

# Update on Mitral Clip: **COAPT and More**

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# Disclosure Statement

**Gregg W. Stone MD**

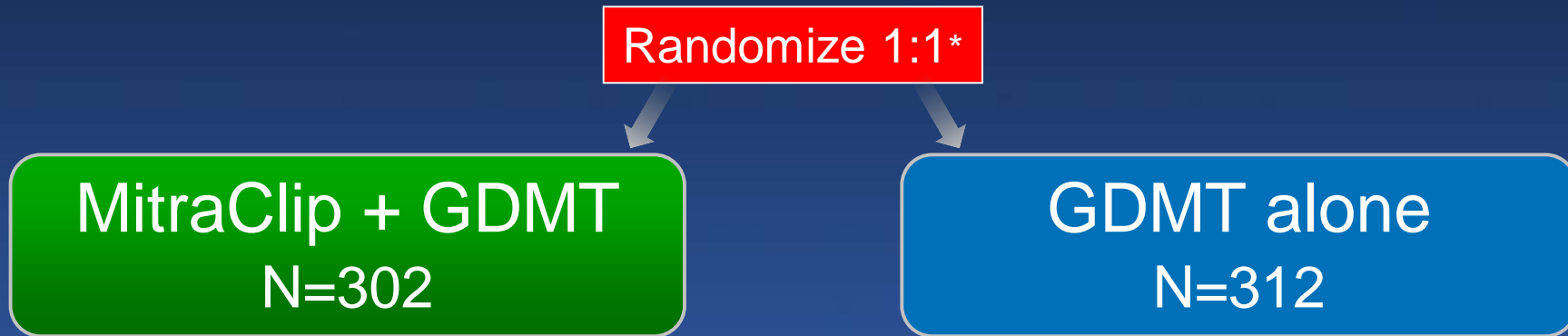
Consulting fees from Neovasc, Valfix, Ancora, Cardiomech  
Equity/options from Ancora, Valfix, Cardiac Success

Principal investigator for the COAPT trial - Uncompensated

# The COAPT Trial

## Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation

A parallel-controlled, open-label, multicenter trial in 614 patients with heart failure and moderate-to-severe (3+) or severe (4+) secondary MR who remained symptomatic despite maximally-tolerated GDMT



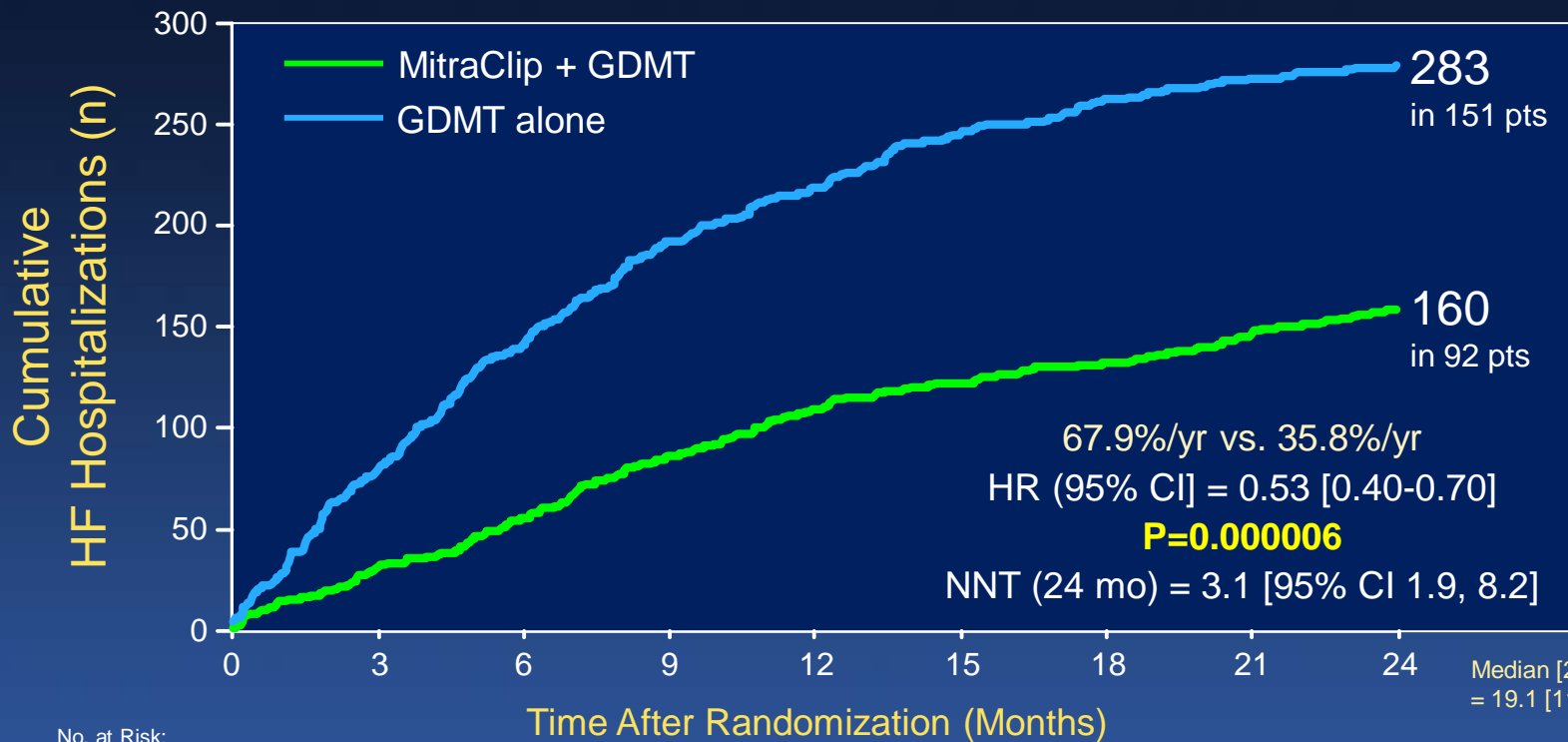
\*Stratified by cardiomyopathy etiology (ischemic vs. non-ischemic) and site

# Key Entry Criteria

1. Ischemic or non-ischemic cardiomyopathy with **LVEF 20%-50%** and **LVEDD  $\leq$ 70 mm**
2. Moderate-to-severe (3+) or severe (4+) secondary MR confirmed by an independent echo core laboratory prior to enrollment (**US ASE criteria**)
3. NYHA functional class II-IVa (ambulatory) despite a stable **maximally-tolerated** GDMT regimen and CRT (if appropriate) per societal guidelines
4. Exclusions: PASP  $>$ 70 mmHg not responsive to vasodilators; mod/sev RV dysfunction; TR requiring surgery

# Primary Effectiveness Endpoint

## All Hospitalizations for HF within 24 months

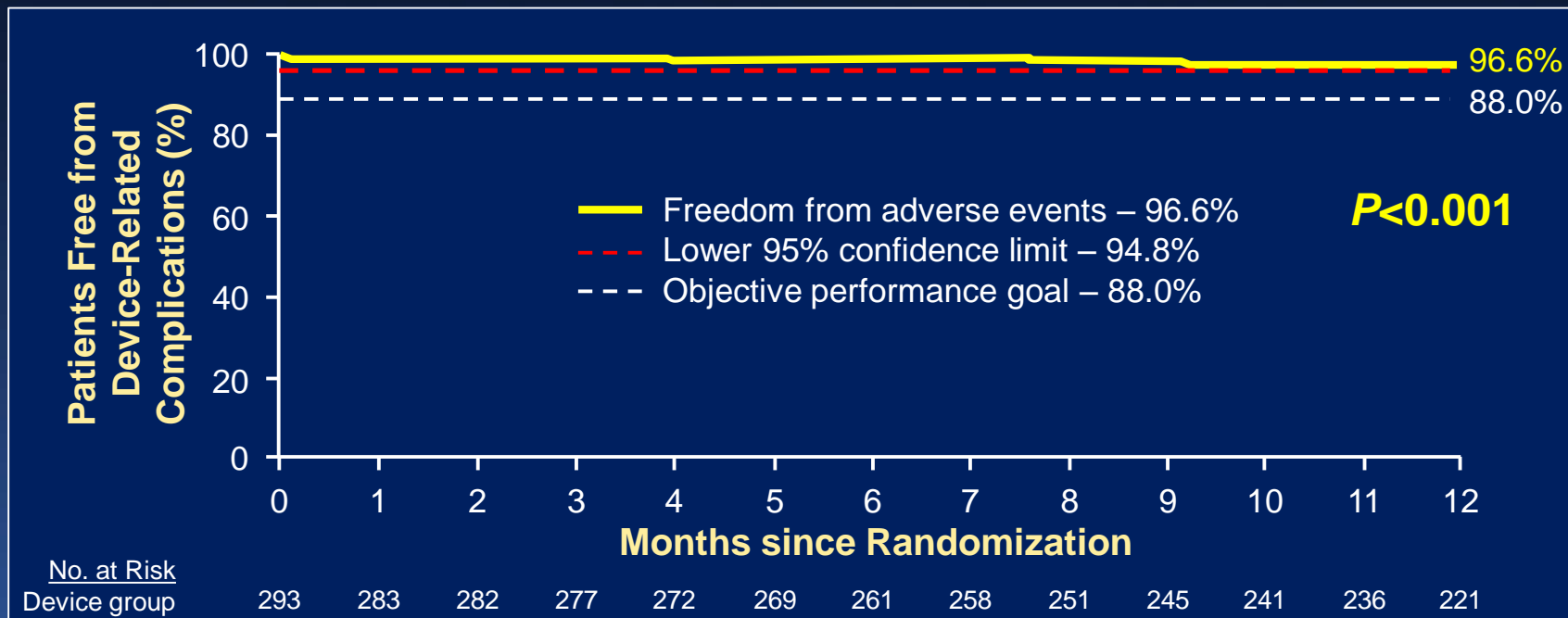


No. at Risk:

	0	3	6	9	12	15	18	21	24
MitraClip	302	286	269	253	236	191	178	161	124
GDMT	312	294	271	245	219	176	145	121	88

