



CLASP IID Trial: A Randomized Comparison of Transcatheter Edge-to-Edge Repair Devices for Degenerative Mitral Regurgitation – Clinical Outcomes and Echo Findings

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on behalf of **The CLASP IID Trial Investigators**



SEPTEMBER 16-19, 2022
BOSTON CONVENTION AND EXHIBITION CENTER
BOSTON, MA



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.

<u>Affiliation/Financial Relationship</u>	<u>Company</u>
D. Scott Lim, MD	
Grant/Research Support	Abbott, Boston Scientific, Edwards Lifesciences, Medtronic
Consulting Fees/Honoraria	Philips, Venus, Valgen
Konstantinos Koulogiannis, MD	
Consulting Fees/Honoraria/Speaker	Edwards Lifesciences, Abbott

PASCAL Transcatheter Valve Repair System

For Mitral Regurgitation

PASCAL Implant



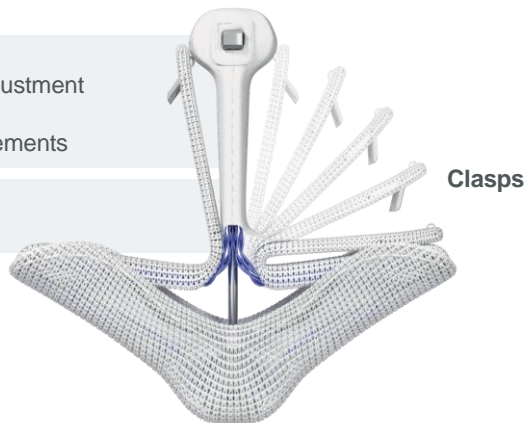
Independent grasping

- Staged leaflet capture and adjustment
- Clasp and reclamp capability with single row of retention elements

Central spacer

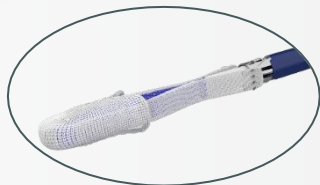
- Bridge the coaptation gap

PASCAL Ace Implant



Nitinol construction

Passive closure,
acute implant flexing



Elongation

Navigate in dense chordae



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

The CLASP IID Randomized Trial

Edwards PASCAL TrAnScatheter Valve RePair System Pivotal Clinical Trial

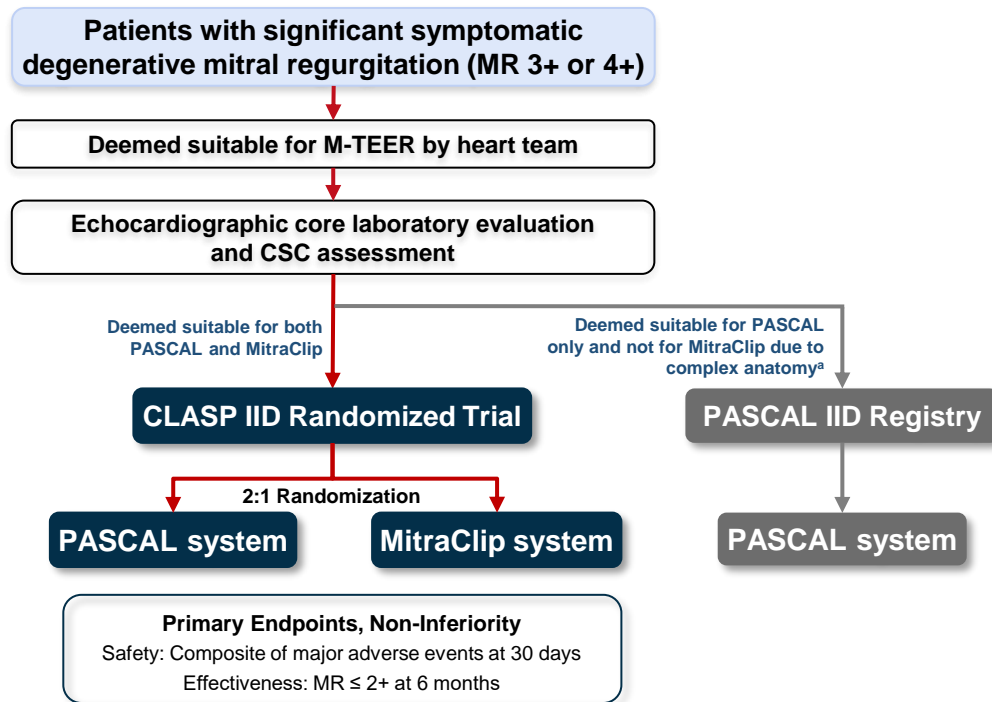
Prospective, multicenter, multinational, randomized, controlled pivotal trial

Purpose:

Evaluate the safety and effectiveness of the PASCAL transcatheter valve repair system compared to the MitraClip system in significant symptomatic DMR patients at prohibitive risk for surgery

IID Trial Oversight:

- Central Screening Committee (CSC)
- Echocardiographic Core Laboratory
- Clinical Events Committee (CEC)
- Data Safety Monitoring Board



Trial Leadership & Oversight

Principal Investigators



Dr. Scott Lim, MD



Jörg Hausleiter, MD



Robert L. Smith, MD



Linda D. Gillam, MD, MPH

Trial Oversight

Echocardiographic Core Laboratory, Atlantic Health System Morristown Medical Center, Morristown, NJ, USA

- Linda D. Gillam, MD, MPH
- Konstantinos Koulogiannis, MD
- Leo Marcoff, MD
- Lillian Aldaia, MD
- Anuj Mediratta, MD

Clinical Events Committee (CEC)

- Pablo A. Quintero Pinzon, MD, *Cardiologist, Heart Failure*
- David E. Thaler, MD, PhD, *Neurologist*
- Carey D. Kimmelstiel, MD, *Interventional Cardiologist*
- Gregory Smaroff, MD, *Cardiothoracic Surgeon*

Data Safety Monitoring Board (DSMB)

- Eugene A. Grossi, MD, *Cardiothoracic Surgery*
- Harold L. Dauerman, MD, *Interventional Cardiology*
- Michael M. Givertz, MD, *Cardiology / Heart Failure*
- Frederick S. K. Ling, MD, *Interventional Cardiology / Cardiovascular Disease*
- John Orav, PhD, *Biostatistics*

Central Screening Committee (CSC)

Cardiac Surgery

- Robert L. Smith, MD
- S. Chris Malaisrie, MD
- Sabine Bleiziffer, MD
- Wilson Y. Szeto, MD
- Vinod H. Thourani, MD
- Howard K. Song, MD, PhD
- Isaac George, MD
- Scott Goldman, MD
- Gorav Ailawadi, MD
- Mubashir Mumtaz, MD

Interventional Cardiology

- D. Scott Lim, MD
- Marvin Eng, MD
- Sammy Elmariah, MD
- Molly Szerlip, MD
- Philipp Lurz, MD, PhD
- Volker Rudolph, MD
- Firas Zahr, MD
- Michael Rinaldi, MD
- Peter Lüdiike, MD
- Brian Whisenant, MD
- Jörg Hausleiter, MD
- Ralph Stephan von Bardeleben, MD, PhD

Echocardiography

- Linda D. Gillam, MD, MPH
- Leo Marcoff, MD
- Lillian Aldaia, MD
- Konstantinos Koulogiannis, MD

