

COAPT

Three-Year Outcomes from a Randomized Trial of Transcatheter Mitral Valve Leaflet Approximation in Patients with Heart Failure and Secondary Mitral Regurgitation

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On behalf of the COAPT Investigators

Disclosure Statement

- **Abbott – Co-PI COAPT Trial**
- **Edwards Lifesciences- Co-PI PARTNER 3 Trial**
- **Medtronic- Study Chair-Apollo Trial**
- **Gore- Consultant**

Background

- In the COAPT trial, treatment of symptomatic patients with heart failure (HF) and severe secondary MR with the MitraClip improved survival at 2 years, reduced HF hospitalizations (HFH), and improved quality of life compared to maximally-tolerated guideline-directed medical therapy (GDMT) alone
- Per protocol, subjects randomized to GDMT were not allowed to crossover to the MitraClip prior to 24 months, but were permitted to do so **after 24 months**

Objectives

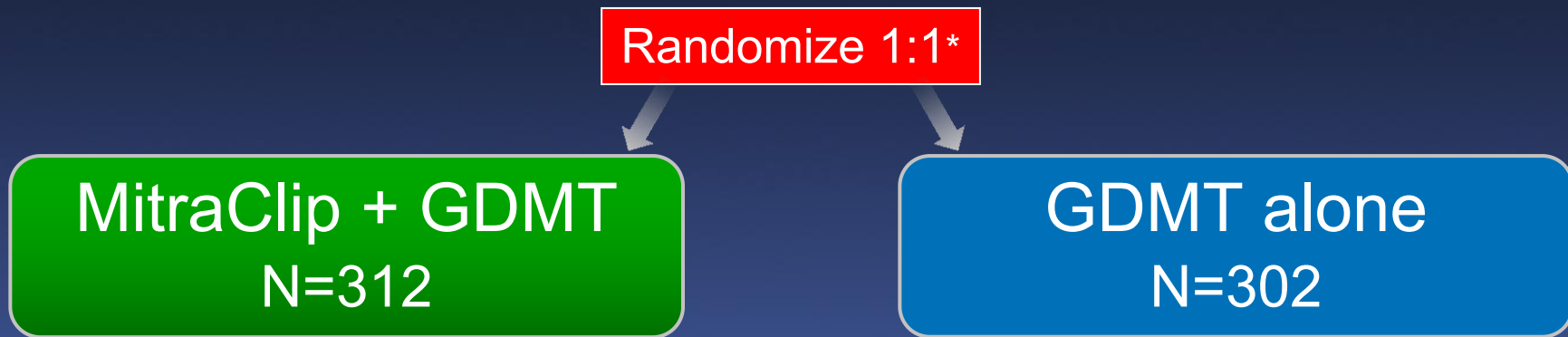
The present study sought to:

- 1) Describe the 3-year clinical outcomes of pts enrolled in the COAPT trial, including those who crossed over to MitraClip (ITT)
- 2) Analyze the impact of MitraClip crossovers in pts assigned to GDMT alone