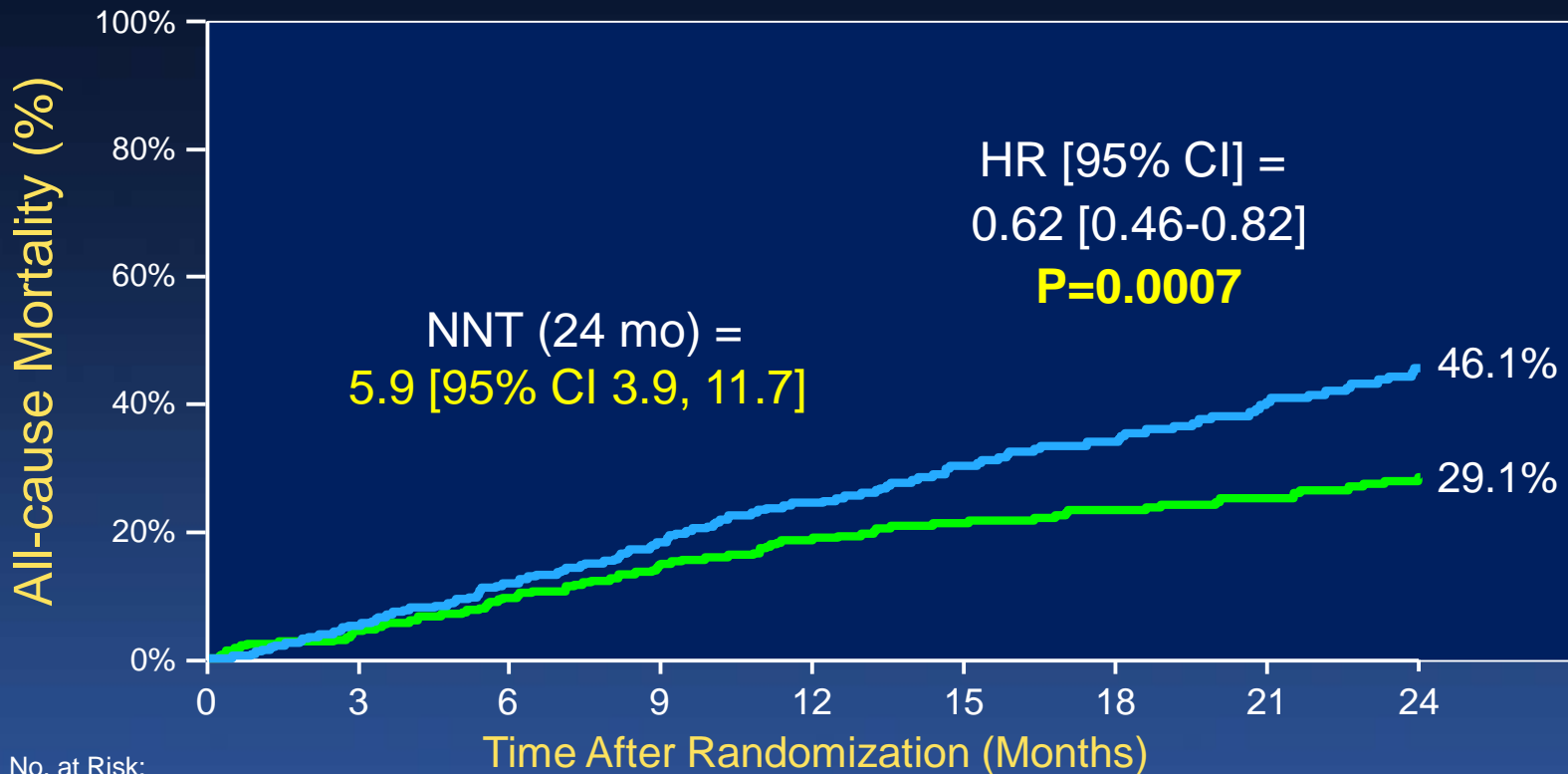
# Primary Safety Endpoint

Freedom from device-related complications\* within 12 months



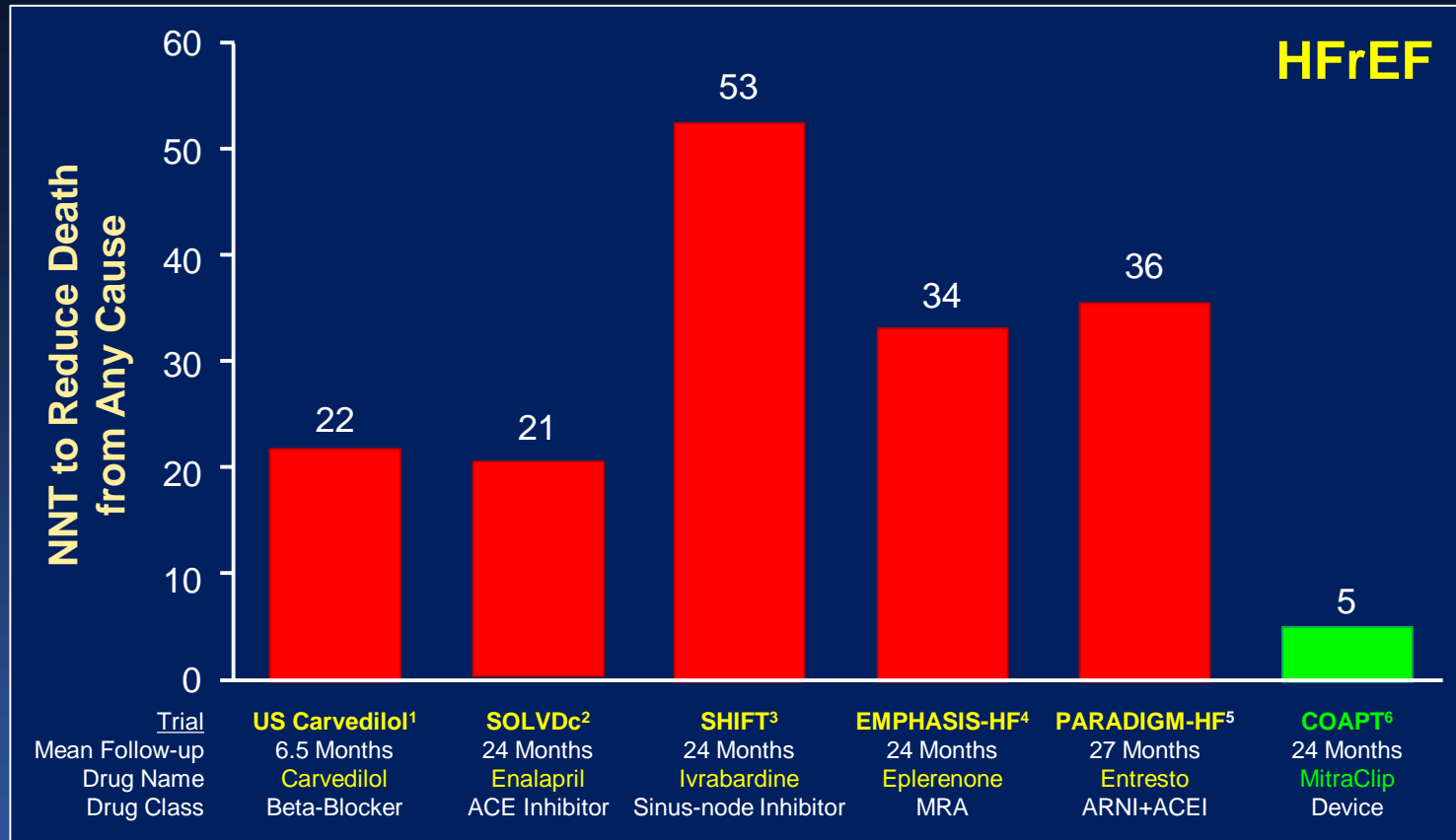
\* SLDA, device embolization, endocarditis or MS requiring surgery, LVAD, OHT, any device-related compl requiring non-elective CV surgery.  $P$  value calculated from Z test with Greenwood's method of estimated variance against a pre-specified OPG of 88%

# All-cause Mortality



No. at Risk:		0	3	6	9	12	15	18	21	24
MitraClip + GDMT	302	286	269	253	236	191	178	161	124	
GDMT alone	312	294	271	245	219	176	145	121	88	

# Number Needed to Treat (NNT) to Prevent 1 Death

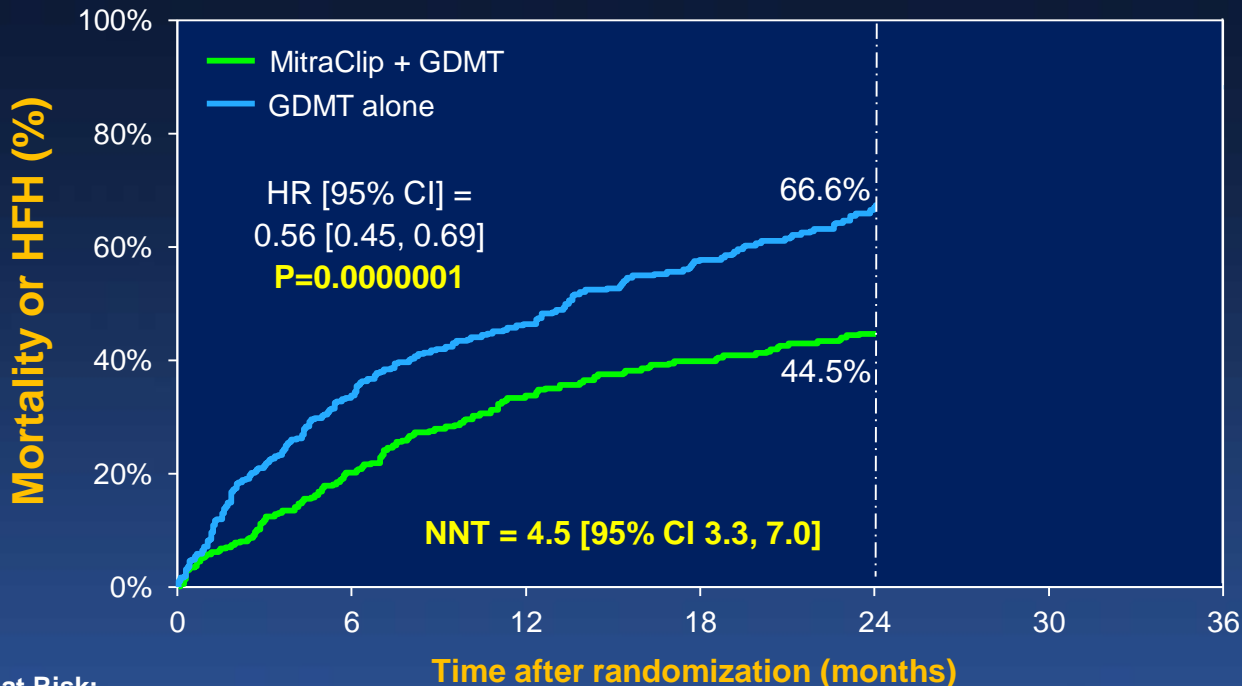


1. Packer M et al. NEJM 1996;334:1349-1355; 2. SOLVD Investigators. NEJM 1991;325:293-302; 3. Swedberg K et al. Lancet 2010;376:1988; 4. Zannad F et al. NEJM 2011;364:11-21; 5. McMurray JJV et al. NEJM 2014;371:993-1004; 6. Stone GW et al. NEJM 2018;379:2307-18.