54 Enrolling Sites in CLASP IID Trial

Canada



United States



Europe



United States	
CA	<ul style="list-style-type: none"> Cedars-Sinai Medical Center Kaiser Permanente San Francisco Los Robles Regional Medical Center Scripps Clinic Stanford University Medical Center Sutter Heart & Vascular Institute
CO	<ul style="list-style-type: none"> UC Health Medical Center of the Rockies
DC	<ul style="list-style-type: none"> MedStar Washington Hospital Center
FL	<ul style="list-style-type: none"> Cardiac and Vascular Institute
GA	<ul style="list-style-type: none"> Emory University Hospital Piedmont Heart Institute
IL	<ul style="list-style-type: none"> Northwestern University
IN	<ul style="list-style-type: none"> St. Vincent Heart Center of Indiana
MA	<ul style="list-style-type: none"> Beth Israel Deaconess Medical Center Brigham and Women's Hospital Massachusetts General Hospital
MI	<ul style="list-style-type: none"> Henry Ford Hospital
MN	<ul style="list-style-type: none"> Mayo Clinic
MO	<ul style="list-style-type: none"> Saint Luke's Mid America Heart Institute
NC	<ul style="list-style-type: none"> Atrium Health Carolinas Medical Center
NJ	<ul style="list-style-type: none"> Atlantic Health System Morristown Medical Center Rutgers Robert Wood Johnson Medical School
NY	<ul style="list-style-type: none"> Columbia University Medical Center Montefiore Medical Center Northwell-Lenox Hill
OH	<ul style="list-style-type: none"> The Christ Hospital Cleveland Clinic Foundation
OK	<ul style="list-style-type: none"> Oklahoma Heart Institute
OR	<ul style="list-style-type: none"> Oregon Health & Science University
PA	<ul style="list-style-type: none"> Lankenau Medical Center University of Pennsylvania Medical Center UPMC Pinnacle
TN	<ul style="list-style-type: none"> Ascension Saint Thomas Hospital Tristar Centennial Medical Center
TX	<ul style="list-style-type: none"> Baylor Scott & White: Heart Hospital Plano HCA Houston Healthcare Houston Methodist DeBakey Heart & Vascular Center University of Texas Health Science Center
UT	<ul style="list-style-type: none"> Intermountain Medical Center
VA	<ul style="list-style-type: none"> Sentara Norfolk General Hospital University of Virginia Health System Hospital
WA	<ul style="list-style-type: none"> Swedish Medical Center
Europe	
CH	<ul style="list-style-type: none"> Inselspital University of Bern Heart Center Leipzig at University of Leipzig Helios Klinikum Siegburg Klinikum der Universität München Ruhr-Universität Bochum
DE	<ul style="list-style-type: none"> University Heart and Vascular Center Hamburg University Medical Centre Mainz University of Ulm West German Heart and Vascular Center, University Hospital Essen
Canada	
BC	<ul style="list-style-type: none"> St. Paul's Hospital, University of British Columbia
ON	<ul style="list-style-type: none"> St. Michael's Hospital
QC	<ul style="list-style-type: none"> Laval Hospital

Top 20 Enrolling Sites in CLASP IID Trial

Site Principal Investigator(s)	
1	Firas Zahr, MD and Scott Chadderdon, MD Oregon Health & Science University, Portland, OR
2	Raj Makkar, MD Cedars-Sinai Medical Center, Los Angeles, CA
3	Ralph Stephan von Bardeleben, MD, PhD University Medical Centre Mainz, Mainz, Germany
4	Robert M. Kipperman, MD Atlantic Health System Morristown Medical Center, Morristown, NJ
5	Andrew N. Rassi, MD Kaiser Permanente San Francisco Medical Center, San Francisco, CA
6	Jörg Hausleiter, MD Klinikum der Universität München, Munich, Germany
7	Robert L. Smith, MD and Molly Szerlip, MD Baylor Scott and White: The Heart Hospital Plano, Plano, TX
8	Scott Goldman, MD Lankenau Medical Center, Wynnewood, PA
9	D. Scott Lim, MD University of Virginia Health System Hospital, Charlottesville, VA
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11	Pradeep Yadav, MD Piedmont Heart Institute, Atlanta, GA
12	Philipp Lurz, MD, PhD Heart Center Leipzig at University of Leipzig, Leipzig, Germany
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14	Mubashir Mumtaz, MD and Hemal Gada, MD UPMC Pinnacle, Harrisburg, PA
15	Saibal Kar, MD Los Robles Regional Medical Center, Thousand Oaks, CA
16	Susheel K. Kodali, MD Columbia University Medical Center, New York, NY
17	Roger Laham, MD Beth Israel Deaconess Medical Center, Boston, MA
18	William Hiesinger, MD Stanford University Medical Center, Palo Alto, CA
19	Neil P. Fam, MD St. Michael's Hospital, Toronto, Ontario, Canada
20	Mirjam Keßler, MD University of Ulm, Ulm, Germany

Key Inclusion / Exclusion Criteria

Inclusion Criteria

- Age ≥ 18 years
- Prohibitive risk for mitral valve surgery
- Candidate for M-TEER with both the PASCAL system and the MitraClip system
- Degenerative mitral regurgitation (3+ to 4+)
- Suitable valve and regurgitant jet morphology
- LVEF $\geq 20\%$, LVEDD ≤ 80 mm

Exclusion Criteria

- TEE is contraindicated or screening TEE is unsuccessful
- Severe right ventricular dysfunction
- Active rheumatic heart disease or rheumatic MR etiology
- Other severe valve disorders requiring intervention or left ventricular outflow obstruction
- Clinically significant, untreated coronary artery disease
- Requiring chronic renal replacement therapy or eGFR ≤ 25 mL/min

Anatomical Exclusion Criteria^a

Presence of any of the following:

- Moderate to severe calcification in the grasping area
- Significant cleft or perforation in the grasping area
- ≥ 2 independent significant jets
- One significant jet in the commissural area
- Mitral valve orifice area < 4.0 cm²
- Leaflet mobility length < 8 mm
- Severe bileaflet/multi scallop prolapse involvement

Primary Endpoints

Safety

The PASCAL system is not inferior to the MitraClip system with respect to the **composite Major Adverse Event (MAE) rate at 30 days** comprising:

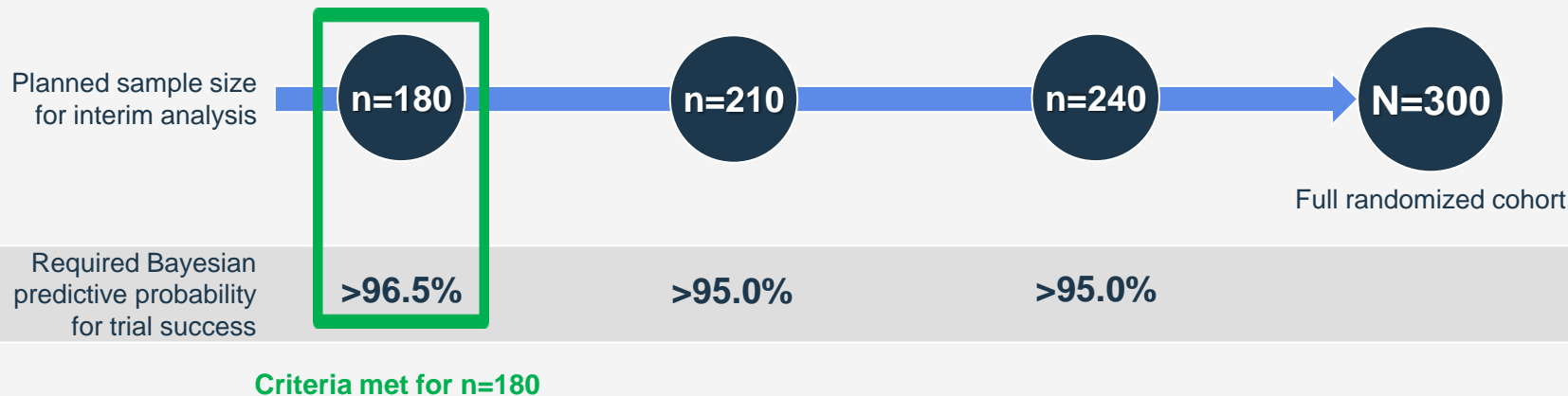
Cardiovascular mortality, stroke, myocardial infarction, new need for renal replacement therapy, severe bleeding^a and non-elective mitral valve re-intervention (either percutaneous or surgical)