The COAPT Trial

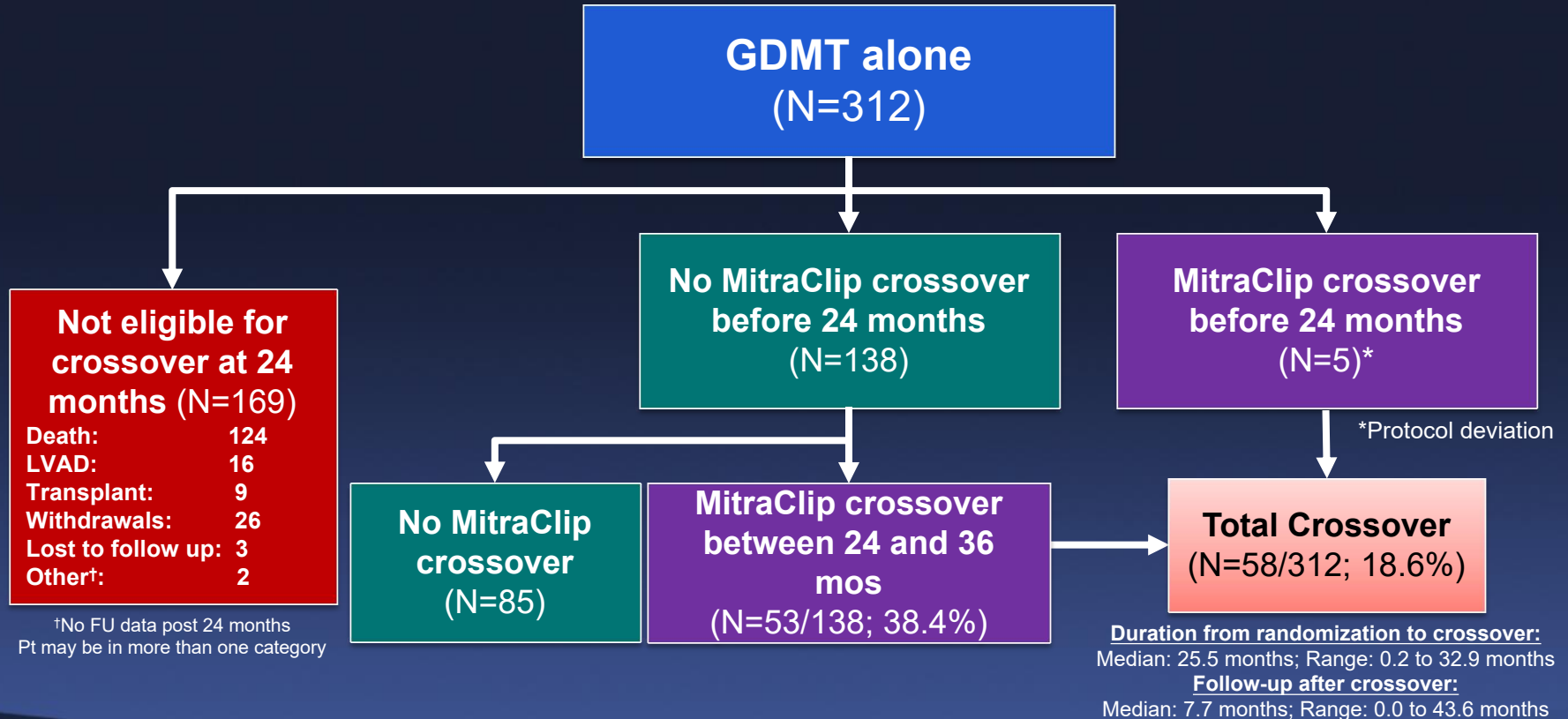
Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation

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



Follow-up at 30d, 6mo, 1y, 18mo, 2y, 3y, 4y, 5y

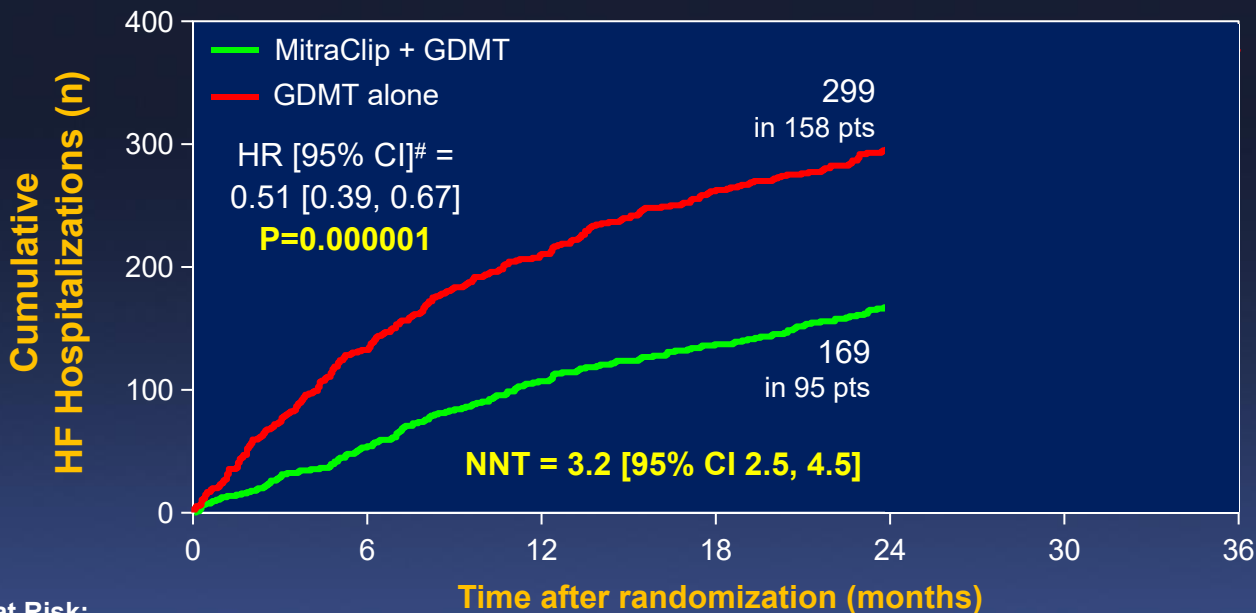
MitraClip Crossovers in GDMT-Assigned Patients