# All-Cause Mortality or HF Hospitalization

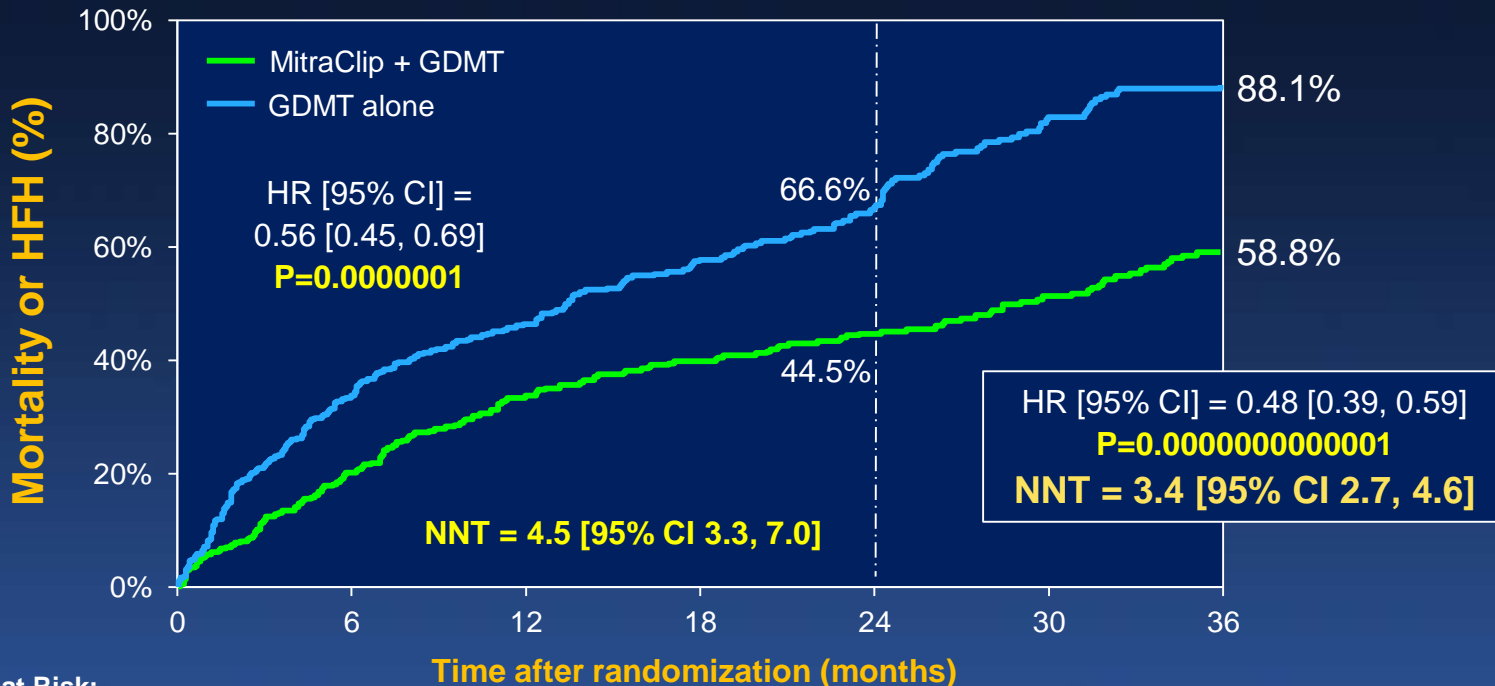
All patients, ITT, including crossovers



# at Risk:	0	6	12	18	24
MitraClip + GDMT	302	238	196	176	148
GDMT alone	312	206	156	120	87

# All-Cause Mortality or HF Hospitalization

All patients, ITT, including crossovers

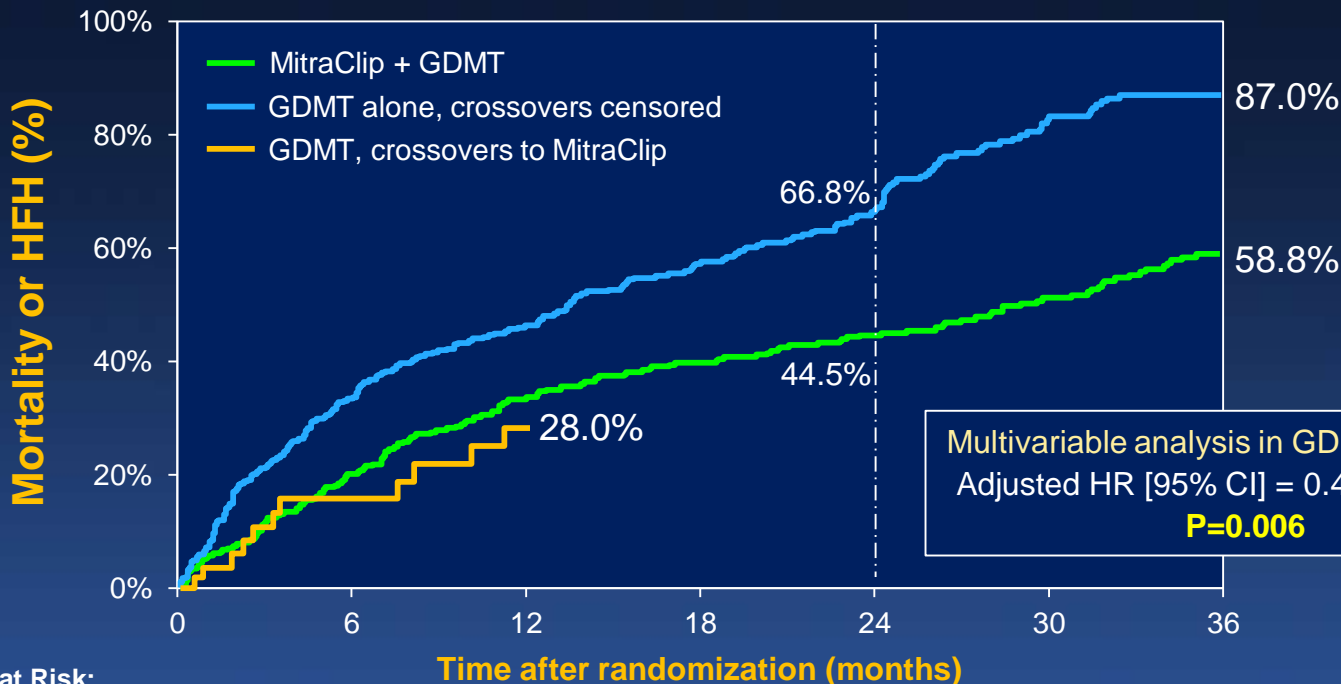


**# at Risk:**

MitraClip + GDMT	302	238	196	176	148	101	66
GDMT alone	312	206	156	120	87	37	20

# All-Cause Mortality or HF Hospitalization

GDMT pts censored at time of crossover; crossovers landmarked at MitraClip procedure

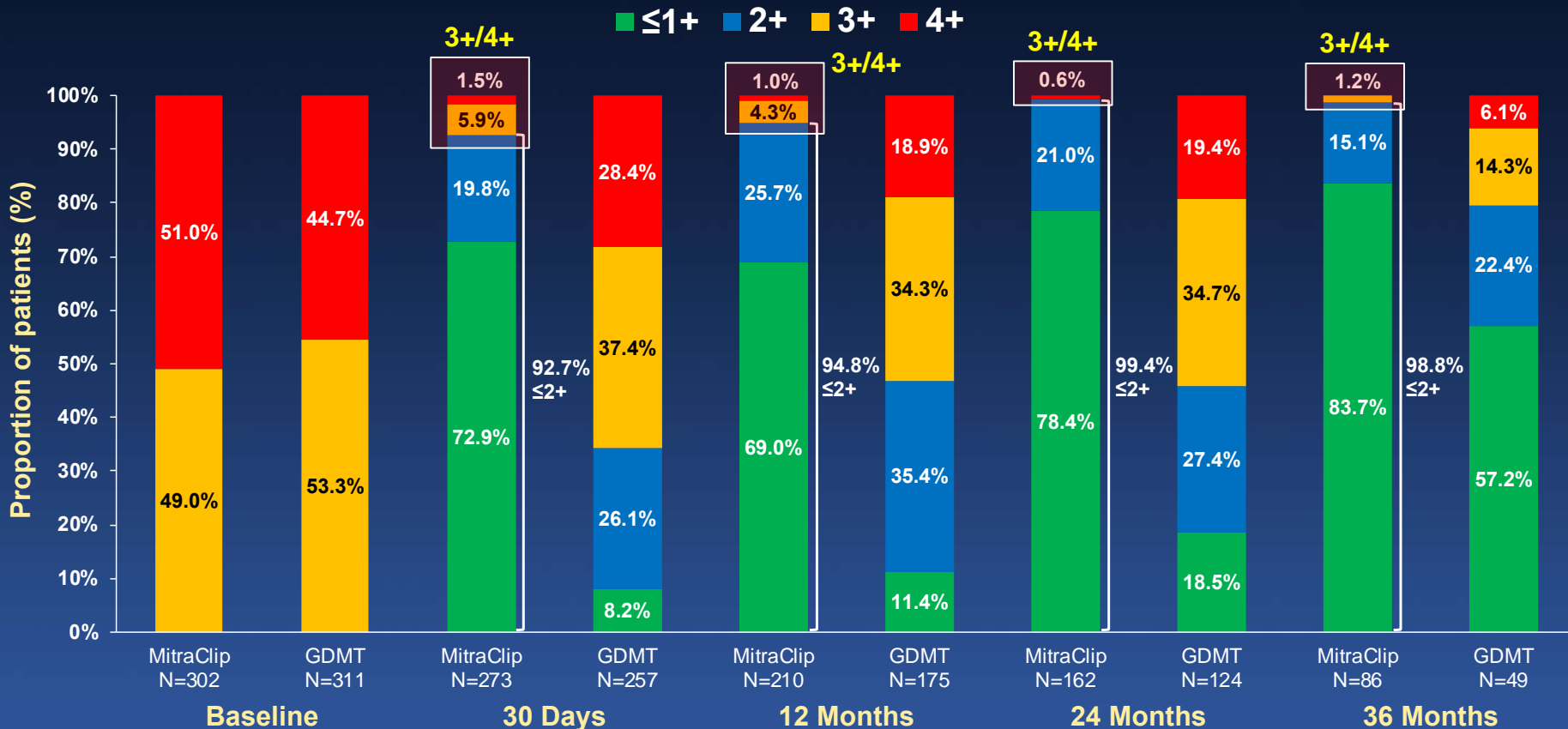


**# at Risk:**

	0	6	12	18	24	30	36
MitraClip + GDMT	302	238	196	176	148	101	66
GDMT only, crossovers censored	312	205	155	119	85	33	19
GDMT crossovers to MitraClip	58	30	22				