Effectiveness

The PASCAL system is not inferior to the MitraClip system with respect to the **proportion of patients with MR $\leq 2+$ at 6 months**

Statistical Analysis

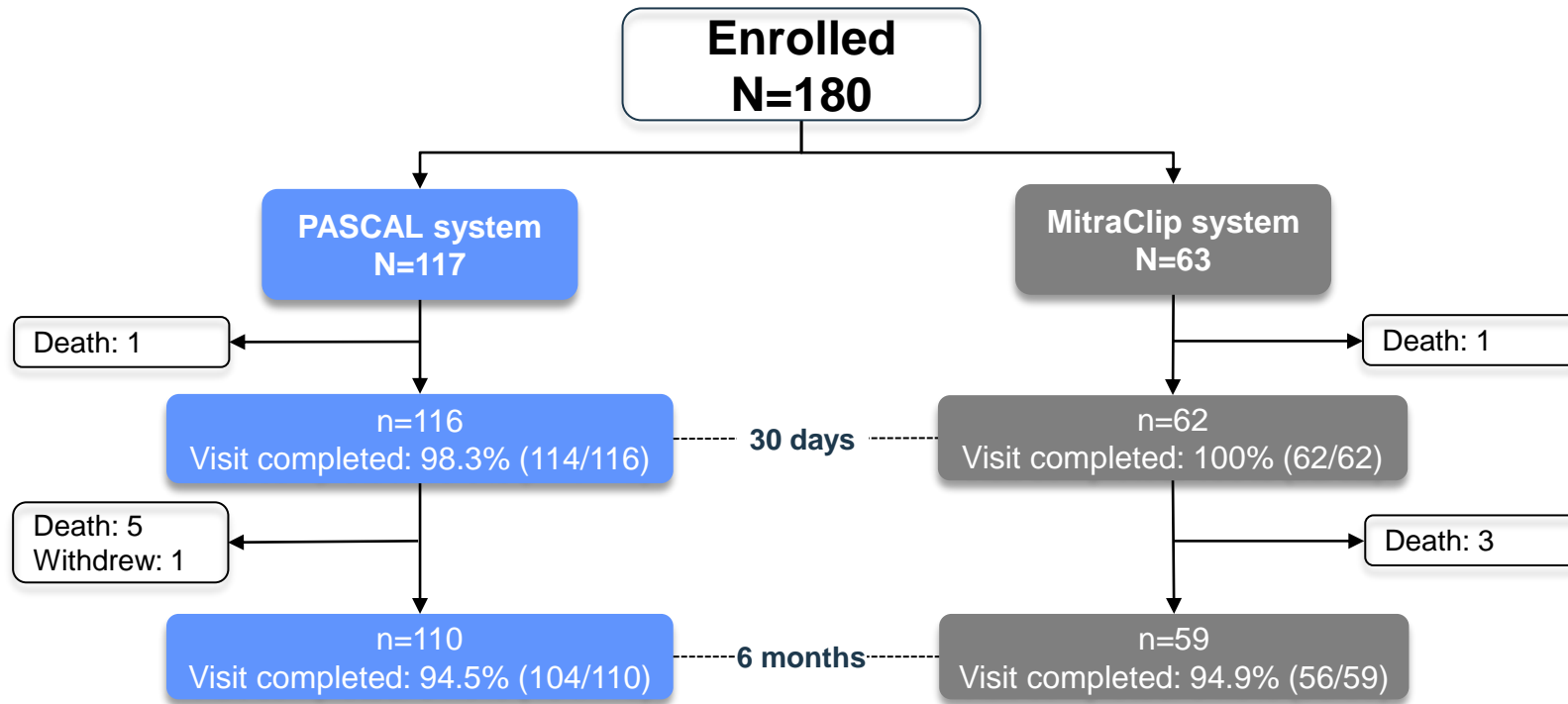
Interim analysis per Bayesian adaptive design



Primary endpoint outcomes and trial success reported for n=180 patients

Primary Endpoints and Clinical Outcomes

Study Flow

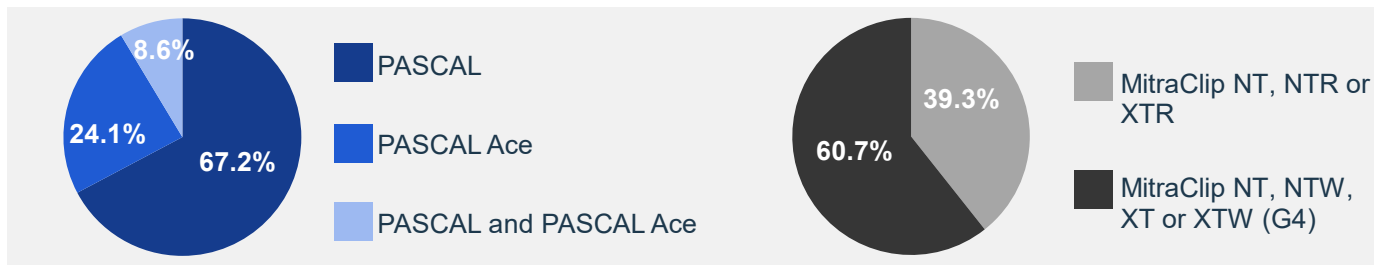


Baseline Characteristics

	PASCAL (N=117)	MitraClip (N=63)	p value
Age (years)	81.1 ± 6.9	81.2 ± 6.2	0.926
Male	66.7%	68.3%	0.869
NYHA class III/IV	60.7%	61.9%	1.000
STS score for mitral valve repair (%)	4.1 ± 2.8	3.6 ± 2.2	0.476
EuroScore II (%)	3.9 ± 2.9	4.1 ± 3.1	0.736
MR severity ≥3+	100%	100%	-
Atrial fibrillation	57.3%	60.3%	0.752
Renal insufficiency	35.0%	42.9%	0.335
Pulmonary hypertension	45.3%	47.6%	0.876
HFH (≥1 in past 12 months)	34.2%	39.7%	0.516
Aortic valve surgery/intervention	12.0%	3.2%	0.056

