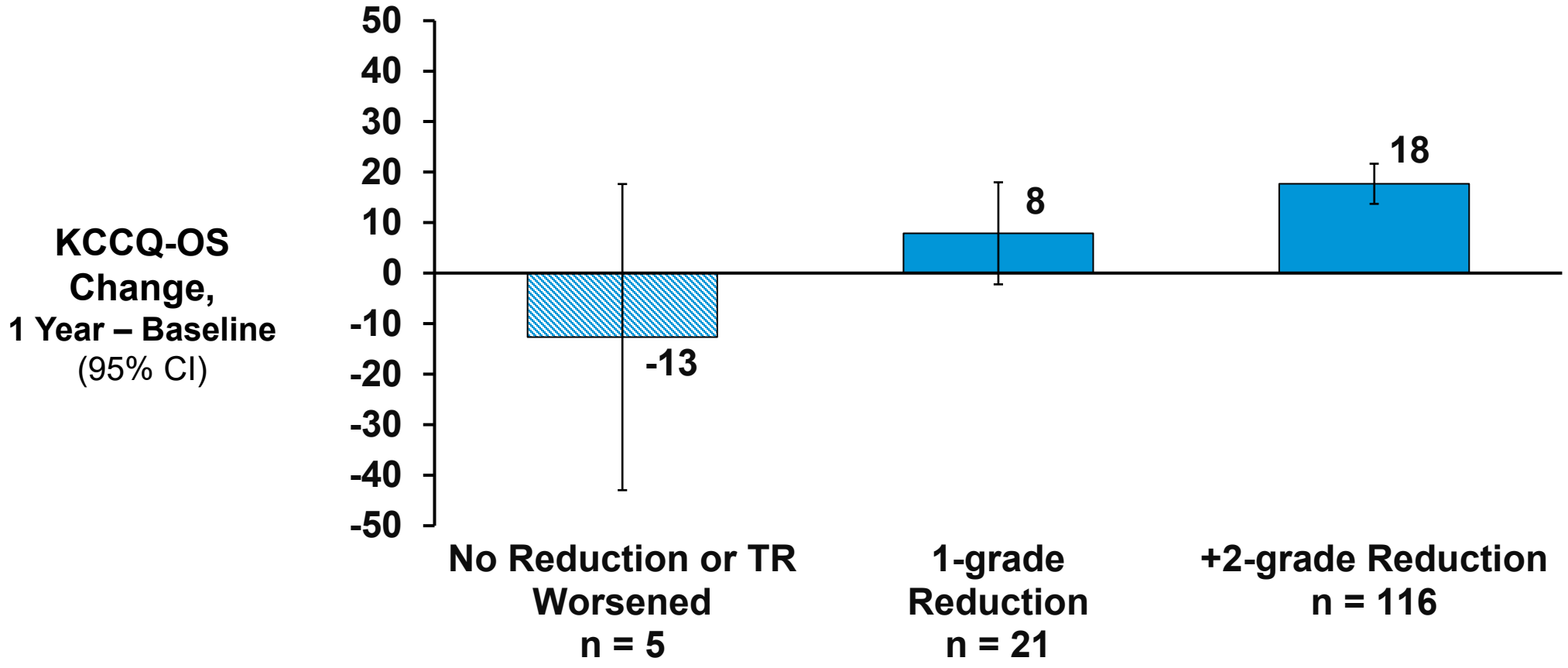
Patients who underwent TV surgery before 12-month follow-up were excluded from this analysis

Edema and Ascites Improvement for TriClip vs Control



CI not adjusted for multiple testing

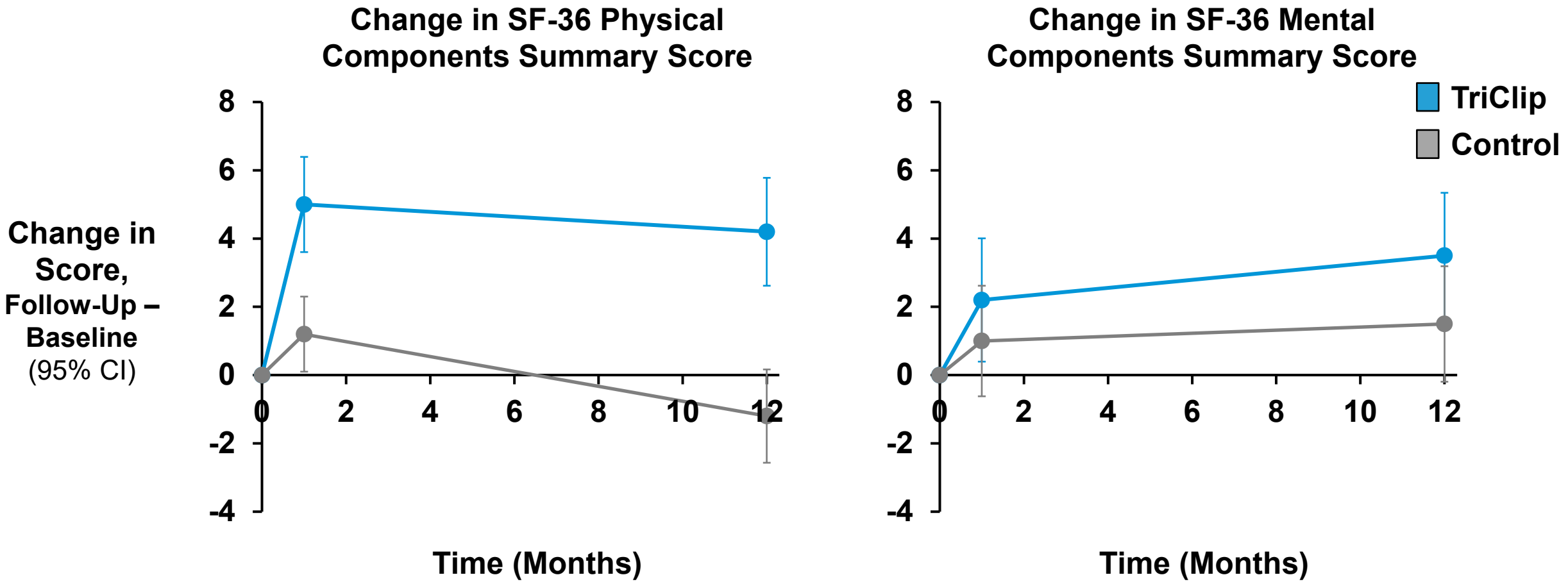
Change in TR Associated with Change in KCCQ-OS