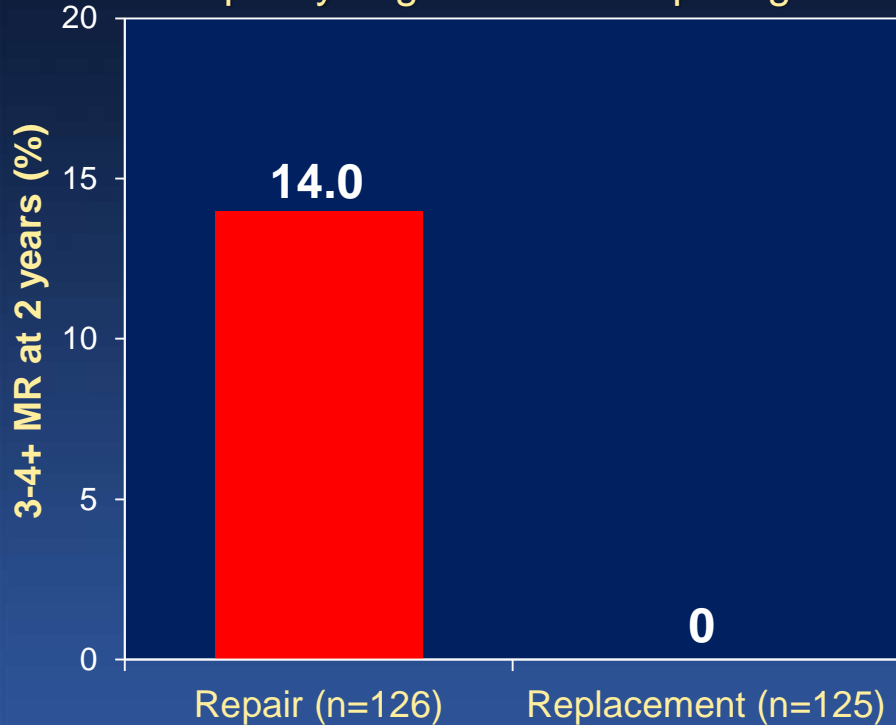
# MR Severity

**All FU P<0.0001**  
for trend and for  $\leq 2+$



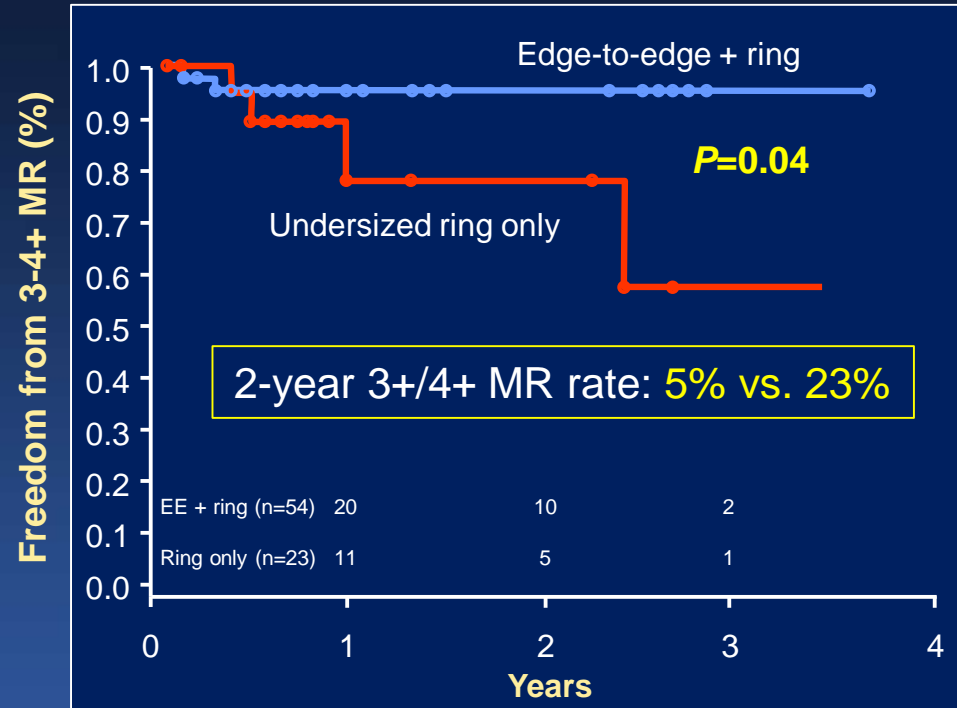
# Recurrent Severe MR After Surgical TMVr

CTSN trial: 251 pts with FMR were randomized to MV repair with downsized annuloplasty ring vs. chordal-sparing MVR



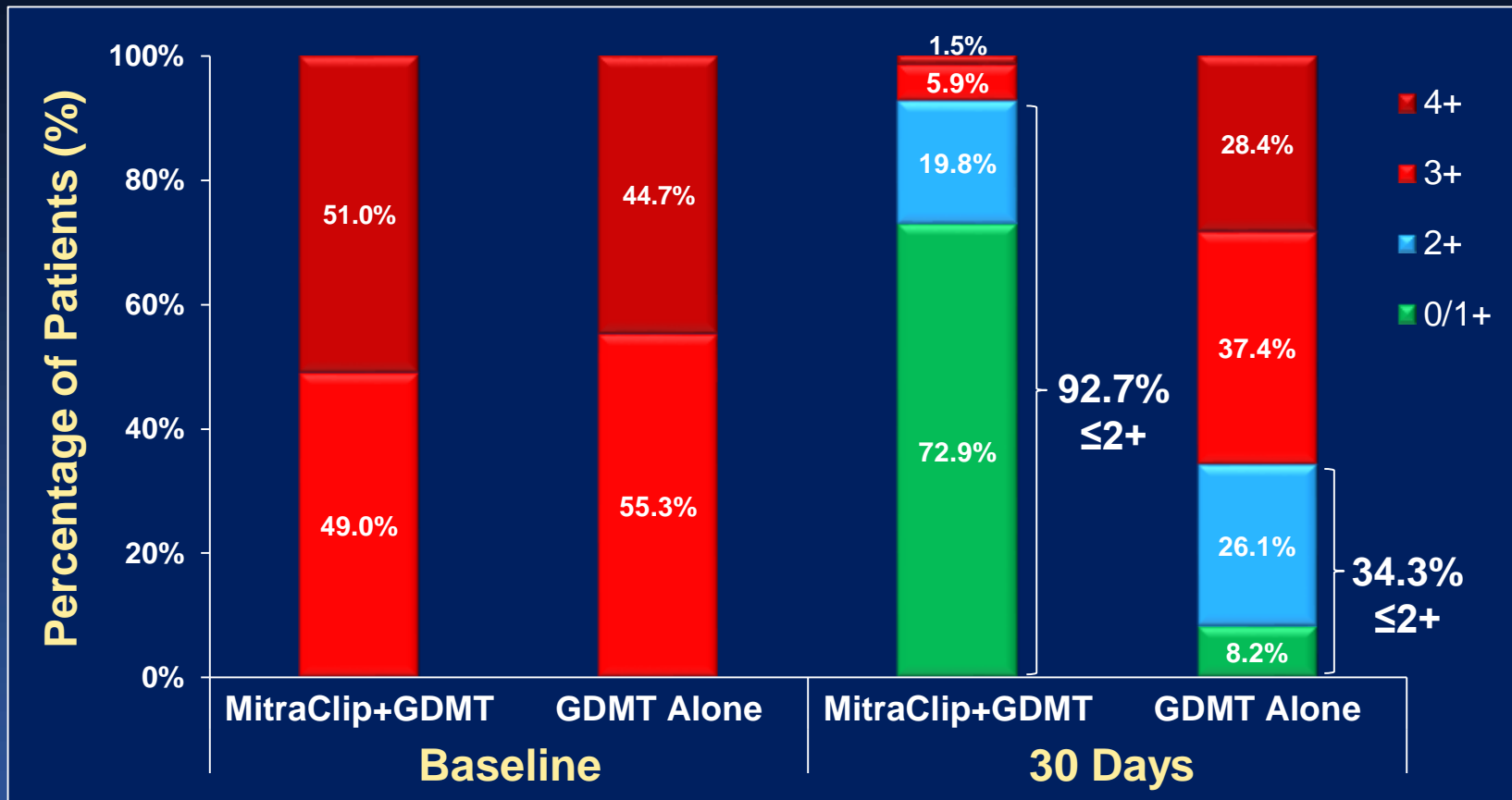
Goldstein D et al. *NEJM* 2016;374:344-353

77 pts with FMR underwent MV repair with downsized annuloplasty ring with or without Alfieri edge-to-edge stitch