Procedural Characteristics

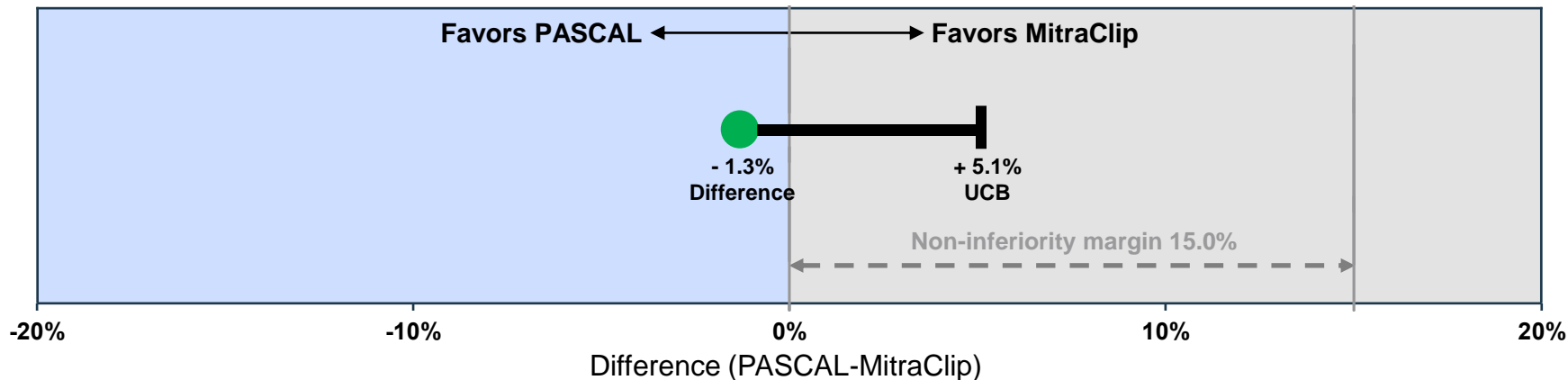
	PASCAL (N=117)	MitraClip (N=63)	p value
	Mean ± SD, Median [Q1, Q3], %		
Successful implant rate ^a	99.1%	100.0%	1.000
Procedure time (min) ^b	88.0 [68.5, 122.0]	79.0 [58.0, 106.0]	0.023
Device time (min) ^c	60.0 [38.0, 96.0]	41.0 [26.0, 67.0]	<0.001
Mean no. of devices implanted ^d	1.5 ± 0.6	1.6 ± 0.7	0.215
Total length of stay for the index procedure (days)	1.0 [1.0, 2.0]	1.0 [1.0, 2.0]	0.505



Primary Safety Endpoint Met

Composite MAE rate at 30 days: 3.4% for PASCAL vs. 4.8% for MitraClip

PASCAL (n=117)	MitraClip (n=63)	Difference	One-sided 95% UCB
3.4% (4/116)	4.8% (3/63)	- 1.3%	+ 5.1%



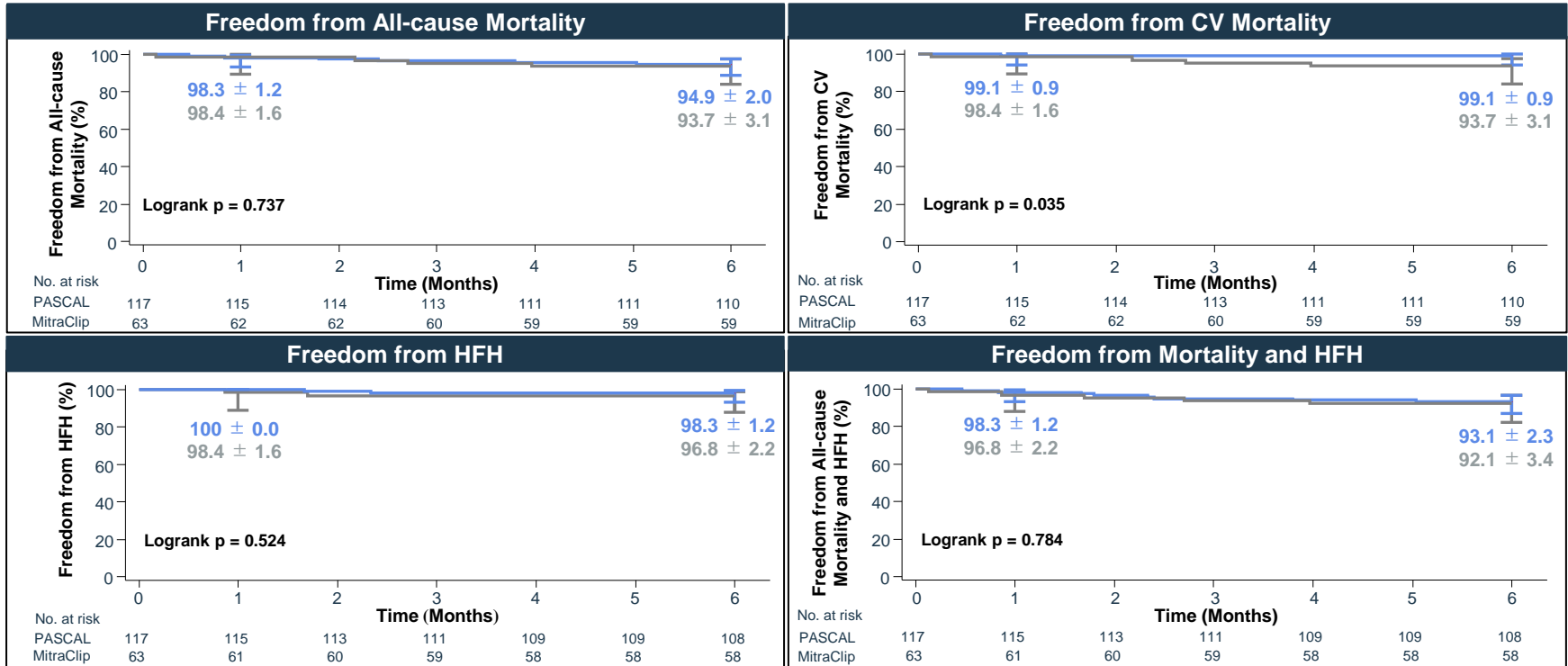
CEC-adjudicated Major Adverse Events

Low event rates to 30 days

	PASCAL N=117 ^a	MitraClip N=63
	Patients n (%)	
Composite MAE rate at 30 days	4 (3.4%)	3 (4.8%)
Cardiovascular mortality	1 (0.9%)	1 (1.6%)
Stroke	0 (0.0%)	0 (0.0%)
Myocardial Infarction	0 (0.0%)	0 (0.0%)
New need for renal replacement therapy	0 (0.0%)	0 (0.0%)
Non-elective mitral valve re-intervention (percutaneous or surgical)	1 (0.9%)	0 (0.0%)
Severe bleeding ^b	3 (2.6%)	2 (3.2%)

CEC-adjudicated Freedom from Mortality and HFH¹

High survival and low HFH to 6 months



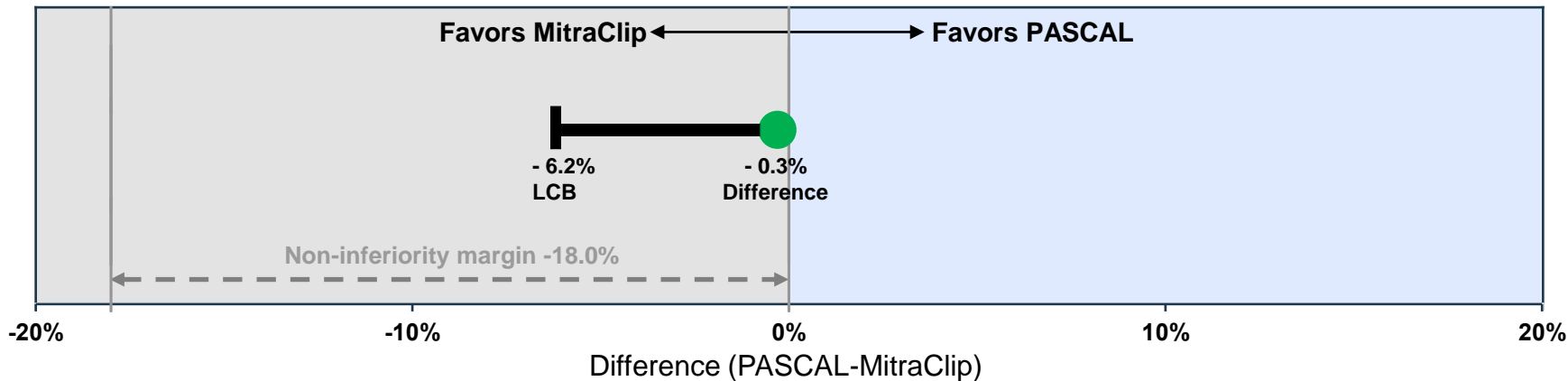
— PASCAL — MitraClip

¹Graph shows Kaplan-Meier analysis time to first event (KM estimate ± SE) and error bars represent 95% CI. CEC: Clinical events committee; HFH: Heart failure hospitalization; CV: Cardiovascular.