Hashed lines represent low sample size

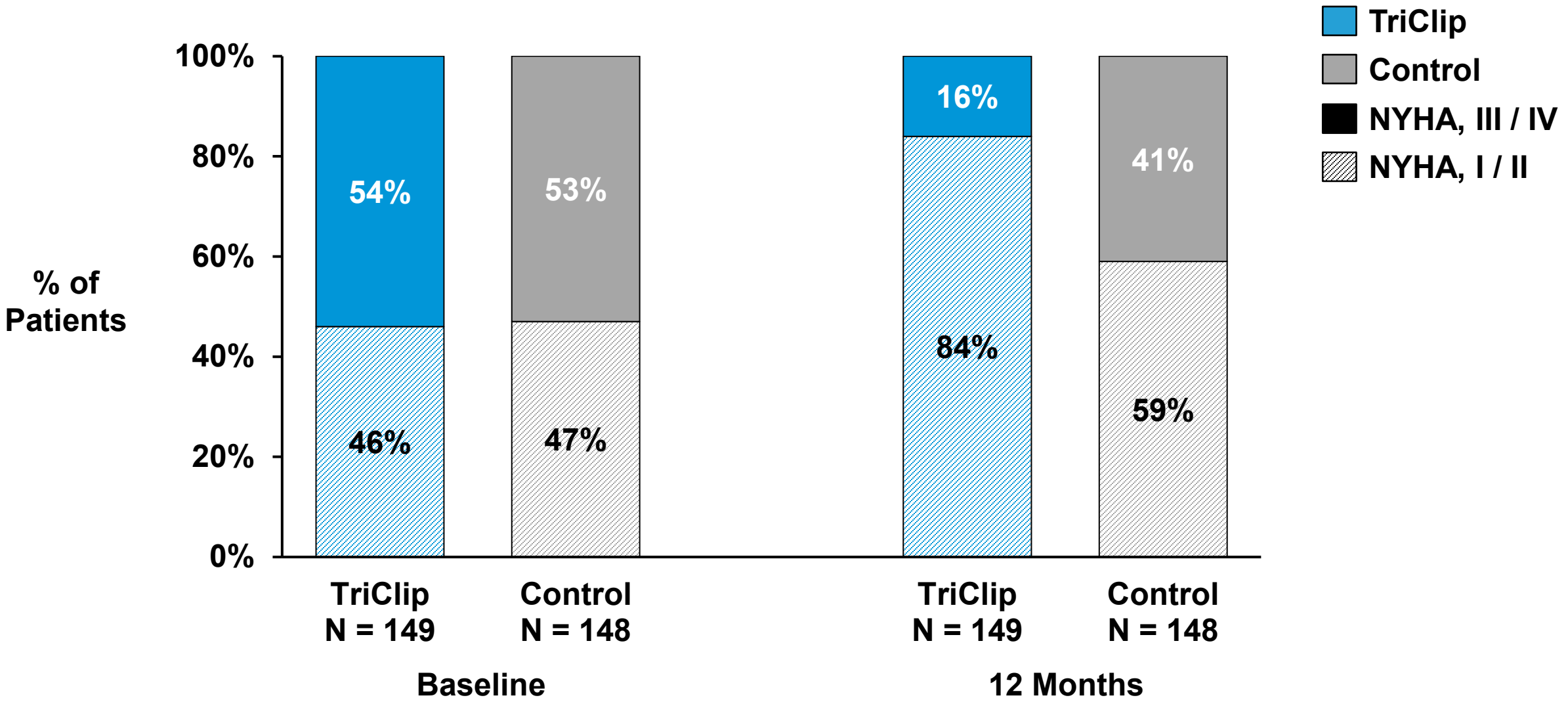
CI not adjusted for multiple testing

Other Health Status Measures (SF-36) Supportive of Device Benefit

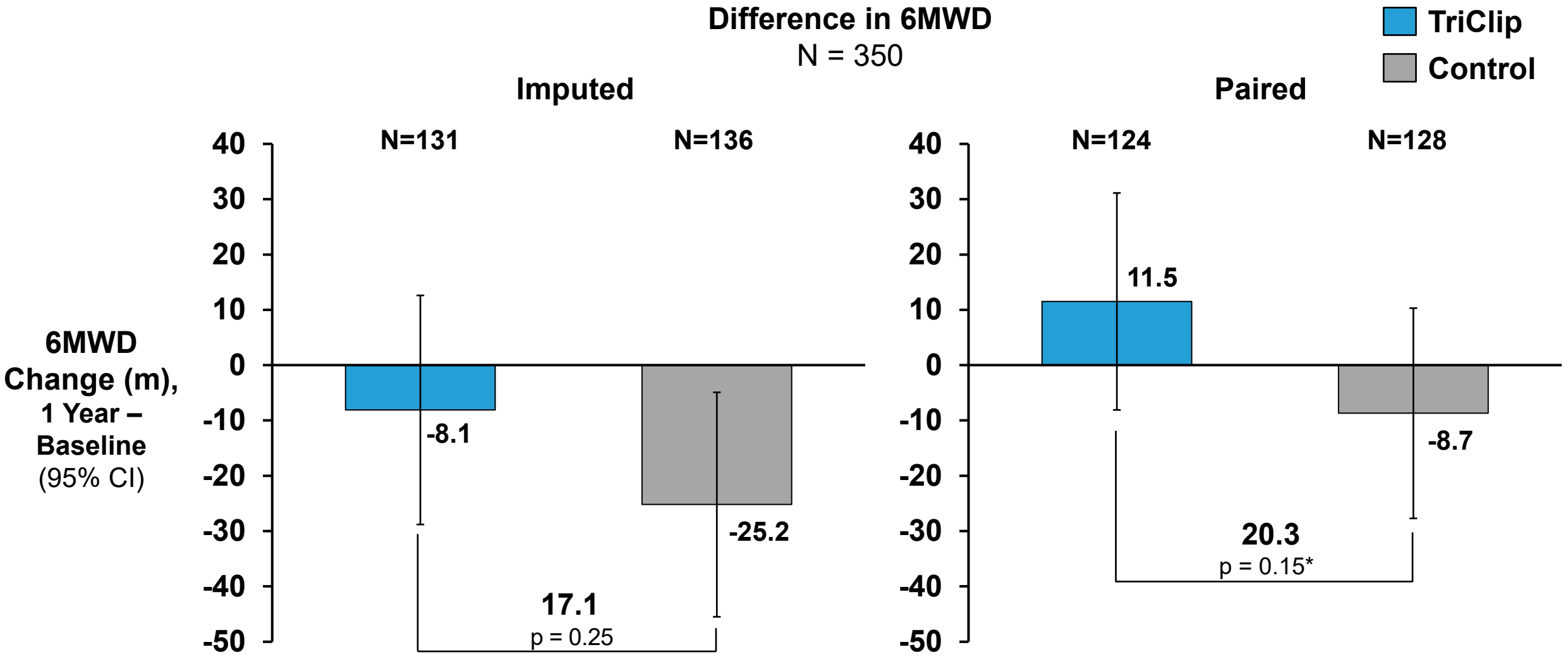


CI not adjusted for multiple testing

Symptom Relief (NYHA) Greater in Device Patients



6 Minute Walk Distance (6MWD)



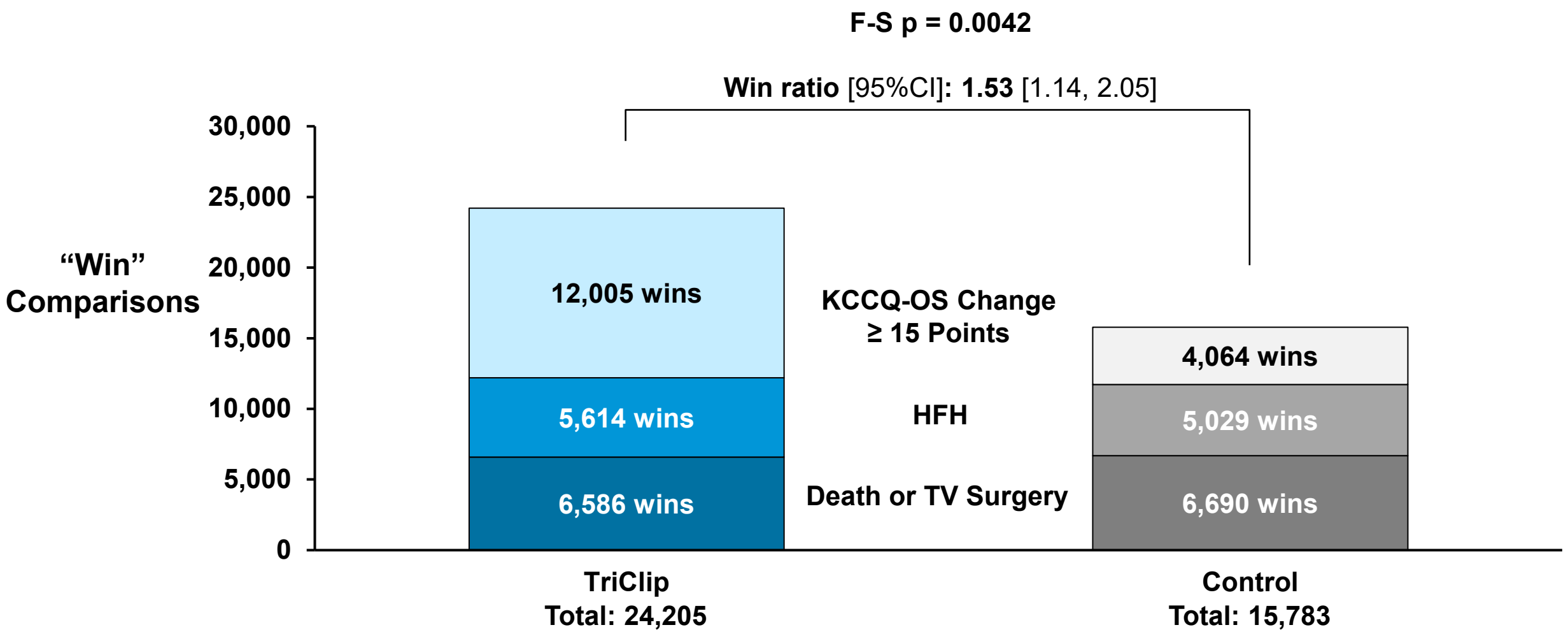
Secondary endpoint # 4: Change in 6MWD at 12 months not met, p=0.25

*p-value not adjusted for multiple testing

Full Randomized Cohort (N=572)