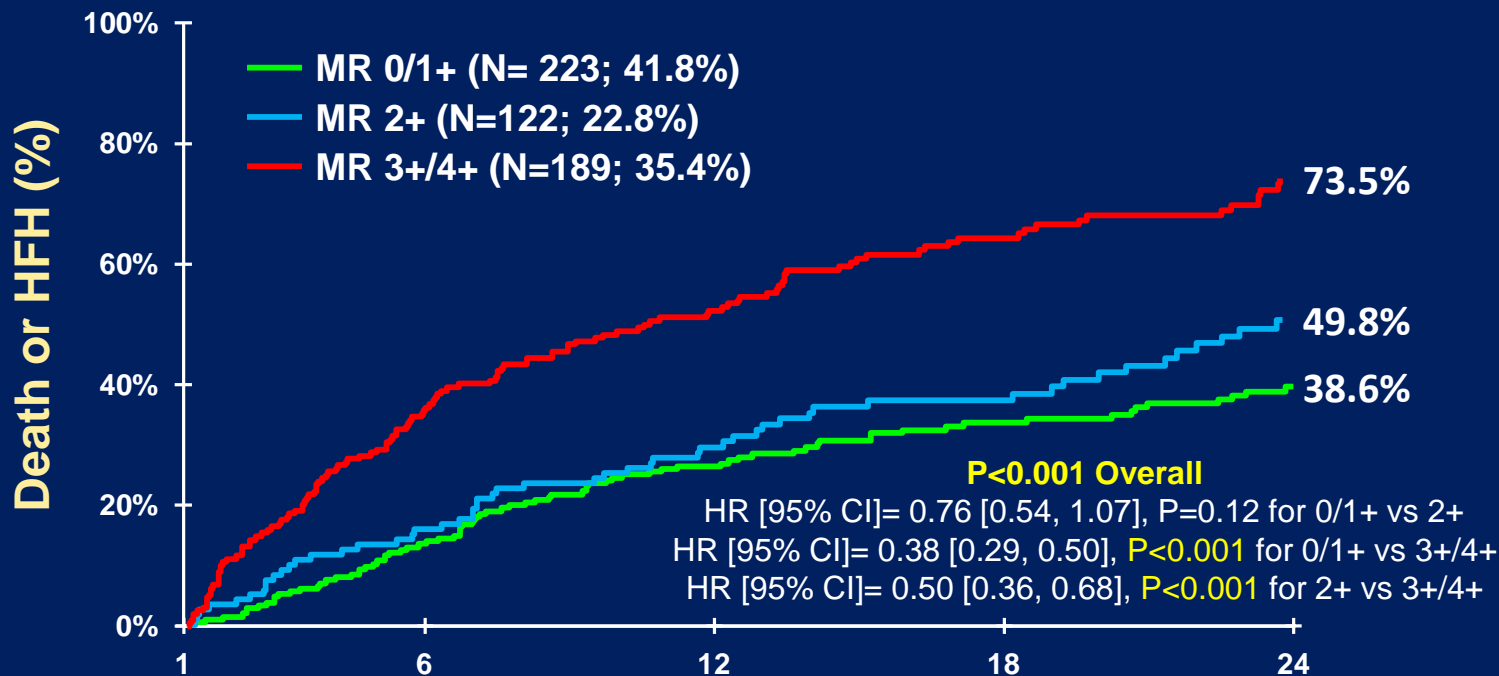
De Bonis M et al. *Circulation* 2005;112[suppl I]:I-402-8

# MR Reduction in COAPT



# Time to Death or First HF Hosp

Pooled population, stratified by 30-day residual MR



**# At Risk**

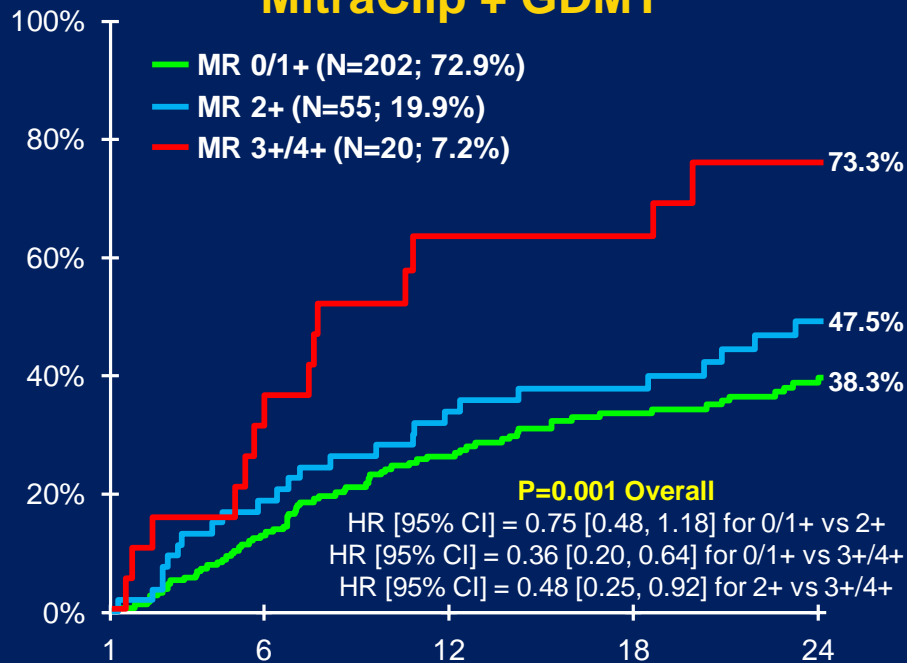
	1	6	12	18	24
MR 0/1+	223	192	152	117	73
MR 2+	122	101	81	57	36
MR 3+/4+	189	120	83	51	30

# Time to Death or First HF Hosp

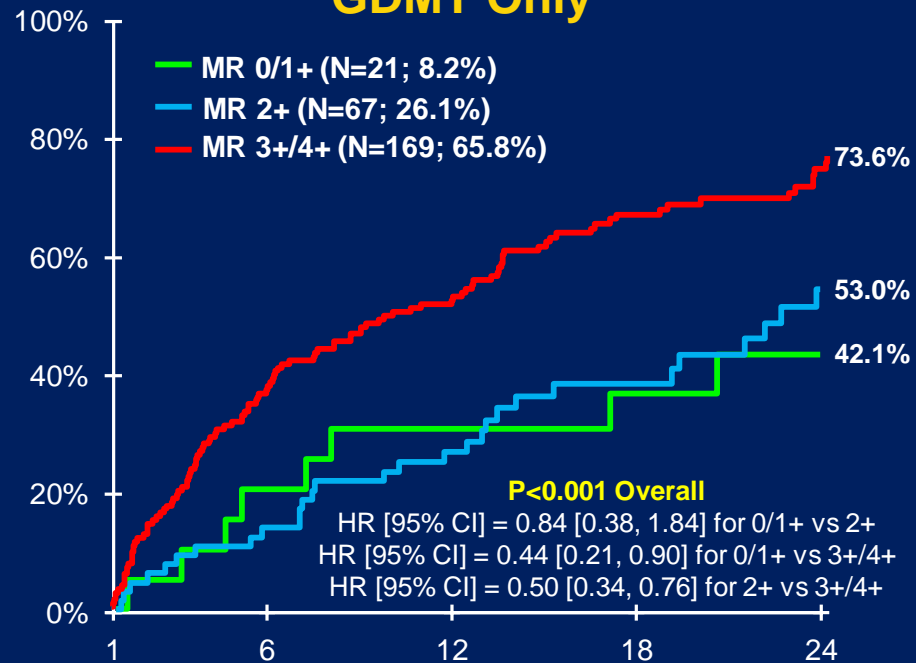
Randomization groups stratified by 30-day residual MR

$P_{int}=0.93$

## MitraClip + GDMT



## GDMT Only



# At Risk

	1	6	12	18	24
MR 0/1+	202	176	139	106	66
MR 2+	55	45	37	31	21
MR 3+/4+	20	13	7	7	4

Follow-up Duration (Months)

# At Risk

	1	6	12	18	24
MR 0/1+	21	16	13	11	7
MR 2+	67	56	44	26	15
MR 3+/4+	169	107	76	44	26

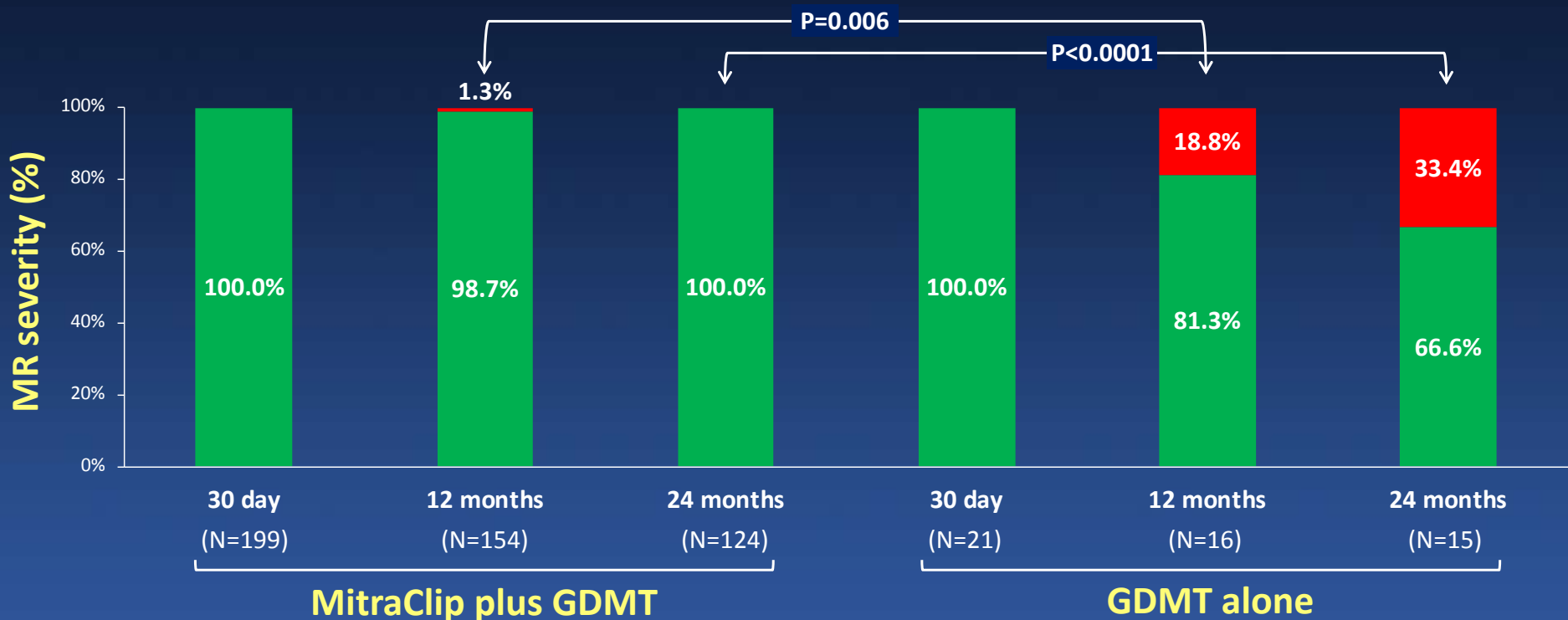
Follow-up Duration (Months)