Primary Effectiveness Endpoint Met

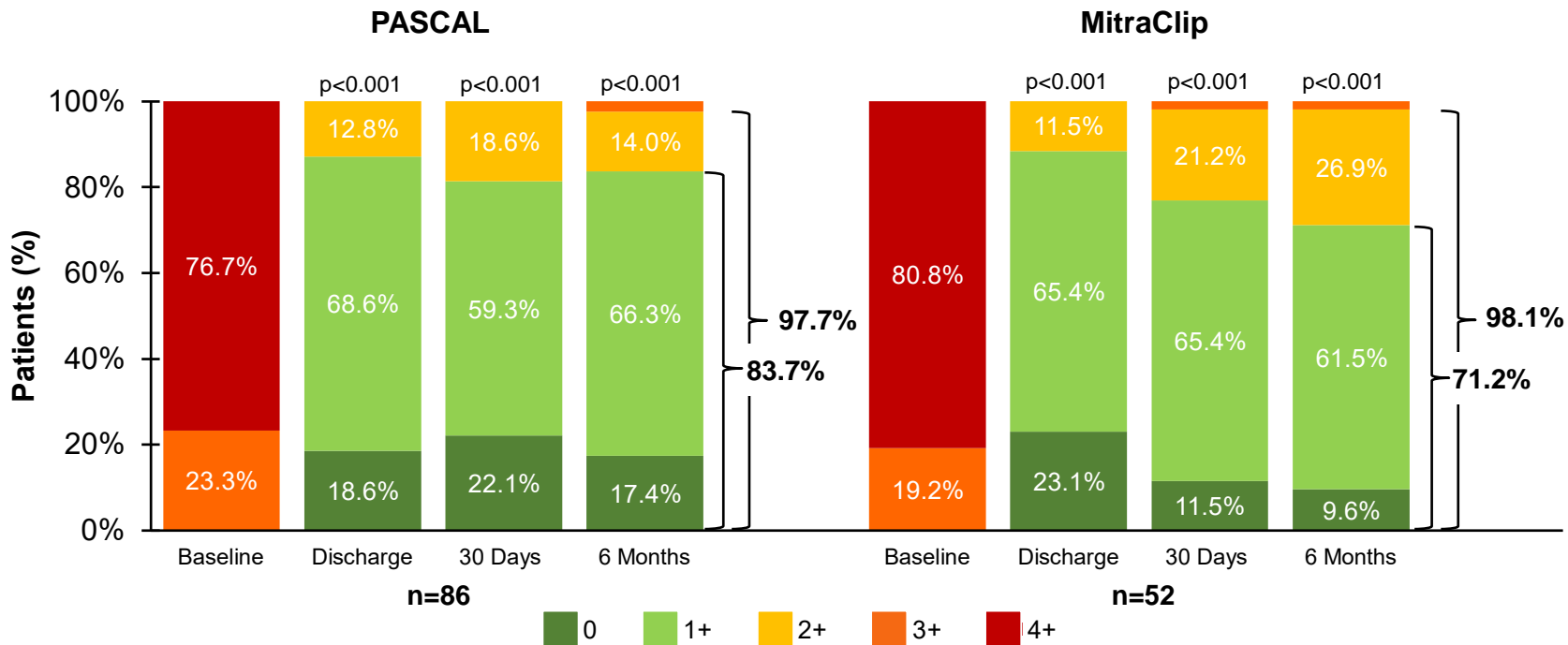
MR ≤2+ at 6 months: 96.5% for PASCAL vs. 96.8% for MitraClip

PASCAL (n=117)	MitraClip (n=63)	Difference	One-sided 95% LCB
96.5% (110/114)	96.8% (60/62)	- 0.3%	- 6.2%



MR Reduction by Core Lab¹

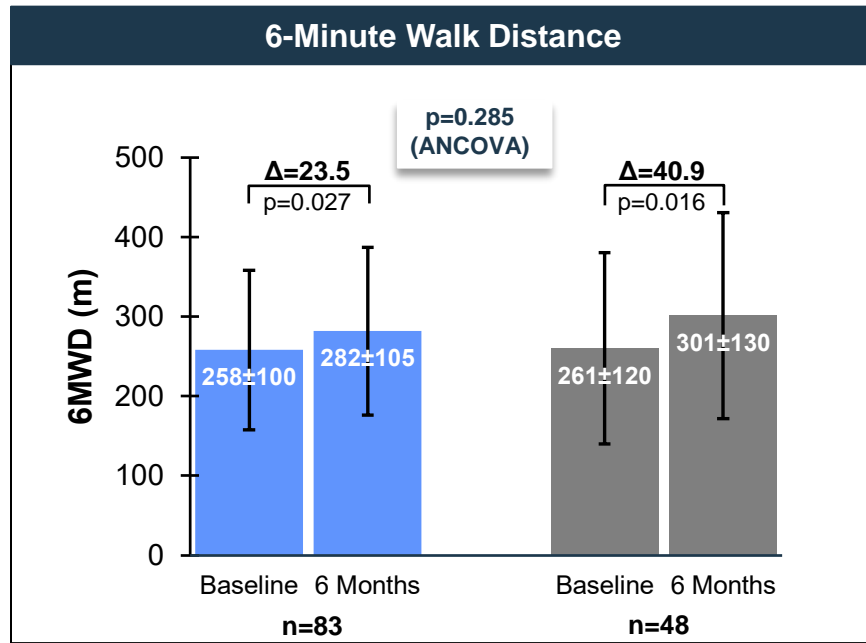
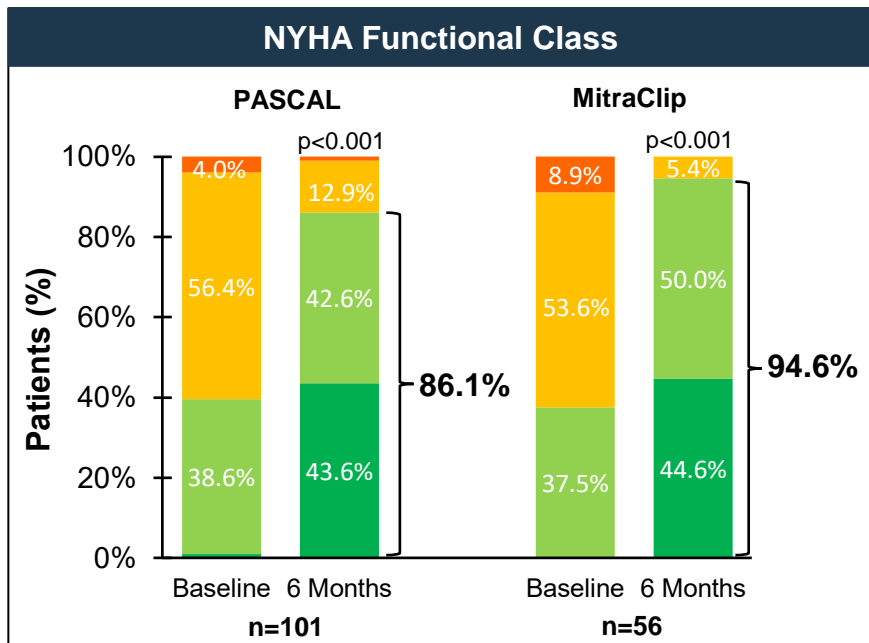
Significant MR reduction: 97.7% with MR ≤2+ at 6 months