Primary Endpoint: Full Randomized Cohort (N=572)*

Device patients 53% more likely to have better outcome



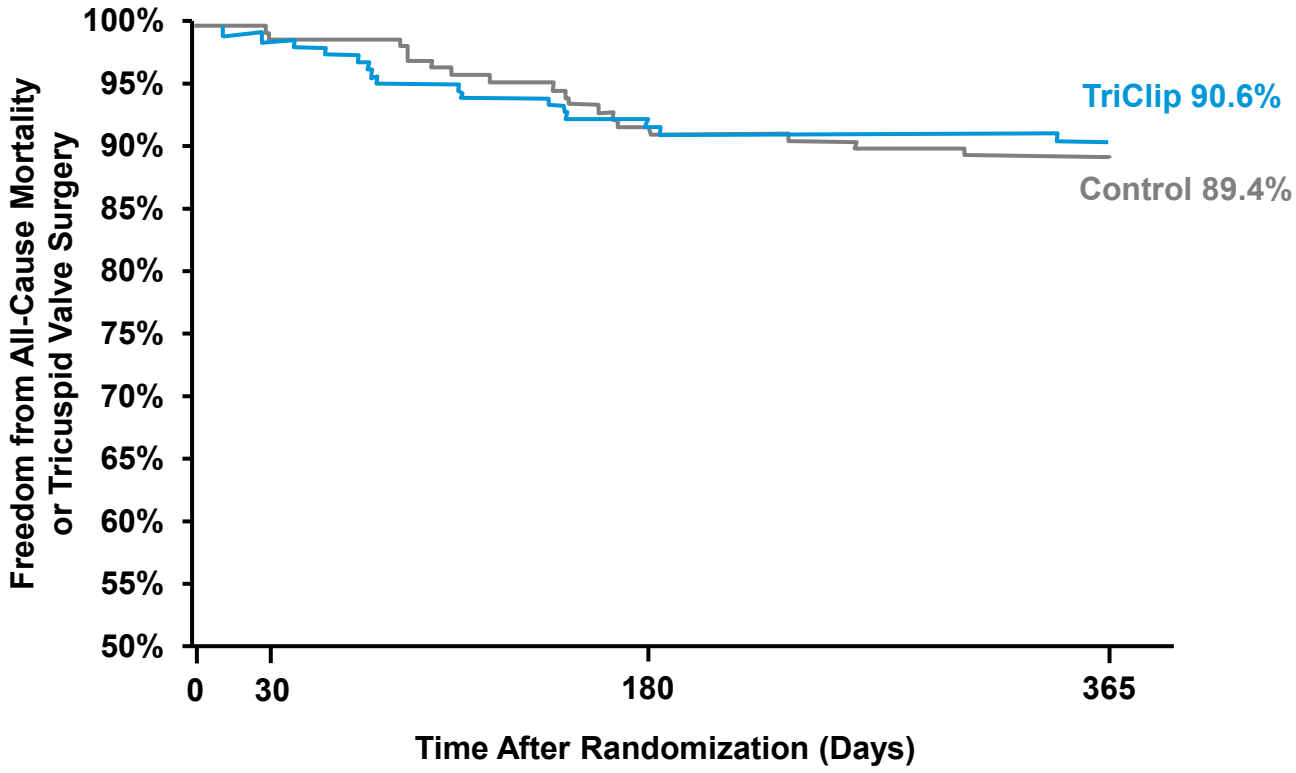
*56 patients pending 1 year visit F-S = Finkelstein-Schoenfeld

p value not adjusted for multiple testing

No Difference in All-Cause Mortality or TV Surgery: Full Randomized Cohort Consistent with Primary Analysis