Primary Effectiveness Endpoint

All Hospitalizations for HF within 36 months

All patients, ITT, including crossovers



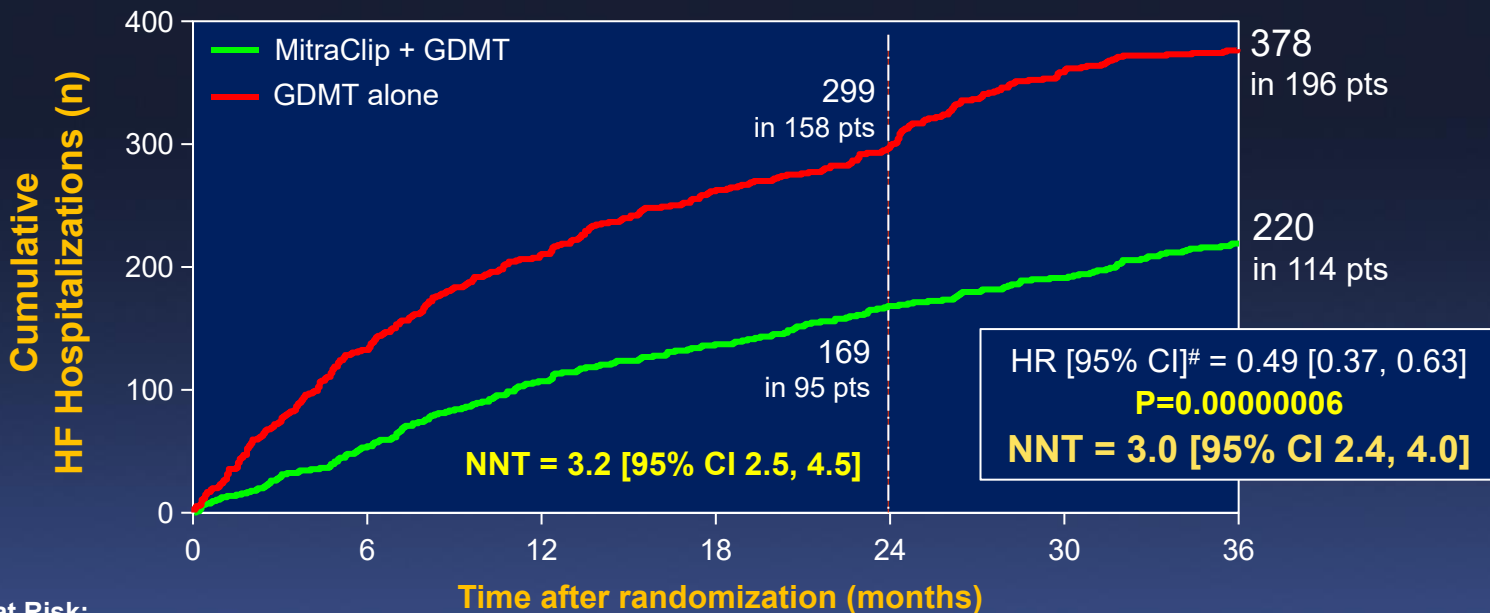
at Risk:

MitraClip + GDMT	302	269	238	219	189
GDMT alone	312	272	223	185	144

Primary Effectiveness Endpoint

All Hospitalizations for HF within 36 months

All patients, ITT, including crossovers



at Risk:

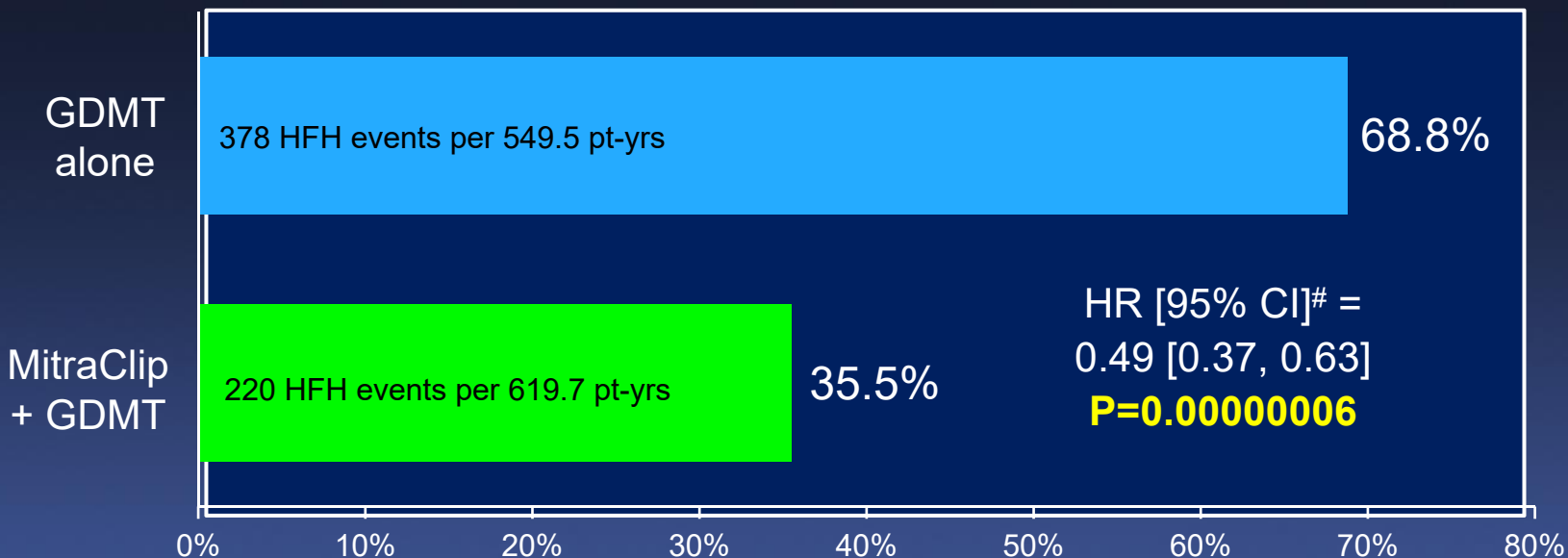
MitraClip + GDMT	302	269	238	219	189	128	93
GDMT alone	312	272	223	185	144	89	68

Primary Effectiveness Endpoint

Annualized Rates of HF Hospitalizations within 36 months

All patients, ITT, including crossovers

NNT= 3.0 [95% CI 2.4, 4.0]



Primary Safety Endpoint (MitraClip arm)

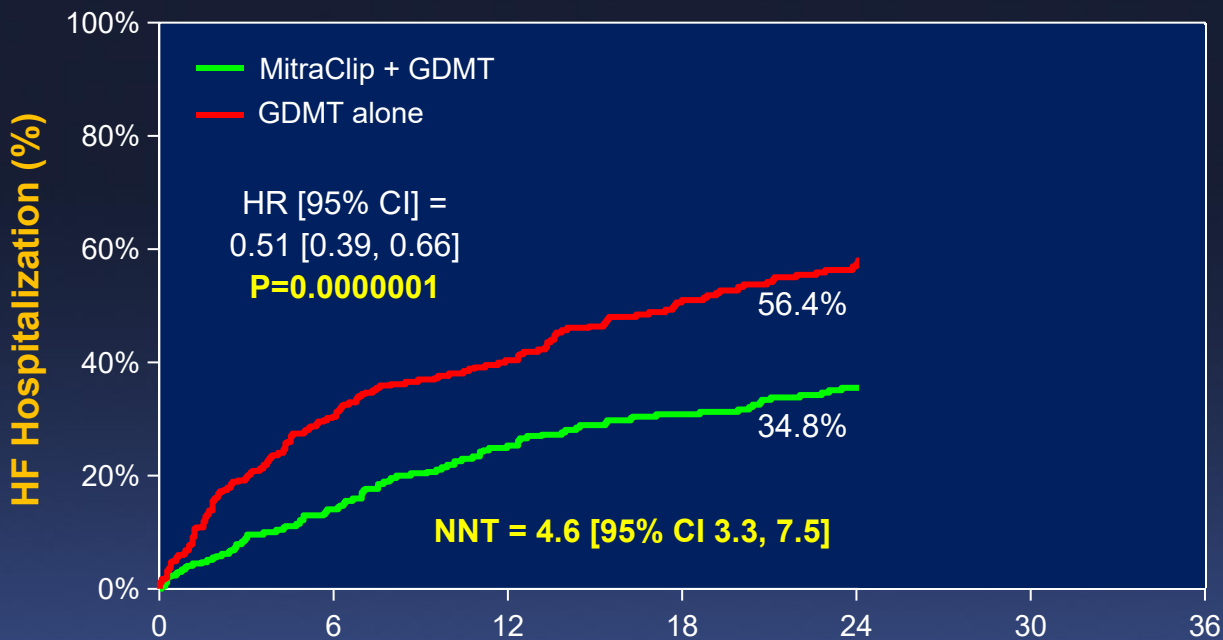
Freedom from Device-related Complications