Paired analysis

Functional Outcomes

Significant improvement in functional capacity at 6 months



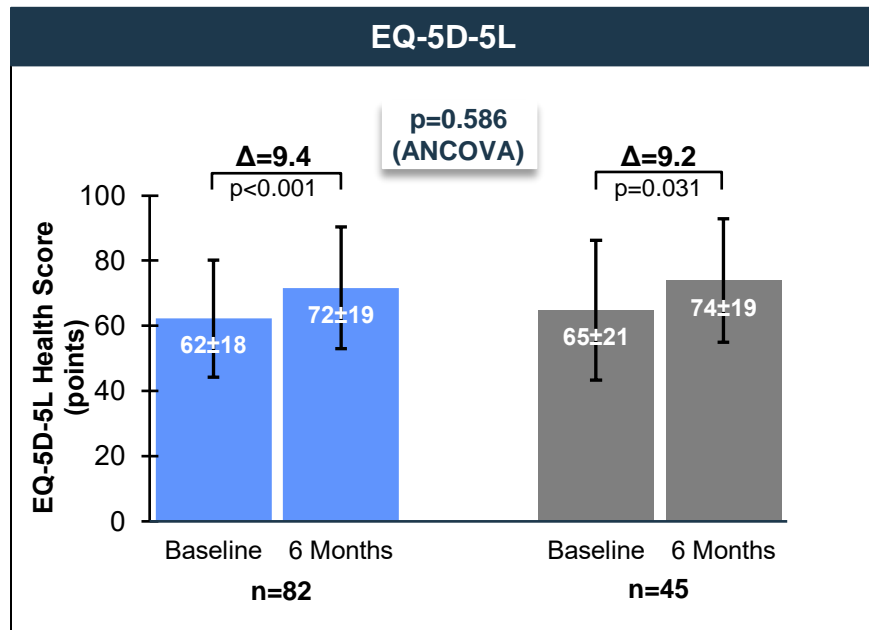
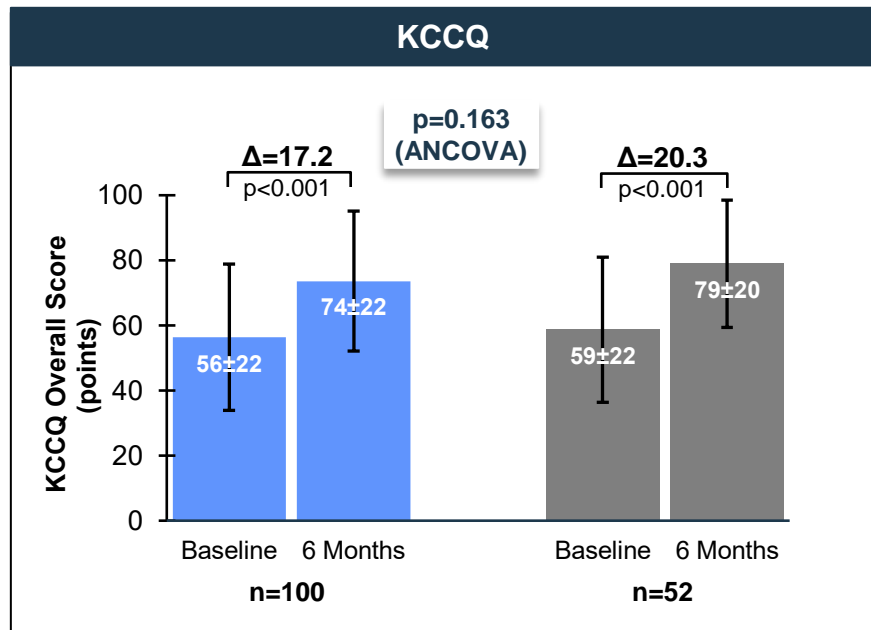
■ Class I
 ■ Class II
 ■ Class III
 ■ Class IV

■ PASCAL
 ■ MitraClip

Paired analysis

Quality of Life Outcomes

Significant improvement in QoL at 6 months



■ PASCAL ■ MitraClip

Paired analysis

■ PASCAL ■ MitraClip

Echocardiographic Outcomes



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Echocardiographic Baseline Characteristics

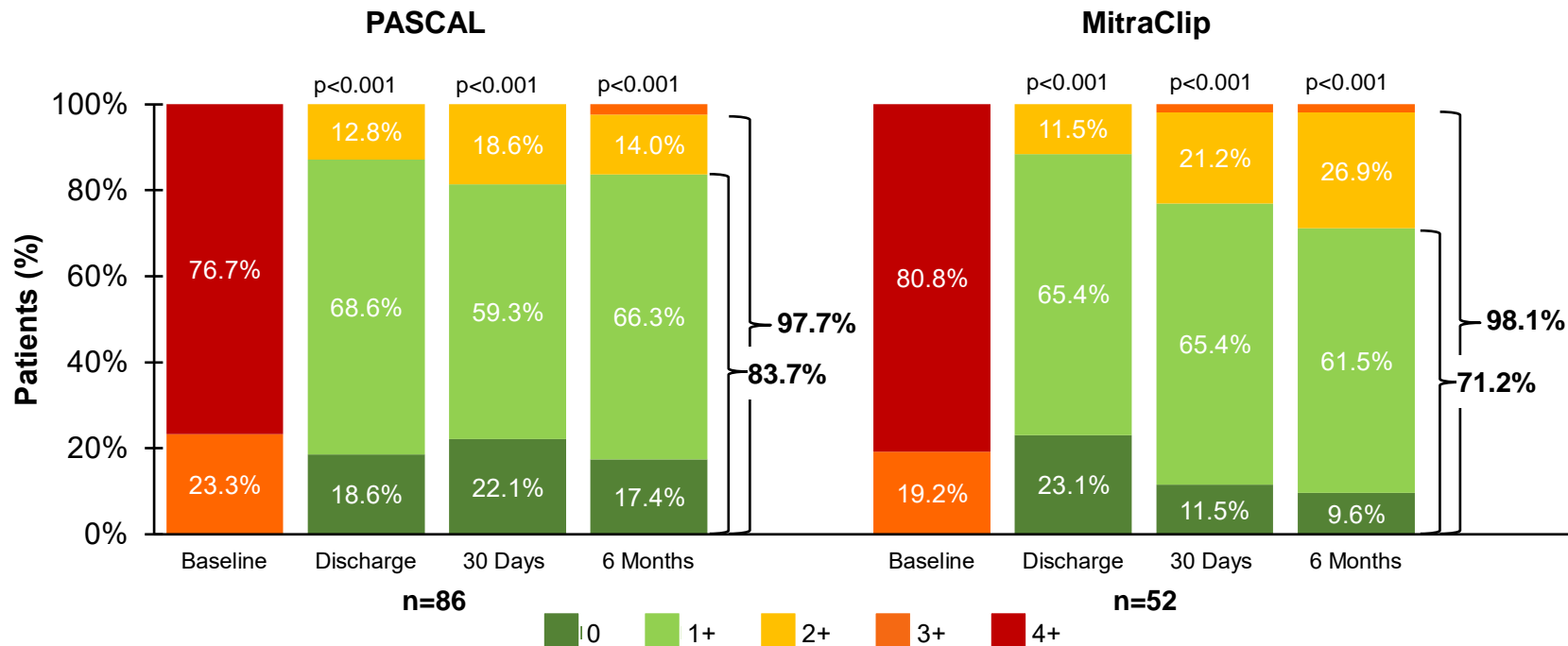
	PASCAL (N=117)	MitraClip (N=63)	p value
MR severity, moderate-severe (3+)	25.2%	20.6%	0.581
MR severity, severe (4+)	74.8%	79.4%	0.581
Left ventricular end-systolic dimension (mm)	38.3 ± 7.7	39.8 ± 7.8	0.215
Left ventricular end-diastolic dimension (mm)	57.1 ± 6.5	57.4 ± 6.5	0.889
Left ventricular end-systolic volume (mL)	59.5 ± 28.8	63.7 ± 27.4	0.196
Left ventricular end-diastolic volume (mL)	143.3 ± 48.6	149.9 ± 44.8	0.180
Left atrial volume (mL)	116.3 ± 37.6	121.3 ± 45.8	0.859
Mean transmitral valve gradient (mmHg)	2.5 ± 1.1	2.4 ± 1.1	0.400
Effective regurgitant orifice area (PISA, cm ²)	0.50 ± 0.15	0.50 ± 0.20	0.857
Regurgitant volume (PISA, mL)	69.9 ± 18.4	71.8 ± 21.6	0.988
Left ventricular ejection fraction (%)	59.6 ± 8.7	58.3 ± 9.0	0.346
Pulmonary vein flow (S reversal)	80.5%	85.4%	0.630
Pulmonary artery systolic pressure	42.3 ± 11.4	45.6 ± 14.6	0.225
Right ventricular systolic function (≥ mild dysfunction)	18.8%	27.4%	0.189
Tricuspid regurgitation severity (3+)	2.6%	4.8%	0.426