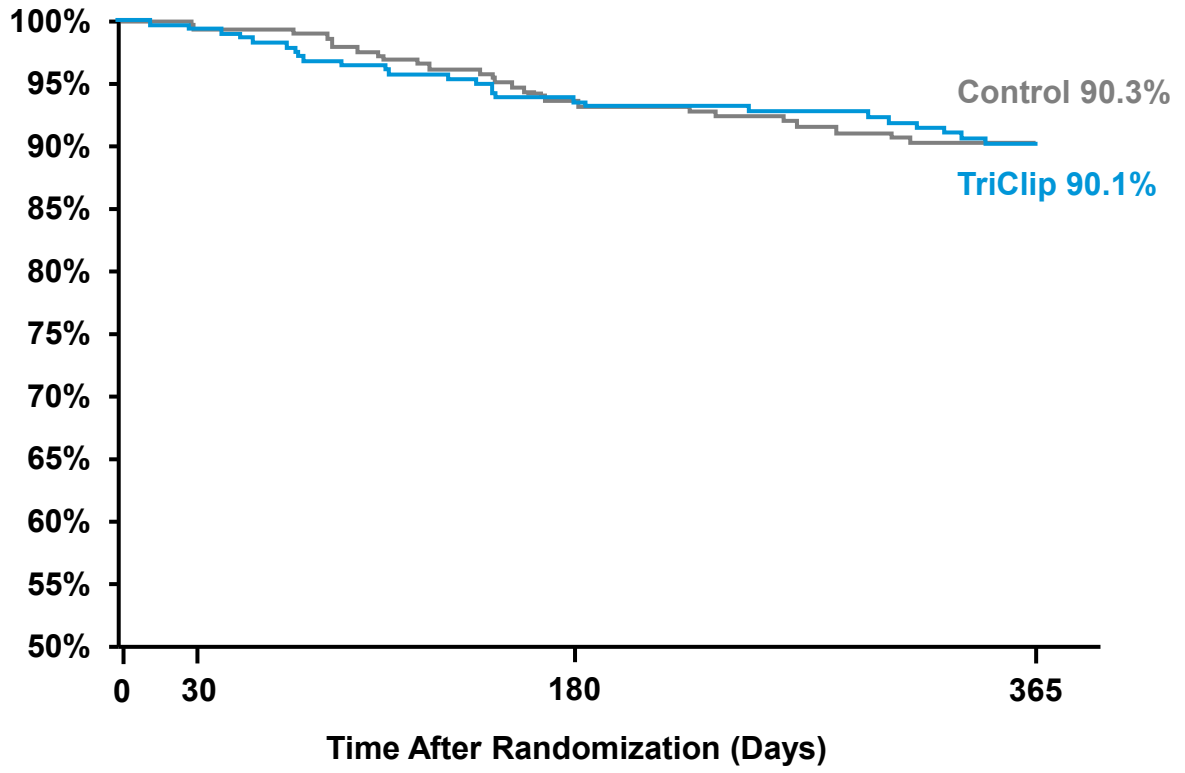
Primary Analysis Cohort

N = 350



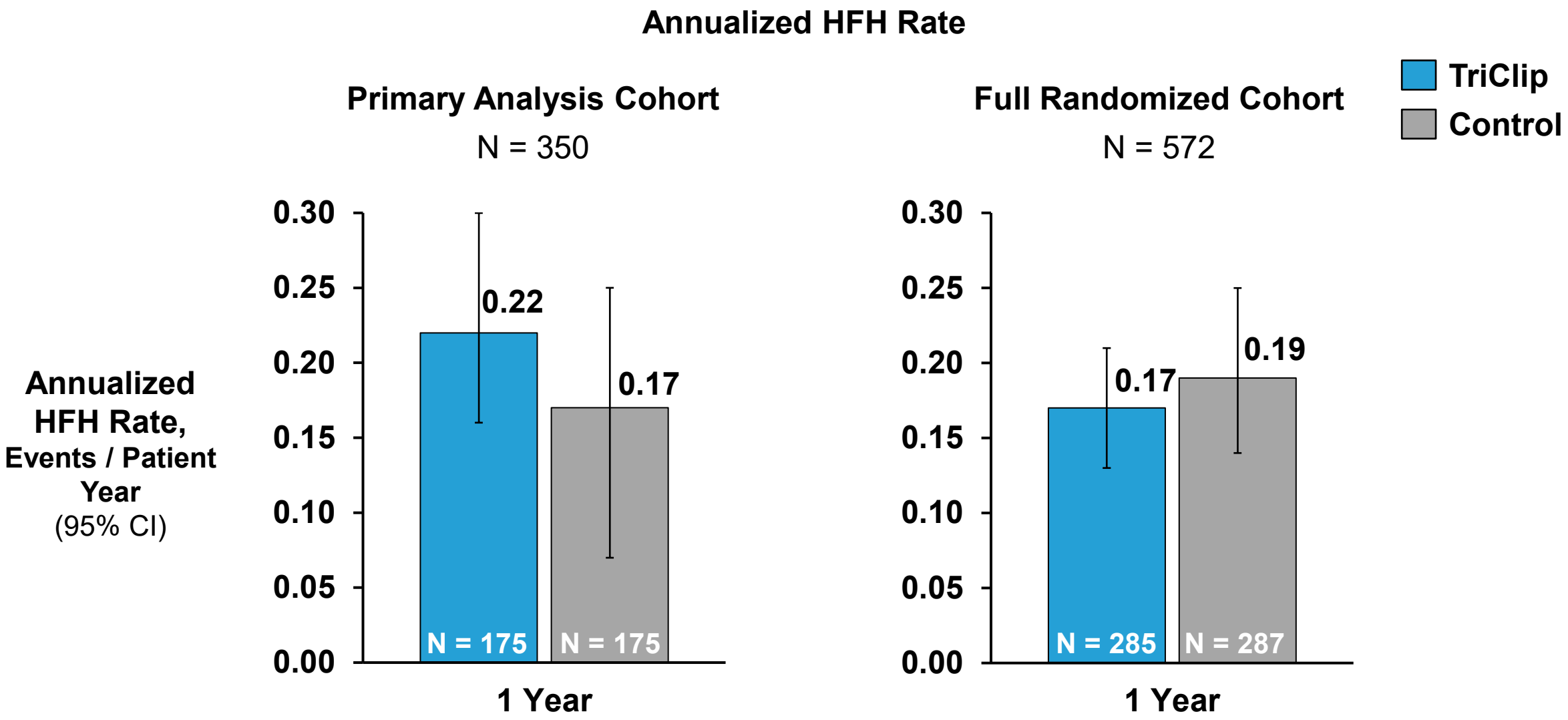
Full Randomized Cohort

N = 572

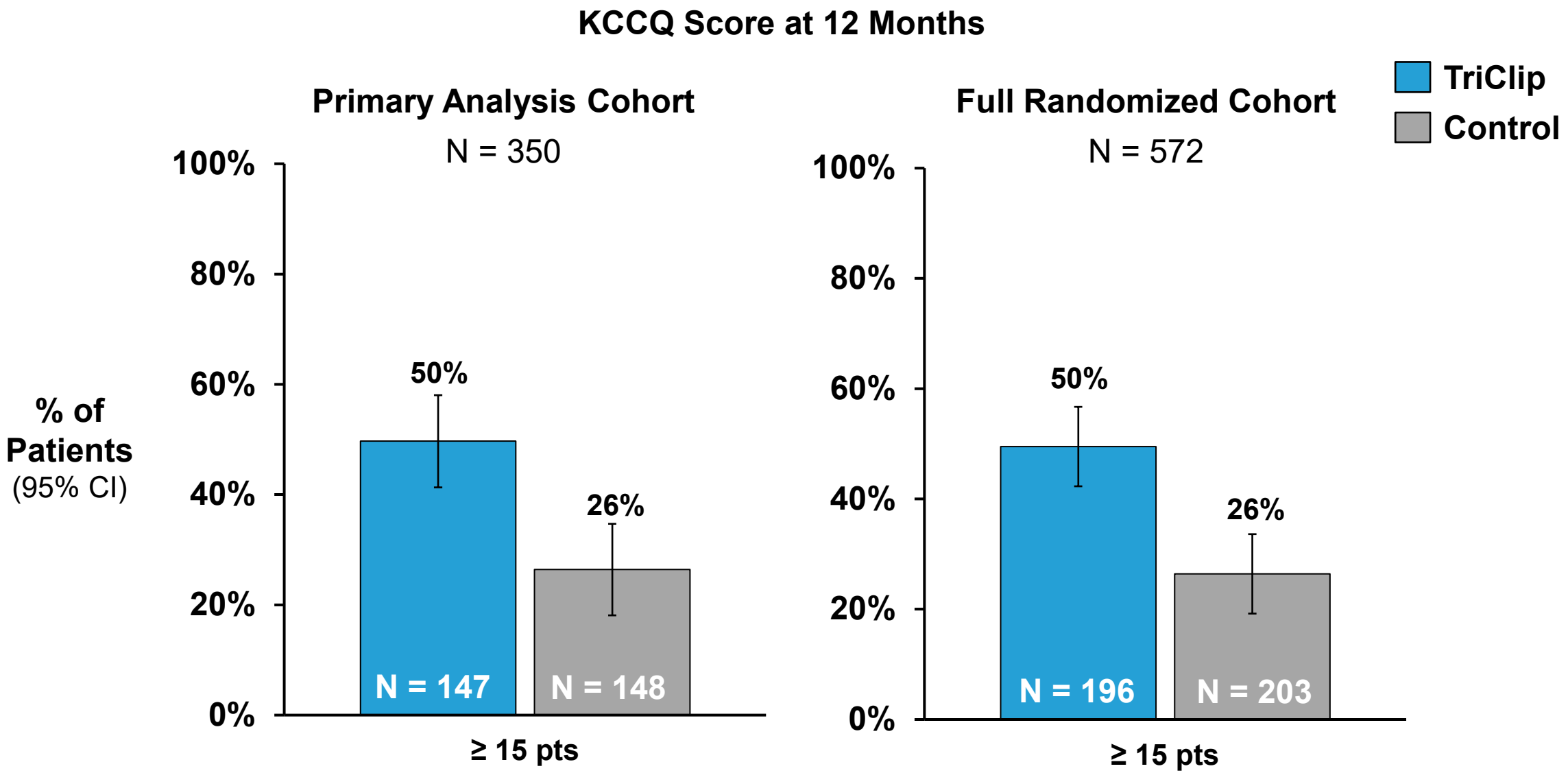


No. at Risk:								
	175	170	158	152	285	278	256	195
	175	173	154	149	287	285	252	201

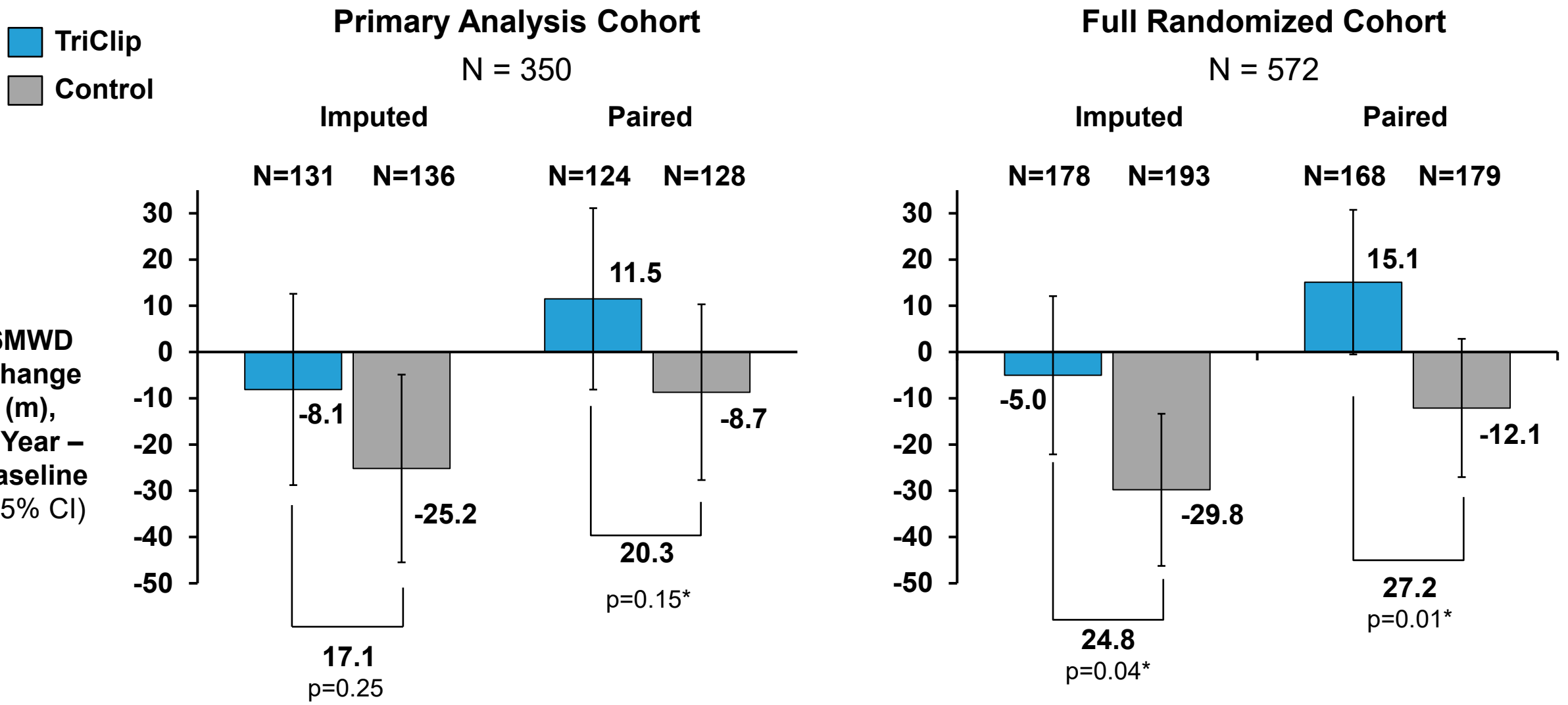
No Difference in HFH: Full Randomized Cohort Consistent with Primary Analysis