# Stability of 30-Day MR Grade

Patients with 30-day residual MR 0/1+

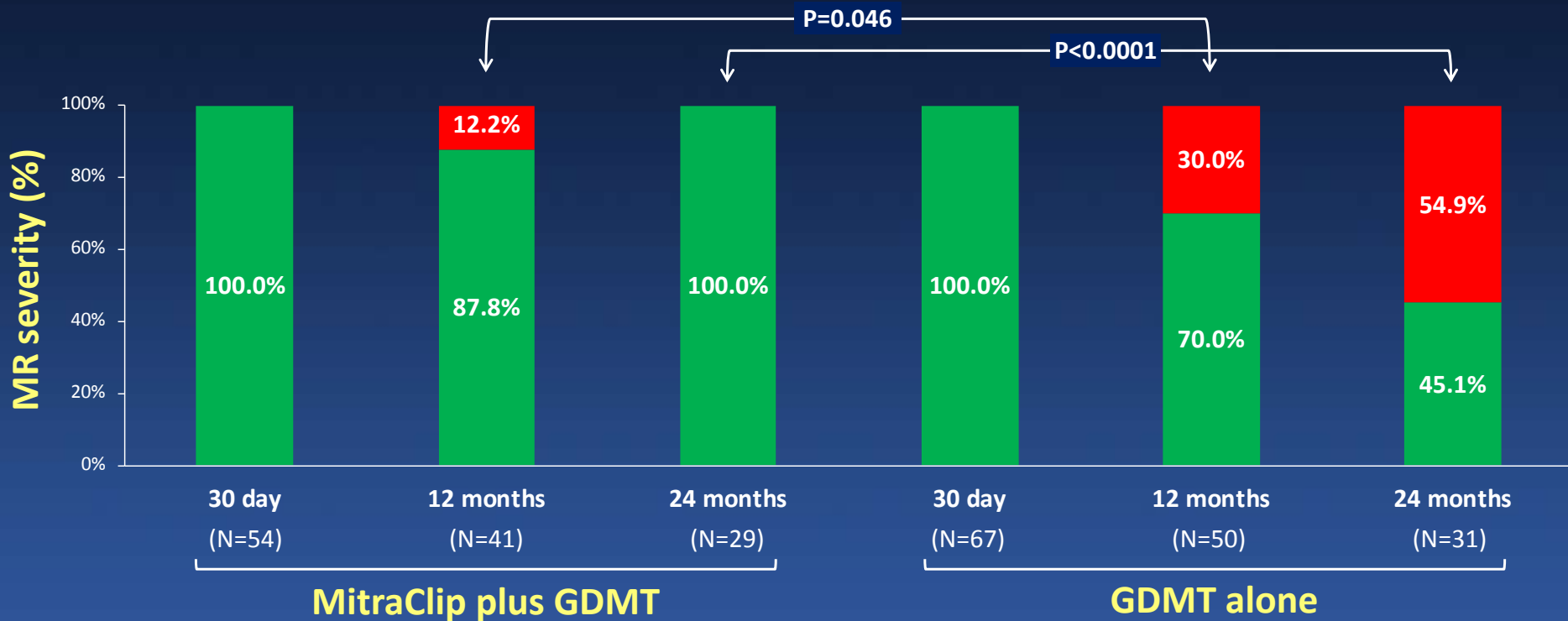
■ MR ≤2+ ■ MR >2+



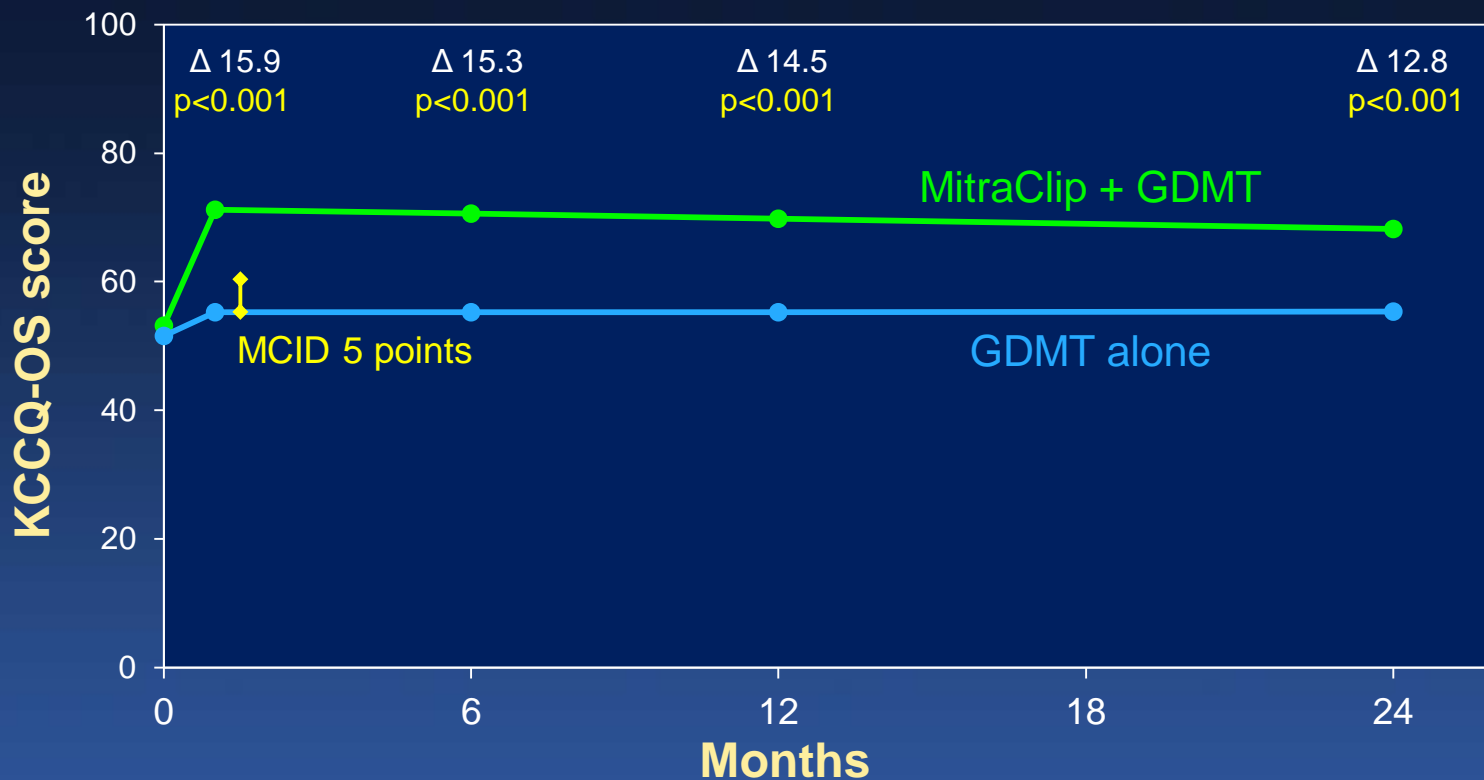
# Stability of 30-Day MR Grade

Patients with 30-day residual MR 2+

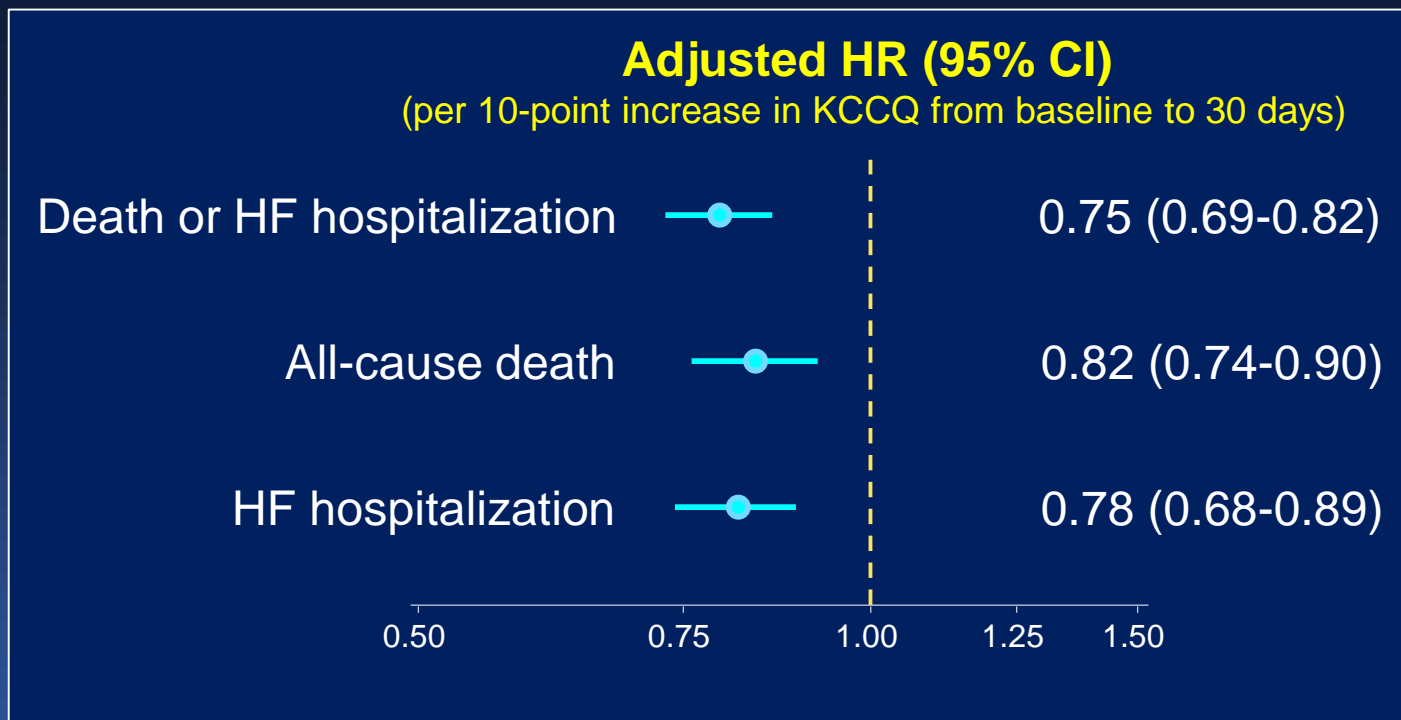
■ MR ≤2+ ■ MR >2+



# Effects of TMVr: Health Status



# Association of 1-Month Change in KCCQ and Outcomes Between 1 Month and 2 Years

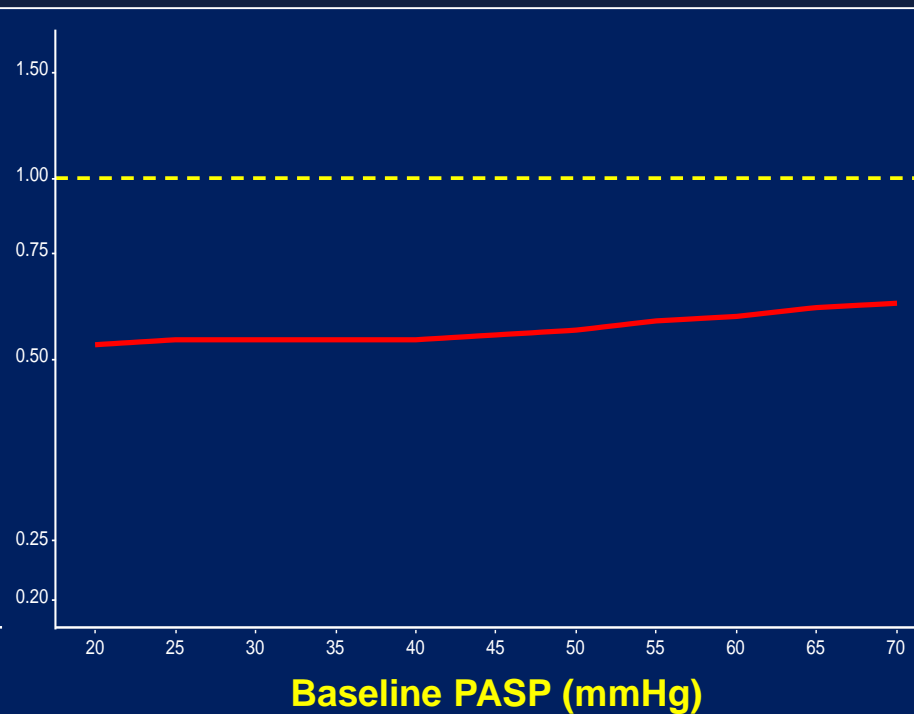
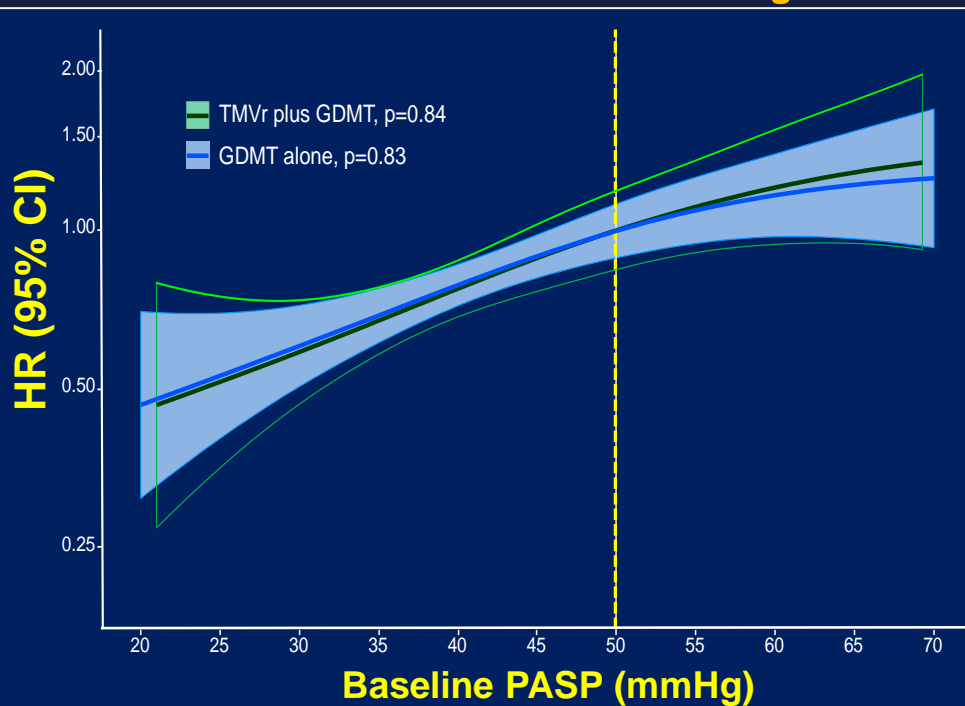