Echocardiographic Baseline Characteristics

	PASCAL (N=117)	MitraClip (N=63)	p value
Vena contracta width – commissural (mm)	10.9 ± 3.7	12.3 ± 4.0	0.090
Mitral valve area (cm ²)	6.1 ± 1.4	6.0 ± 1.6	0.556
Anatomical measures			
Prolapse	20.0%	20.6%	1.000
Flail	80.0%	77.8%	0.847
Severe bileaflet prolapse	0.0%	1.6%	0.354
Mitral valve cleft in grasping area	4.7%	0.0%	0.161
PML length (mm)	12.3 ± 3.4	11.7 ± 3.4	0.089
Flail width (mm)	9.9 ± 3.1	10.2 ± 3.1	0.412
Flail gap (mm)	4.3 ± 1.9	4.0 ± 1.6	0.561
Jet location A2-P2	87.2%	82.5%	0.505

MR Reduction by Core Lab¹

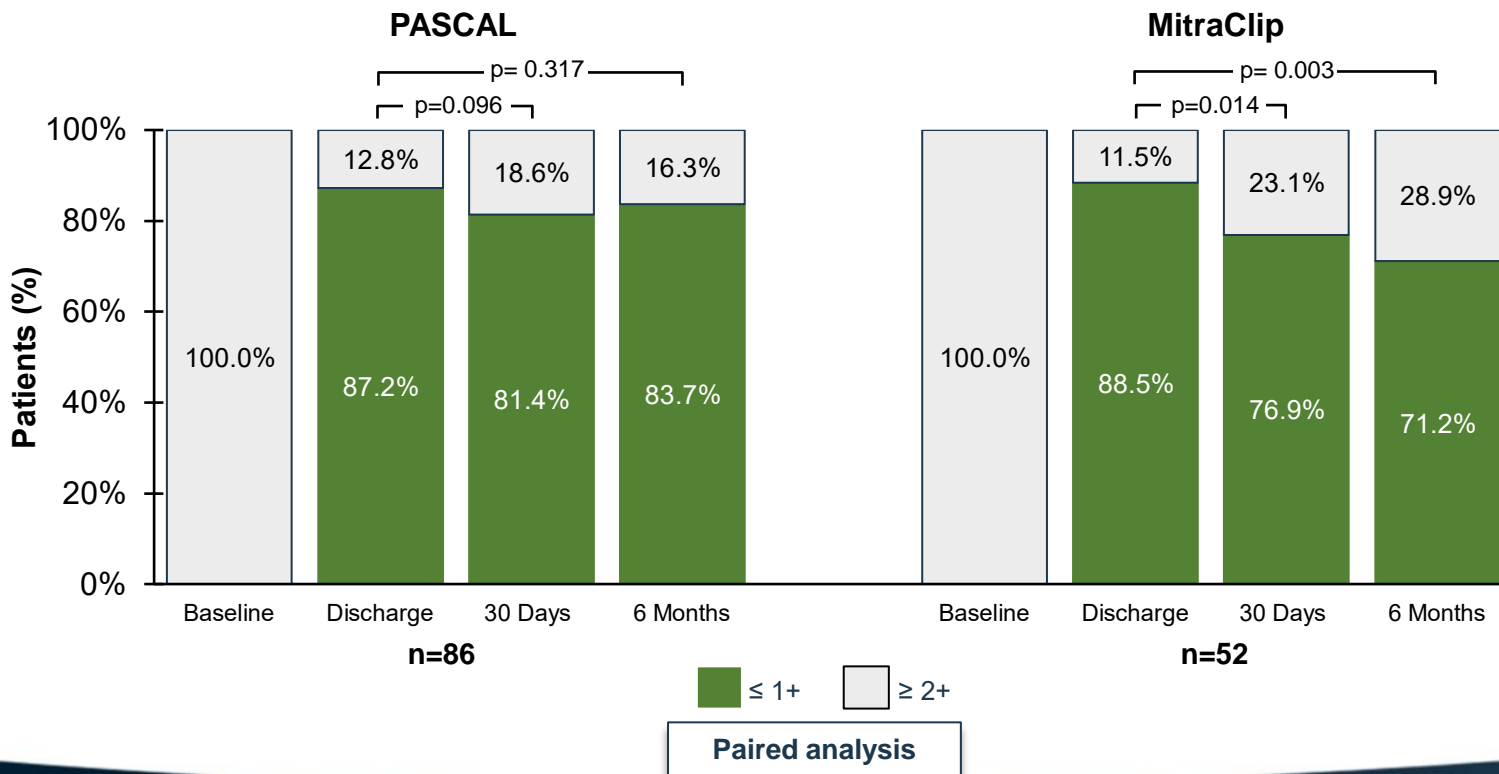
MR ≤1+ at 6 months: 83.7% for PASCAL and 71.2% for MitraClip