KCCQ Improvements: Full Randomized Cohort Consistent with Primary Analysis



6 Minute Walk Distance (6MWD) Trends in Favor of TriClip



*p value not adjusted for multiple testing

Single-Arm Cohort

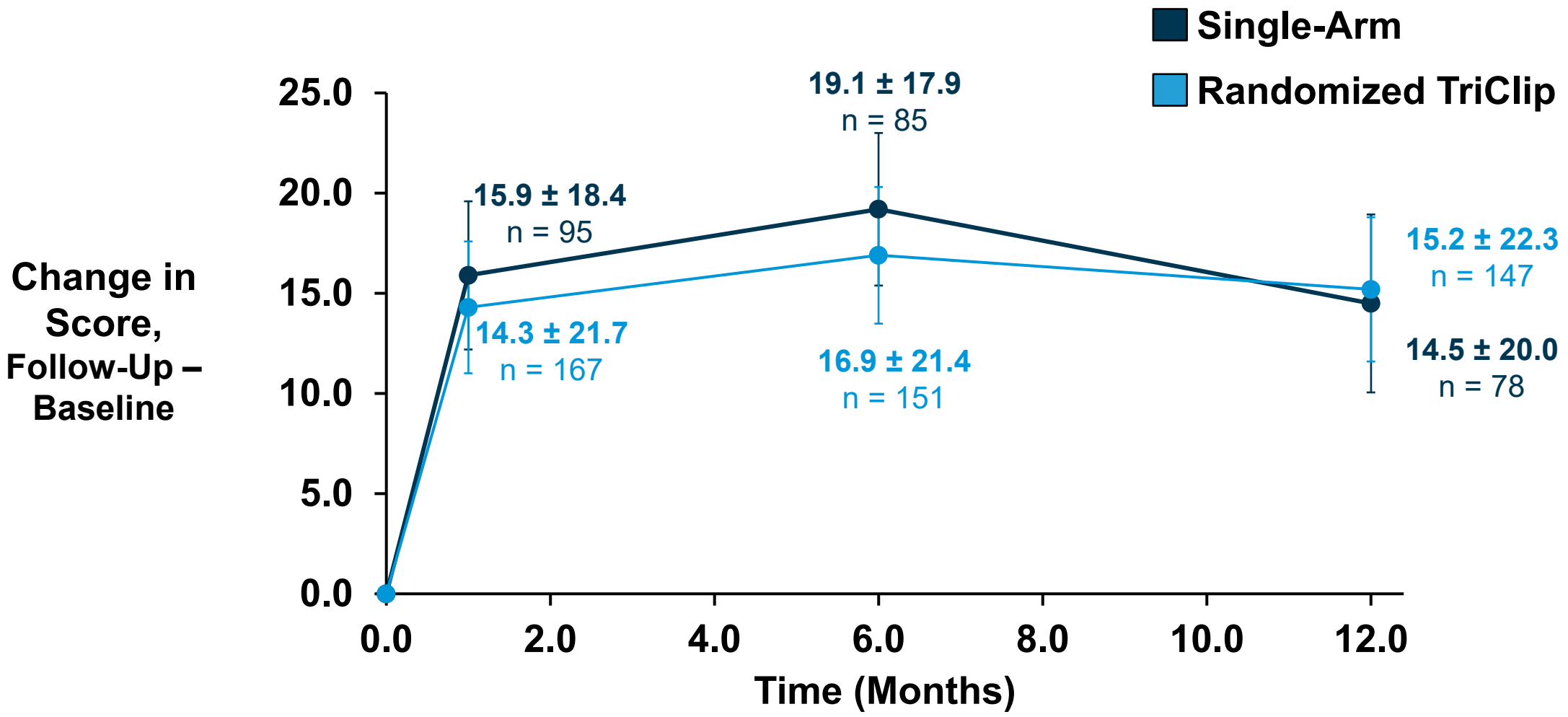
Patients in Single-Arm Cohort had More Advanced Disease than those in Randomized Cohort

	Randomized Cohort N = 350	Single-Arm Cohort N = 100
Age, mean ± SD (years)	**77.9 ± 7.3**	**80.4 ± 6.2**
Myocardial infarction	4.0%	9.0%
Stroke	8.6%	12.0%
Hypertension	80.9%	83.0%
COPD	**12.3%**	**22.0%**
HFH within previous year	25.1%	22.0%
CRT / ICD / permanent pacemaker	**14.9%**	**35.0%**
Prior mitral/aortic intervention	36.9%	44.0%
Torrential TR	**50.9%**	**74.0%**
Coaptation gap (mm), ± SD	**5.4 ± 1.8**	**7.4 ± 2.7**
RVEDD, base (cm), ± SD	**5.0 ± 0.8**	**5.4 ± 0.9**
RA volume (mL), ± SD	**148.1 ± 84.3**	**181.7 ± 103.7**
LVEF (%), ± SD	59.0 ± 9.9	58.9 ± 9.5
NYHA III / IV	57.4%	59.0%
KCCQ-OS score, ± SD	55.1 ± 23.8	54.5 ± 22.6
Six-minute walk distance (m), ± SD	247.1 ± 123.3	237.7 ± 120.4

Single-Arm Cohort Met Primary Endpoint

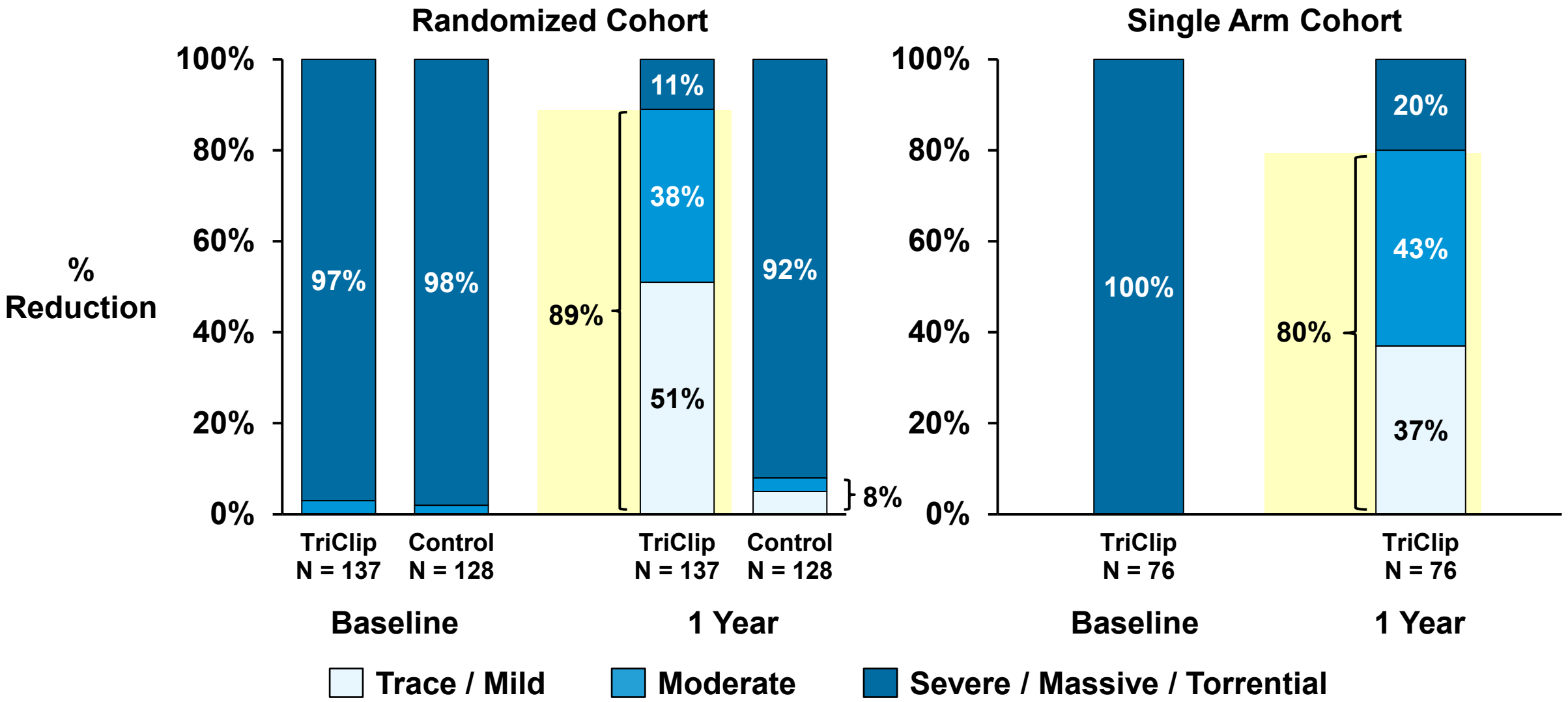
	Estimate n/N (%)	Lower Limit for One-Sided 98.75% CI	Performance Goal	p-value
Primary Endpoint: Survival at 12 months with ≥ 10-point improvement in KCCQ-OS	**42 / 91 (46.2%)**	**34.3%**	**30%**	**0.0008**

KCCQ Improvements: Single-Arm Cohort Consistent with Randomized Cohort



95% CI, not adjusted for multiple testing

Significant and Sustained TR Reduction in Single Arm



No MAEs in Single Arm Cohort at 30 Days

	Estimate	Lower Limit for Two-Sided 95% CI	Performance Goal	p-value
Freedom from MAE through 30 Days	**100%**	**96.3%**	**80%**	**< 0.0001**

Major Adverse Events (MAE) through 30-Days Post-Procedure	TriClip N = 100
Any MAE	**0**
New-onset renal failure	**0**
Cardiovascular mortality	**0**
Endocarditis requiring surgery	**0**
Non-elective CV surgery, TriClip-related AE	**0**