# Impact of Pulmonary HTN

## 2-year Death or HFH after MitraClip vs. GDMT alone

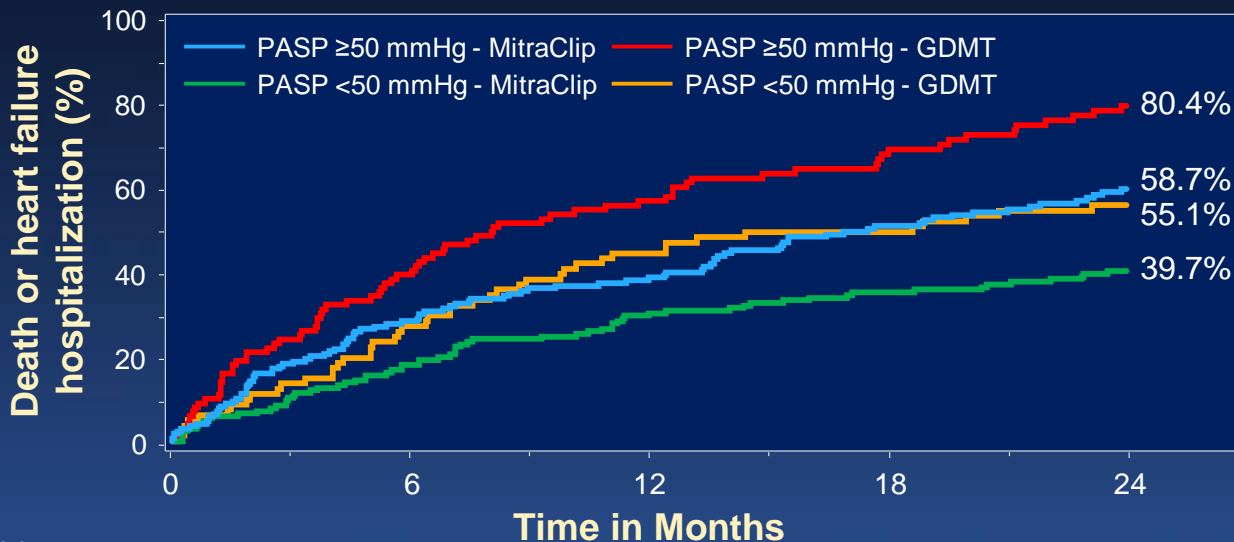
HR for MitraClip and GDMT alone separately, referenced to PASP 50 mmHg

HR for MitraClip vs. GDMT alone



# Impact of Pulmonary HTN

Median PASP (echo) was 43.1 [34.0, 53.0] mmHg, range 13.0 - 112.0 mmHg



## MitraClip vs GDMT:

**PASP ≥50 mmHg:**

HR (95%CI) =  
0.54 (0.39, 0.98)

**P=0.0009**

**PASP <50 mmHg:**

HR (95%CI) =  
0.59 (0.46, 0.75)

**P=0.0008**

**P<sub>int</sub> = 0.78**

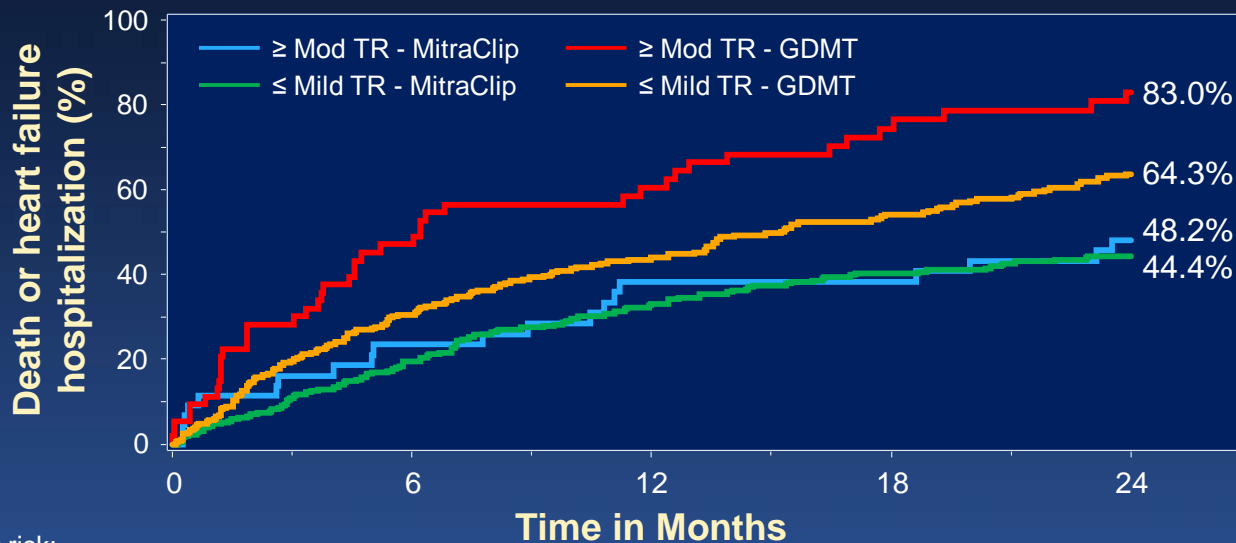
Number at risk:

PASP ≥50 - MitraClip	82	60	45	41	34
PASP ≥50 - GDMT	102	61	41	30	19
PASP <50 - MitraClip	171	137	117	107	92
PASP <50 - GDMT	173	124	119	77	58

# Impact of Baseline TR

TR severity: None/trace 2.0%; Mild 81.6%; Mod 15.4% Mod/sev 0.8%; Sev 0.2%

**83.6% had  $\leq$  Mild TR and 16.4% had  $\geq$  ModTR**



Number at risk:

$\geq$ Mod TR - MitraClip	44	31	25	25	19
$\geq$ Mod TR - GDMT	54	28	20	12	8
$\leq$ Mild TR - MitraClip	255	204	169	149	129
$\leq$ Mild TR - GDMT	246	170	129	102	74

## MitraClip vs GDMT:

In pts with  $\geq$  Mod TR:

HR (95%CI) =  
0.40 (0.23, 0.68)

**P=0.0005**

In pts with  $\leq$  Mild TR:

HR (95%CI) =  
0.59 (0.46, 0.75)

**P<0.0001**

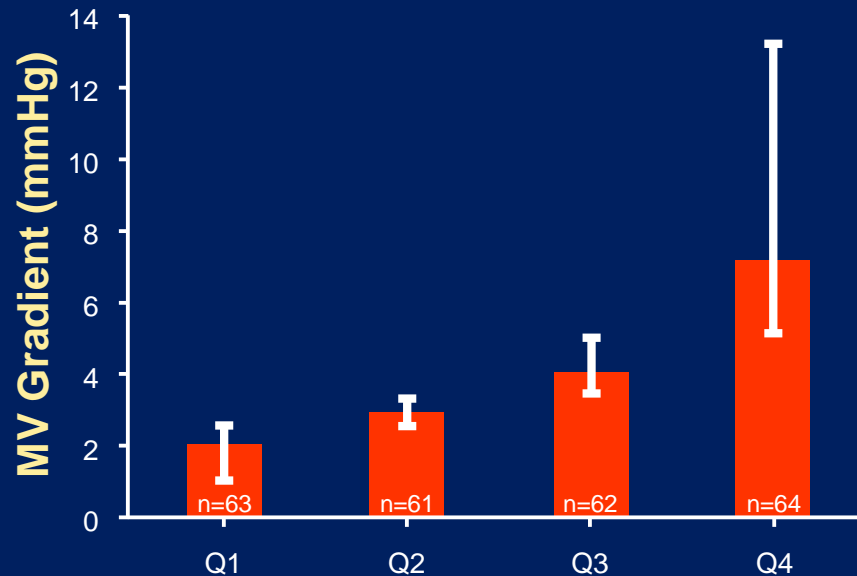
**P<sub>int</sub> = 0.16**

# Impact of Post-MitraClip Gradient

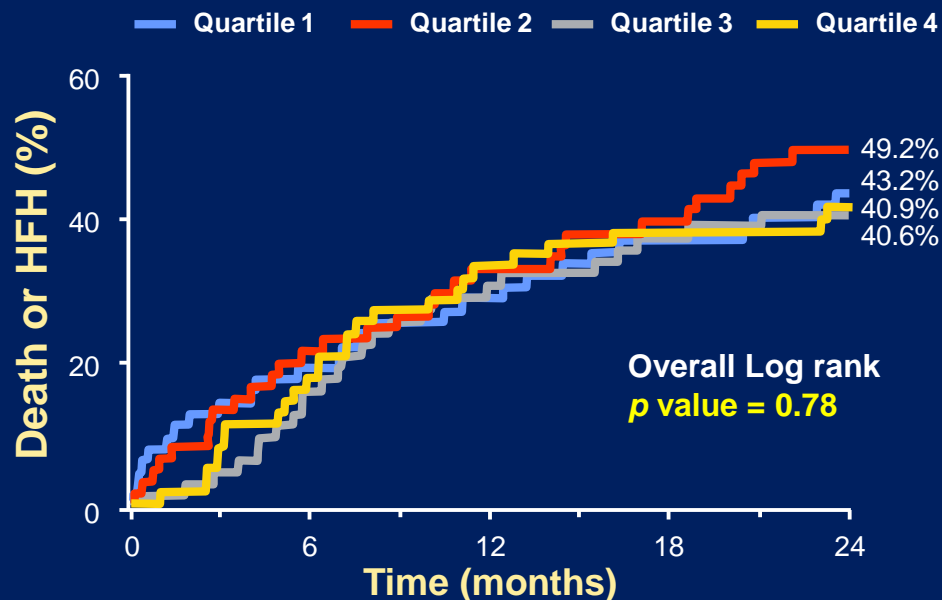
Mean discharge TTE MVG after MitraClip was  $4.2 \pm 2.2$  mmHg (range 1 to 13.2 mmHg)\*

Mean MVG in quartiles:  $2.1 \pm 0.4$ ,  $3.0 \pm 0.2$ ,  $4.2 \pm 0.5$ , and  $7.2 \pm 2.0$  mmHg

## Mitral Valve Gradient by Quartile



## Death or HF Hospitalization





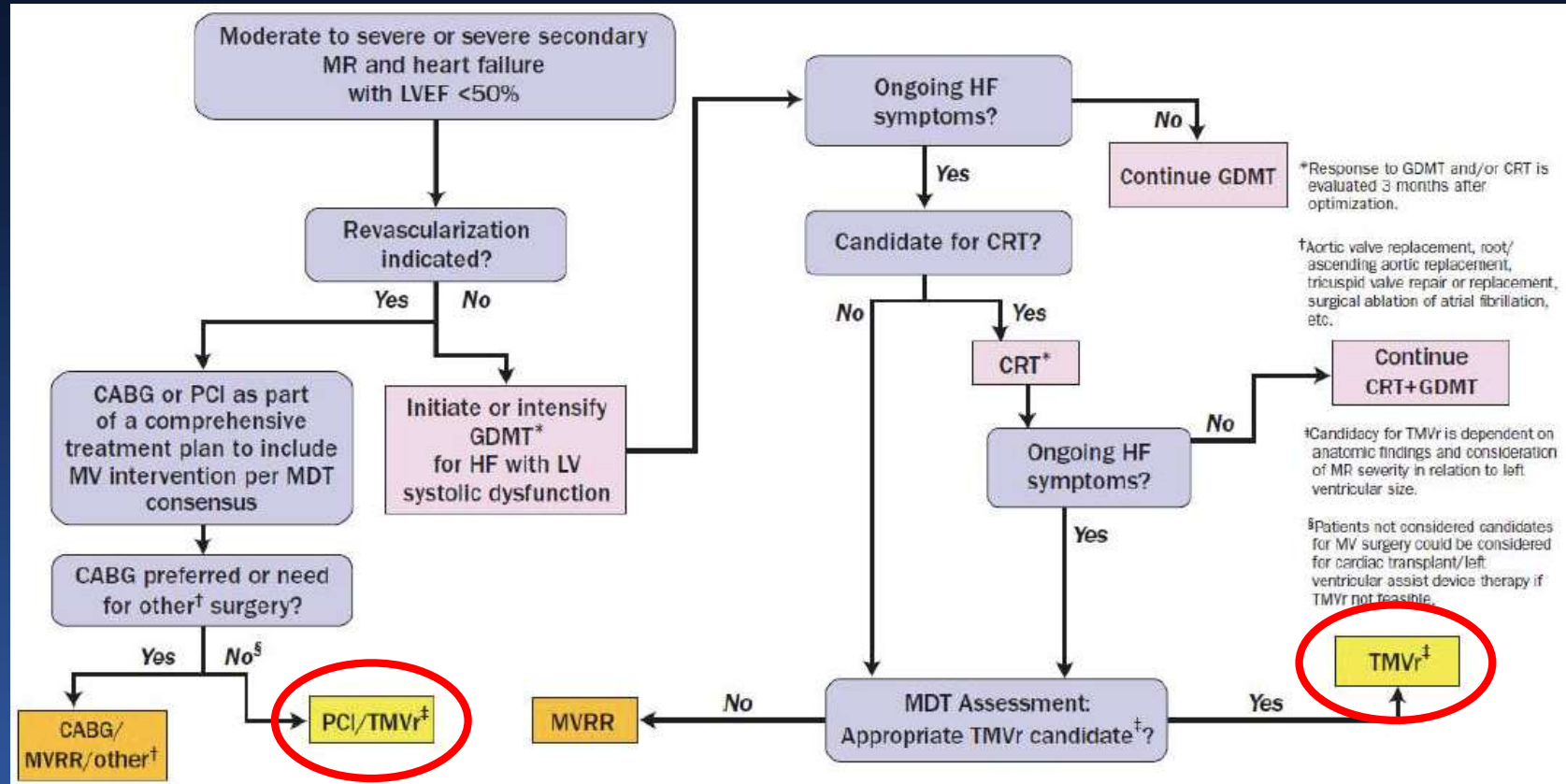
# March 14<sup>th</sup>, 2019

FDA approves  
MitraClip for  
treatment of select  
patients with  
severe secondary  
MR who remain  
symptomatic  
despite GDMT

**Label:** The MitraClip™ NTR/XTR Clip Delivery System, when used with maximally tolerated guideline-directed medical therapy (GDMT), is indicated for the treatment of symptomatic, moderate-to-severe or severe secondary (or functional) mitral regurgitation (MR; MR  $\geq$  Grade III per American Society of Echocardiography criteria) in patients with a left ventricular ejection fraction (LVEF)  $\geq 20\%$  and  $\leq 50\%$ , and a left ventricular end systolic dimension (LVESD)  $\leq 70$  mm whose symptoms and MR severity persist despite maximally tolerated GDMT as determined by a multidisciplinary heart team experienced in the evaluation and treatment of heart failure and mitral valve disease.

# Intervention for Symptomatic Secondary MR

2020 Focused Update of the 2017 ACC Expert Consensus Decision Pathway for MR



# Ascent to Widespread Utilization

Evidence generation  
(COAPT) ✓

FDA approval/  
indication ✓

Guidelines  
adoption ✓

CMS reimbursement



Heart team organization  
(HF, Im, Card, IC, CTS)

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Improved nationwide  
outcomes for  
HF pts with severe MR