Paired analysis

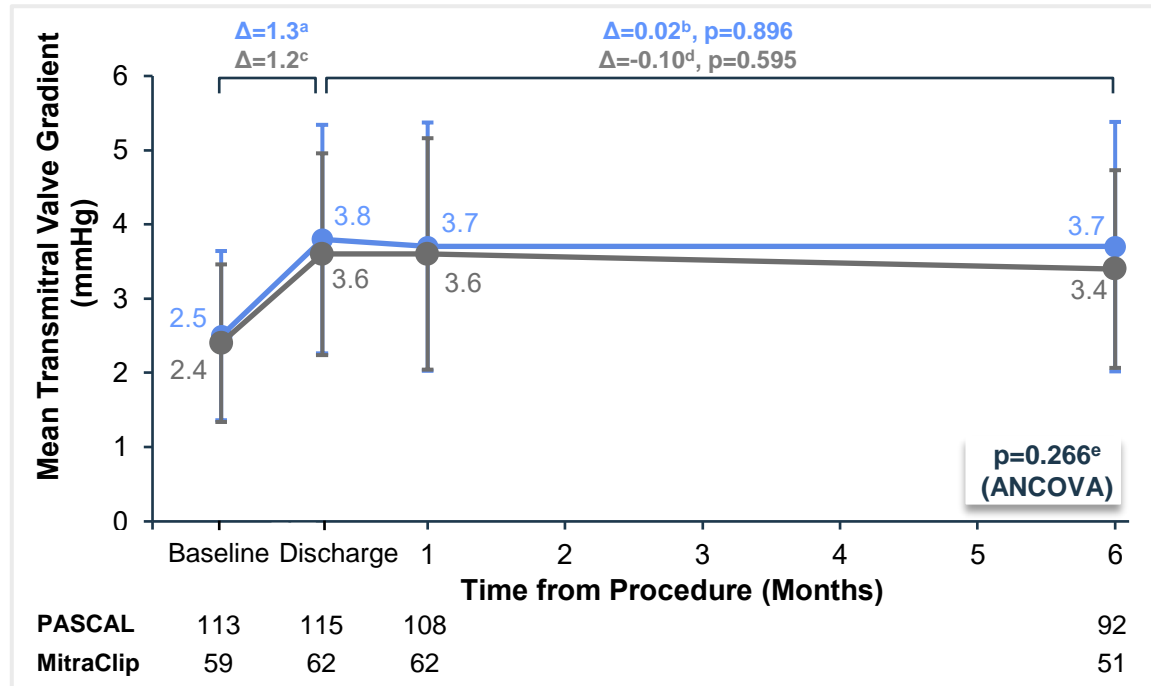
Durability of MR $\leq 1+$ by Core Lab¹

MR $\leq 1+$ sustained to 6 months with the PASCAL system



Transmitral Gradients by Core Lab¹

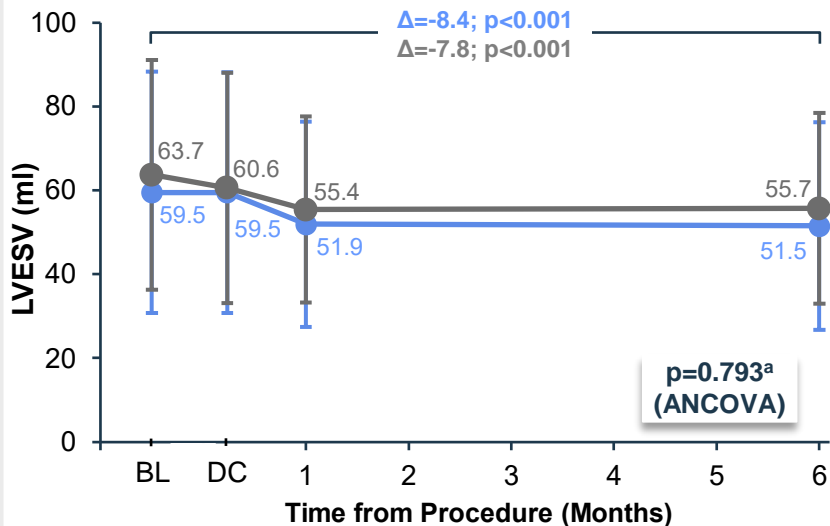
Gradients stable and sustained below 5 mmHg to 6 months



LV Remodeling by Core Lab¹

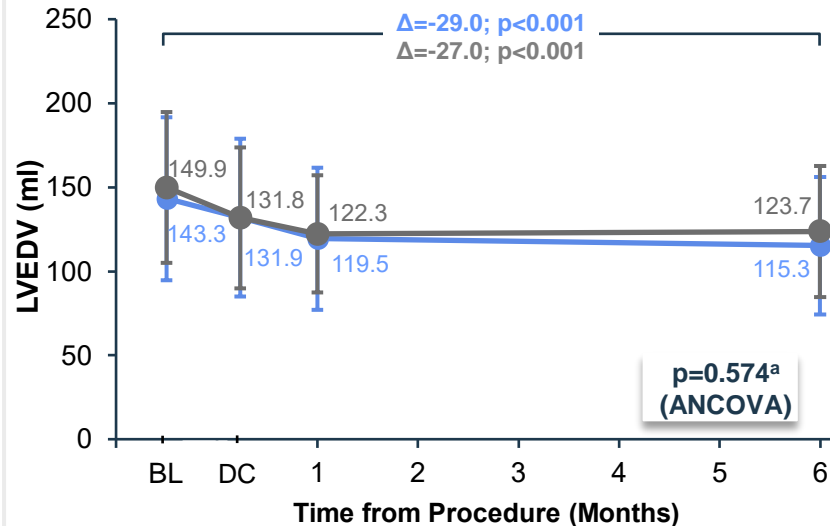
Significant reduction in LVESV and LVEDV to 6 months

LVESV



PASCAL	113	96	101	86
MitraClip	63	56	60	52

LVEDV

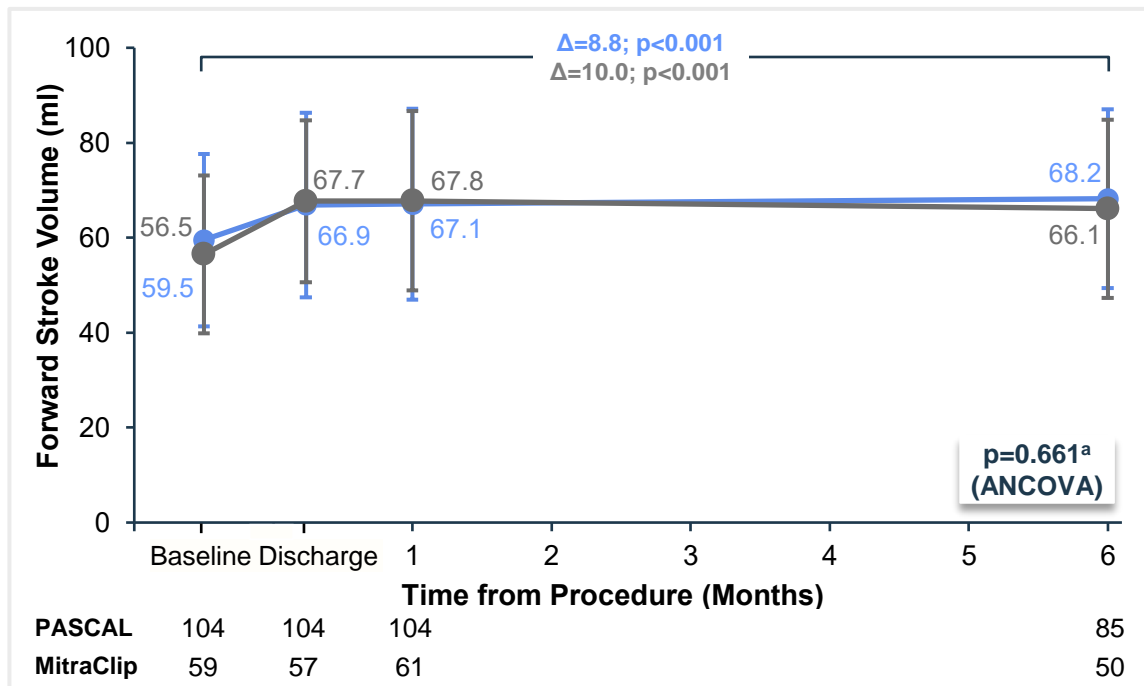


PASCAL	113	96	101	86
MitraClip	63	56	60	52

● PASCAL ● MitraClip

Forward Stroke Volume by Core Lab¹

Significant improvement in forward stroke volume to 6 months



Conclusions

- The CLASP IID trial, the first randomized controlled trial to directly compare two contemporary TEER therapies, further establishes the safety and effectiveness of M-TEER for prohibitive risk DMR patients
- The CLASP IID trial met its primary safety and effectiveness endpoints with the PASCAL system demonstrating:
 - Low composite MAE rate of 3.4% at 30 days
 - Significant and sustained MR reduction with 97.7% patients achieving MR $\leq 2+$ at 6 months
- The PASCAL system demonstrated sustained MR $\leq 1+$ durability with 83.7% patients at MR $\leq 1+$ at 6 months
- Results demonstrated favorable ventricular remodeling with improved forward stroke volume
- Patients experienced significant improvements in functional capacity and quality of life

The PASCAL system is a beneficial therapy for significant symptomatic DMR, expanding transcatheter treatment options for prohibitive surgical risk patients