Physiologic Impact of TR Reduction

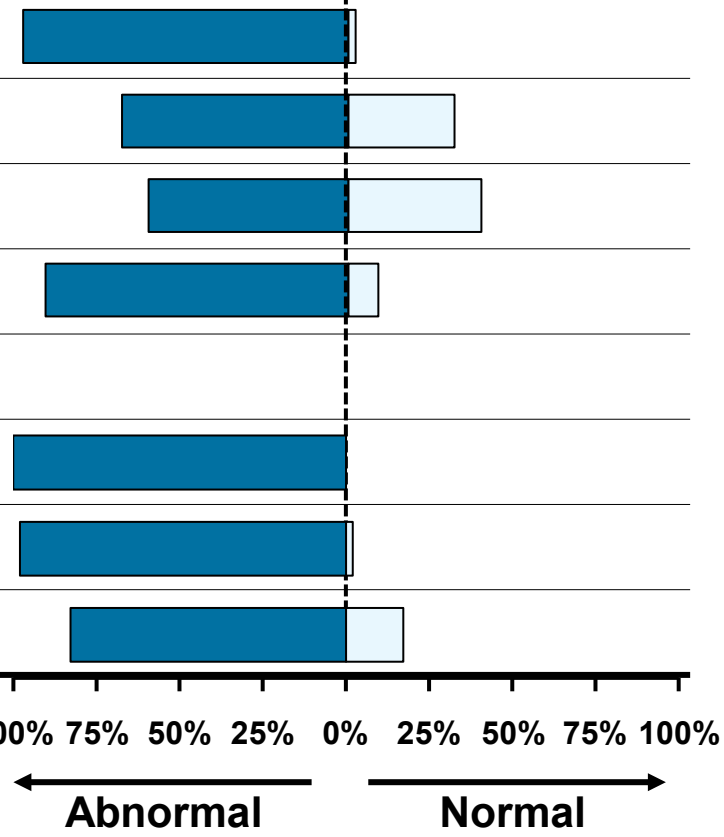
Full Randomized Cohort (N=572)

Last Available Follow-up

Baseline Anatomical Measurements

Echo Measurements		Average (N size)	Normal Threshold
RA Size	RAVI (mL/m^2)	77.5 ± 41.3 (557)	< 25 mL/m^2
Ann. Size	TV Annulus Diameter (cm)	4.3 ± 0.8 (554)	< 4.0 cm
RV Size	RVEDD-mid (cm)	3.7 ± 0.7 (552)	< 3.5 cm
	RVEDD-base (cm)	5.0 ± 0.8 (553)	< 4.1 cm
CT Measurements			
RA Size	RAEDV-I (mL/m^2)	99.7 ± 42.9 (64)	< 25 mL/m^2
Ann. Size	TV Annular Area-I (mm^2/m^2)	1033 ± 241 (64)	< 560 (mm^2/m^2)
RV Size	RVEDV-I (mL/m^2)	136.7 ± 36.6 (64)	< 100 mL/m^2

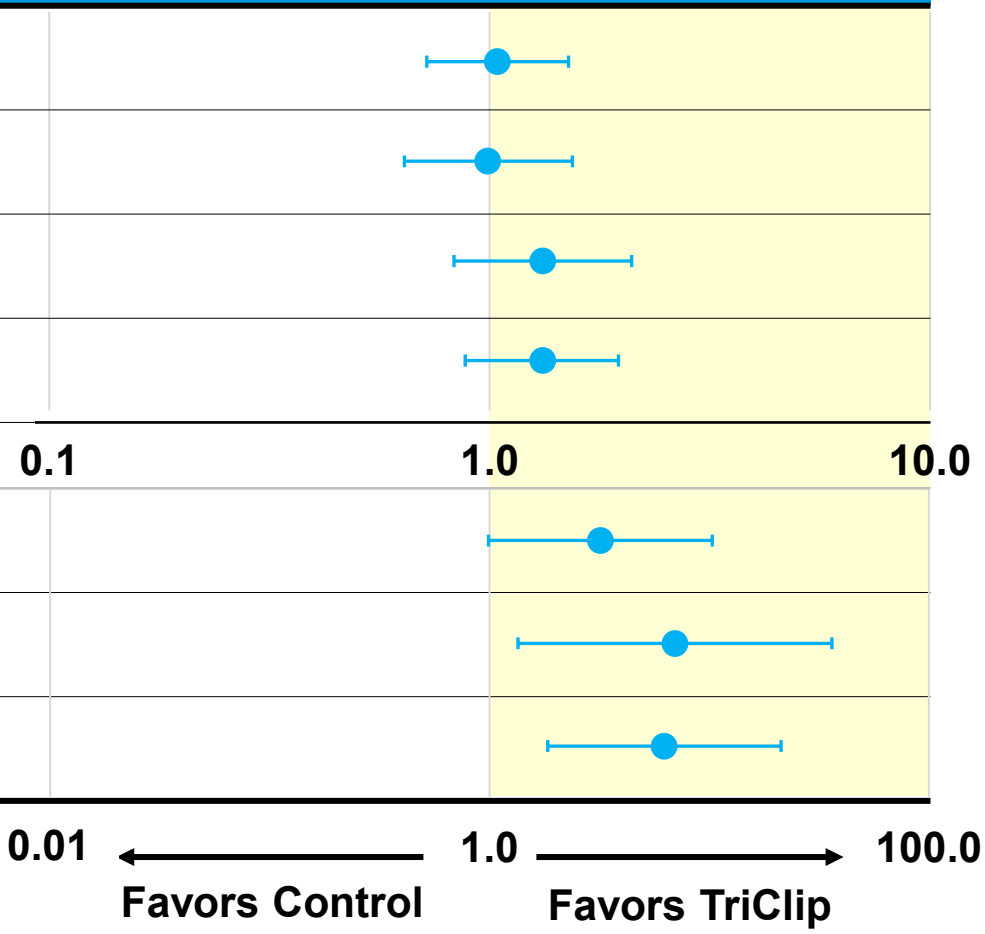
Baseline Distribution*



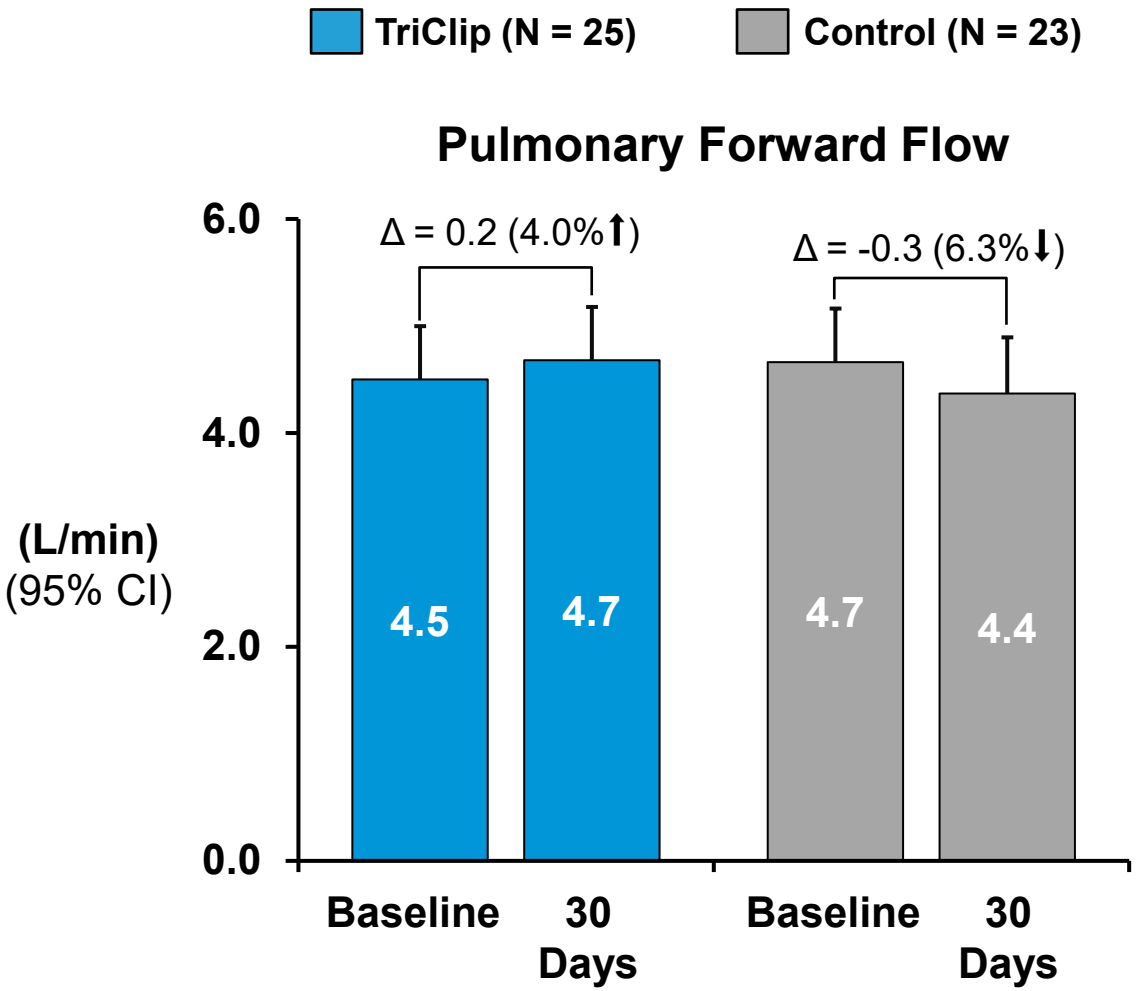
*Includes both TriClip and control patients

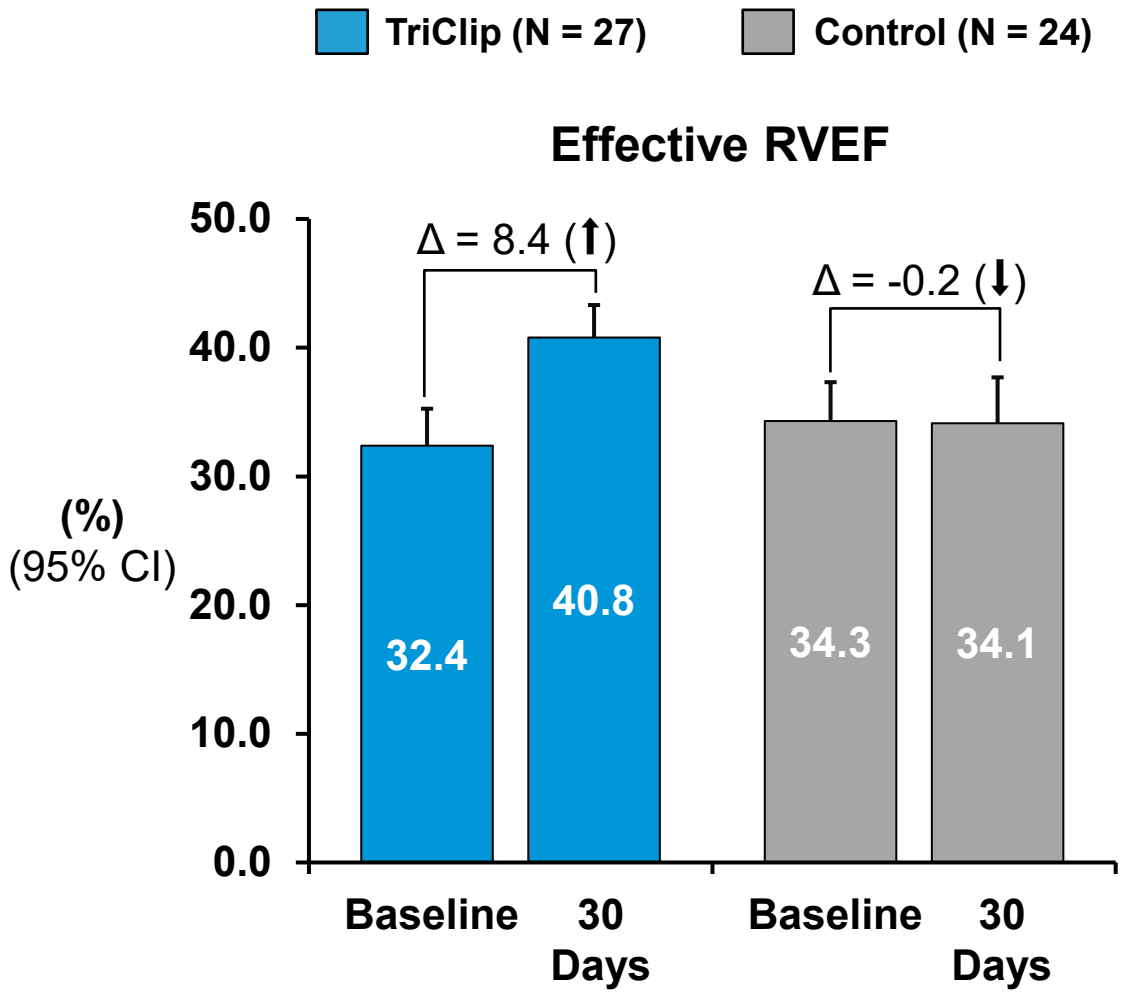
CT Measurements Support Reverse Remodeling

		Δ in Anatomic Measurements Between 12 Months or Last Observation Carried Forward (LOCF) and Baseline (n size)	
Echo Measurements		**Control**	**TriClip**
RA Size	RAV-I (mL/m²)	-1.5 ± 28.7 (262)	1.2 ± 27.6 (270)
Ann. Size	TV Annulus Diameter (cm)	-0.12 ± 0.72 (259)	-0.13 ± 0.64 (271)
RV Size	RVEDD-mid (cm)	0.01 ± 0.80 (257)	-0.14 ± 0.75 (267)
	RVEDD-base (cm)	-0.09 ± 0.72 (257)	-0.17 ± 0.69 (268)
CT Measurements			
RA Size	RAEDV-I (mL/m²)	3.4 ± 22.9 (30)	-11.9 ± 17.5 (27)
Ann. Size	TV Annular Area-I (mm²/m²)	-33 ± 149 (30)	-107 ± 96 (27)
RV Size	RVEDV-I (mL/m²)	-0.4 ± 17.8 (30)	-20.8 ± 15.4 (27)



Pulmonary Forward Flow and Effective RVEF (MRI)
Paired Analysis

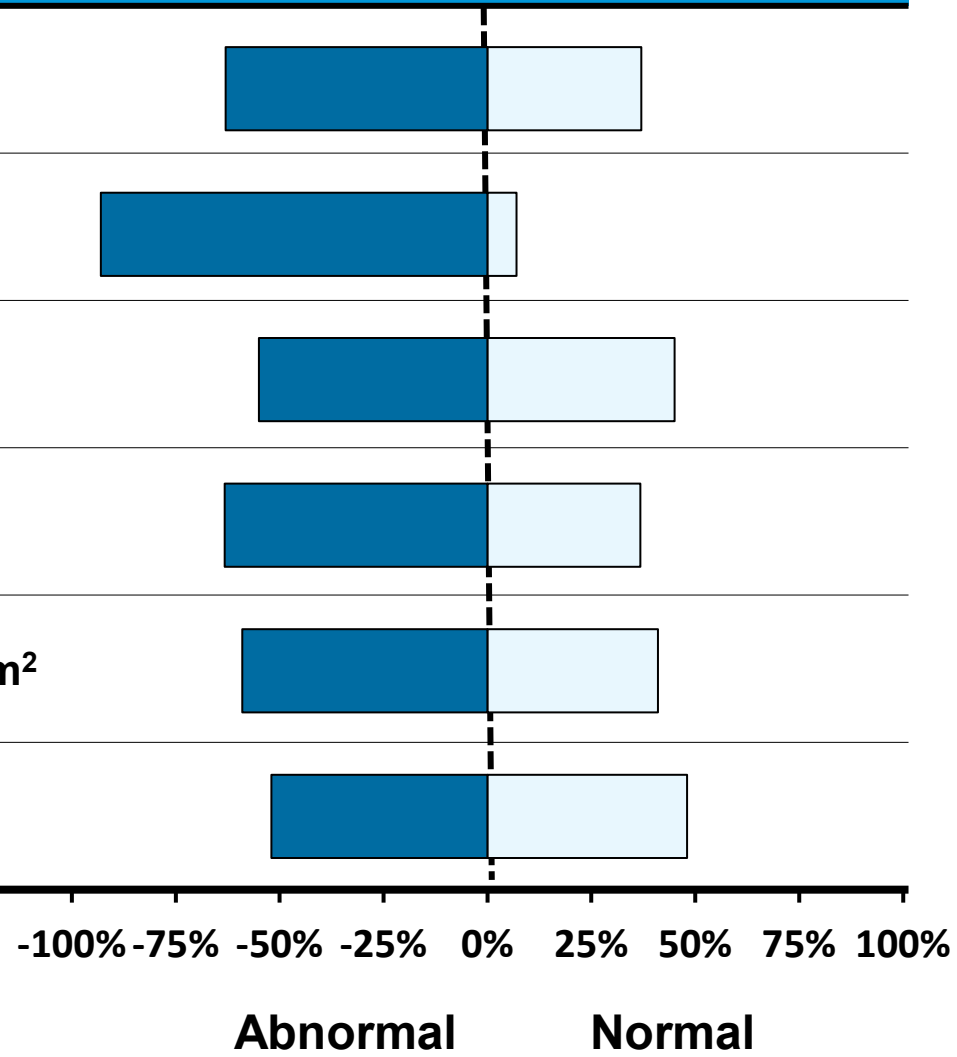




Effective RV EF = Forward Stroke Volume / RVEDV

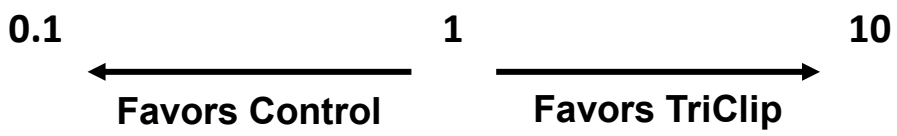
Baseline Biomarkers

Biomarkers		Average (N size)	Normal Threshold
Cardiac Function	BNP (pg/mL)	373.8 ± 356.7 (318)	< 200 pg/mL
	NT-proBNP (pg/mL)	2136 ± 2611 (234)	< 450 pg/mL
Liver Function	MELD-XI	10.3 ± 5.2 (537)	< 9.4
	GGT (U/L)	83.0 ± 87.7 (390)	< 40 U/L
Renal Function	eGFR (mL/min/1.73m^2)	56.7 ± 21.0 (543)	> 60 mL/min/1.73m^2
	BUN (mg/dL)	29.5 ± 16.7 (539)	< 25 mg/dL



Change in Liver and Renal Biomarkers Favor TriClip

		Δ in Biomarker Between 12 Months or Last Observation Carried Forward (LOCF) and Baseline (n size)		Odds of 15% Biomarker Measurement Improvement Between 12 Months or LOCF and Baseline [95% CI]
		Control	TriClip	
Cardiac Function	BNP (pg/mL)	9.8 ± 226.5 (126)	29.6 ± 487.2 (142)	
	NT-proBNP (pg/mL)	-61.5 ± 1752 (106)	438 ± 2195 (116)	
Liver Function	MELD-XI	0.5 ± 3.3 (250)	-0.4 ± 3.3 (263)	
	GGT (U/L)	-1.0 ± 55.3 (179)	-10.9 ± 67.8 (191)	
Renal Function	eGFR (mL/min/1.73m^2)	-2.5 ± 13.9 (253)	0.8 ± 12.8 (266)	
	BUN (mg/dL)	0.9 ± 12.7 (249)	0.1 ± 14.4 (266)	



Effectiveness Summary: TriClip Showed Clinically Meaningful and Sustained TR Reduction

- Primary endpoint met
  - No significant differences in mortality/tricuspid surgery or HFH at 1 year
  - Significant sustained improvement in KCCQ score
- Significant sustained reductions in TR
- KCCQ associated with TR at 1 year
- Secondary endpoints met with exception of 6MWD, although still favoring TriClip
- Totality of data across the single arm cohort, full randomized cohort, and trends in physiological markers substantiates treatment effectiveness

Clinical Perspective

Philipp Lurz, PhD, MD

Director Department of Cardiology

Universitätsmedizin Mainz, Germany

Consistent Favorable Safety Profile

Major Adverse Events (MAE) through 30-Days Post-Procedure	TRILUMINATE CE Mark N = 85[1]	bRIGHT N = 511[2]	TRILUMINATE Pivotal (RCT Device) N = 281	TRILUMINATE Pivotal (Single-Arm) N = 100
Any MAE	**1.2%**	**2.5%**	**1.1%**	**0%**
New-onset renal failure	1.2%	1.4%	0.7%	0
Cardiovascular mortality	0	0.8%	0.4%	0
Endocarditis requiring surgery	0	0	0	0
Non-elective CV Surgery, TVRS for device-related AE	0	0.2%	0	0
Stroke	0	0.4%	-	-
Myocardial Infarction	0	0	-	-

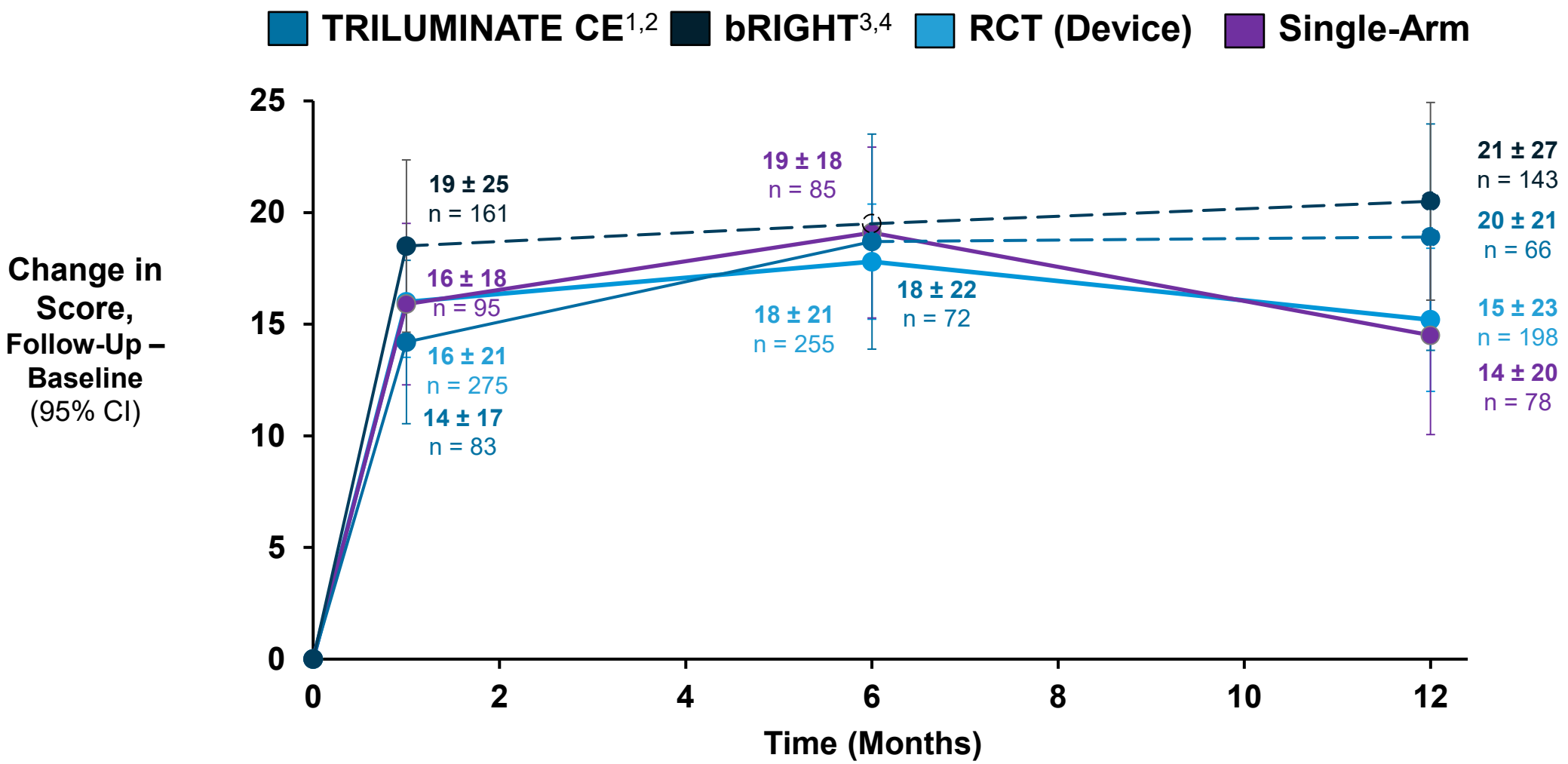
1. Nickenig, 2019; 2. Lurz, 2023

Consistent TR Reduction Across Trials

	TRILUMINATE CE Mark[1] N = 85	bRIGHT[2] N = 511	TRILUMINATE Pivotal RCT Device N = 285	TRILUMINATE Pivotal Single Arm N = 100
% Moderate or less TR at 30 days (Paired from Baseline)	**57%**	**77%**	**89%**	**80%**

1. Nickenig, 2019; 2. Lurz, 2023

Consistent Improvement in KCCQ



1. Nickenig, 2019; 2 Lurz, 2021 JACC; 3.Lurz, 2021 PCR London Valves; 4. Lurz, 2022 PCR London Valves

Clinical Practice has Changed with Availability of TriClip

- Patients need treatment options, demand increasing
- Heterogenous disease with significant comorbidities
  - Come from valve clinic, heart failure hospitalization
- Consistent safety and efficacy demonstrated across trials and over time
- Improvement in QoL directly related to improvement in TR severity

Summary

Lars Sondergaard, MD, DMSc

Chief Medical Officer and Divisional Vice President, Medical Affairs

Abbott

Post Approval Commitments

- Complete follow up for all patients enrolled in TRILUMINATE Pivotal for 5 years (includes both RCT and Single-Arm)
- Upon approval, initiate post approval study in contemporary real-world setting
  - Objective: evaluate patients across spectrum of disease including patients with more advanced disease and better understand various sub-groups
  - Patients will be followed at 30 days, and then annually through 5 years
  - Baseline and Outcomes at 30 days and 1 year will be collected by leveraging TVT registry
  - Outcomes – Survival and HFH data, 2 – 5 years will be collected via CMS linkage to TVT

Totality of Data Observed Supports KCCQ

- TriClip benefit over Control is demonstrated by
  - **KCCQ-OS** improvement substantial, immediate, sustained and improvement observed across all domains
  - Association between **TR and QoL**
  - **SF-36** also shows improvement in QoL
  - Reduced symptom burden through **NYHA**
  - **6MWD** numerical improvement
  - **Anatomical measurements** and liver and kidney **biomarkers** improvement

TriClip Safe and Effective in Treating Patients with Severe TR

Unmet Need

- Severe TR is a progressive disease
- Debilitating symptoms that impact QoL
- High operative risk with surgery
- Medical therapy alone ineffective
- Patients go untreated

Safety

- Favorable safety profile
- 98% free from MAEs
- Low procedural risk
  - No operative mortality
  - No embolization
  - No device thrombosis

Effectiveness

- TRILUMINATE Trial showed clinically meaningful reductions in TR
- Significant improvements in symptoms and health status sustained through 12 mo
- TR reduction correlates with KCCQ
- Supported by extensive OUS experience

TriClip G4 System for Treatment of Patients with Symptomatic, Severe Tricuspid Regurgitation

February 13, 2024

Circulatory System Devices Panel

Abbott