n=293 pts with MitraClip procedure attempted

	0-30 Days	0-12 Months	0-24 Months	0-36 Months
All	1.4% (4)	3.3% (9)	5.2% (13)	8.7% (18)
- Device-related complications	1.4% (4)	1.4% (4)	1.4% (4)	1.4% (4)
• Single leaflet device attachment	0.7% (2)	0.7% (2)	0.7% (2)	0.7% (2)
• Device embolization	0.3% (1)	0.3% (1)	0.3% (1)	0.3% (1)
• Endocarditis requiring surgery	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
• Mitral stenosis requiring surgery	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
• Any device-related complication requiring non-elective CV surgery	0.3% (1)	0.3% (1)	0.3% (1)	0.3% (1)
- Progressive heart failure	0.0% (0)	2.0% (5)	3.8% (9)	7.4% (14)
• Left ventricular assist device implant	0.0% (0)	1.2% (3)	2.6% (6)	5.4% (10)
• Heart transplant	0.0% (0)	0.8% (2)	1.3% (3)	2.6% (5)

First Heart Failure Hospitalization

All patients, ITT, including crossovers



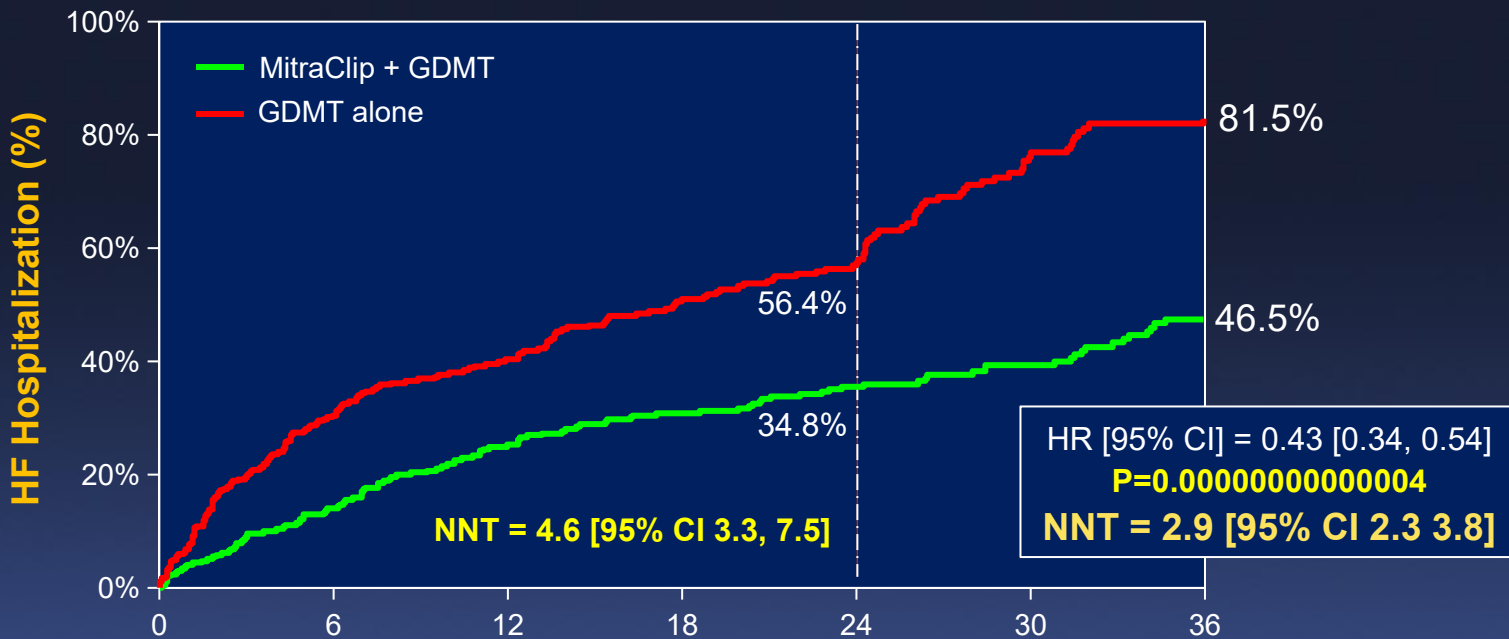
at Risk:

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

Time after randomization (months)

First Heart Failure Hospitalization

All patients, ITT, including crossovers



NNT = 4.6 [95% CI 3.3, 7.5]

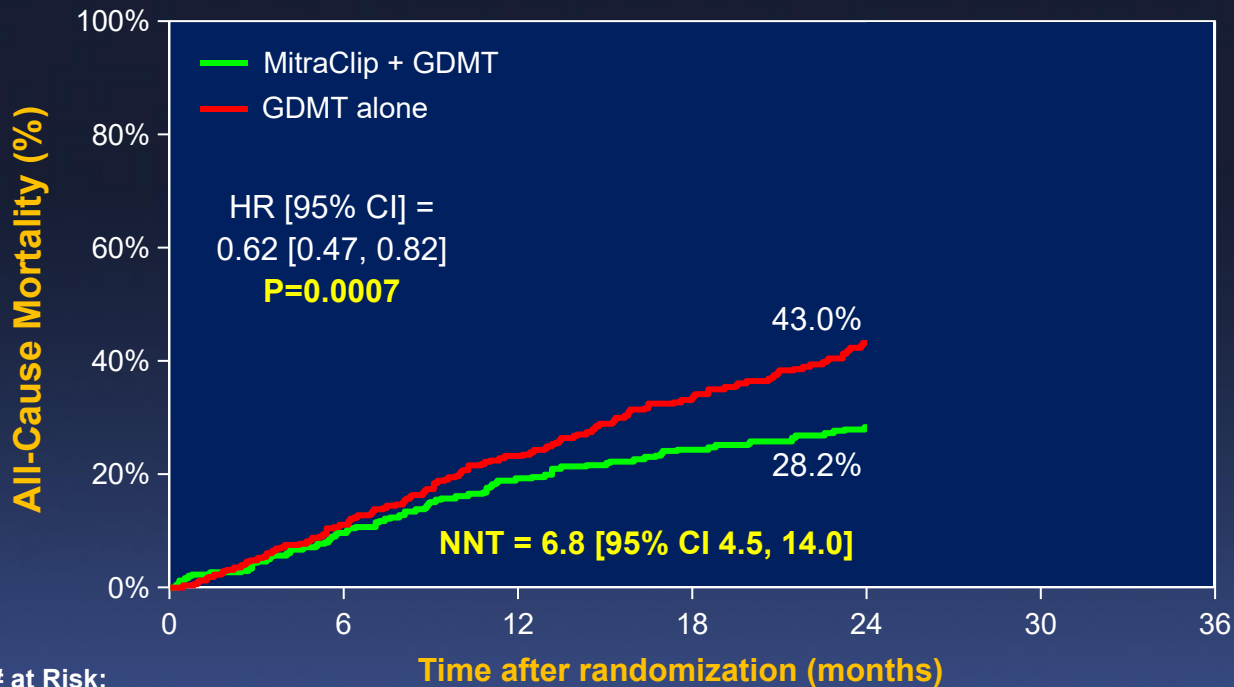
at Risk:

	0	6	12	18	24	30	36
MitraClip + GDMT	302	238	196	176	148	101	66
GDMT alone	312	206	156	120	87	37	20

Time after randomization (months)

All-Cause Mortality

All patients, ITT, including crossovers

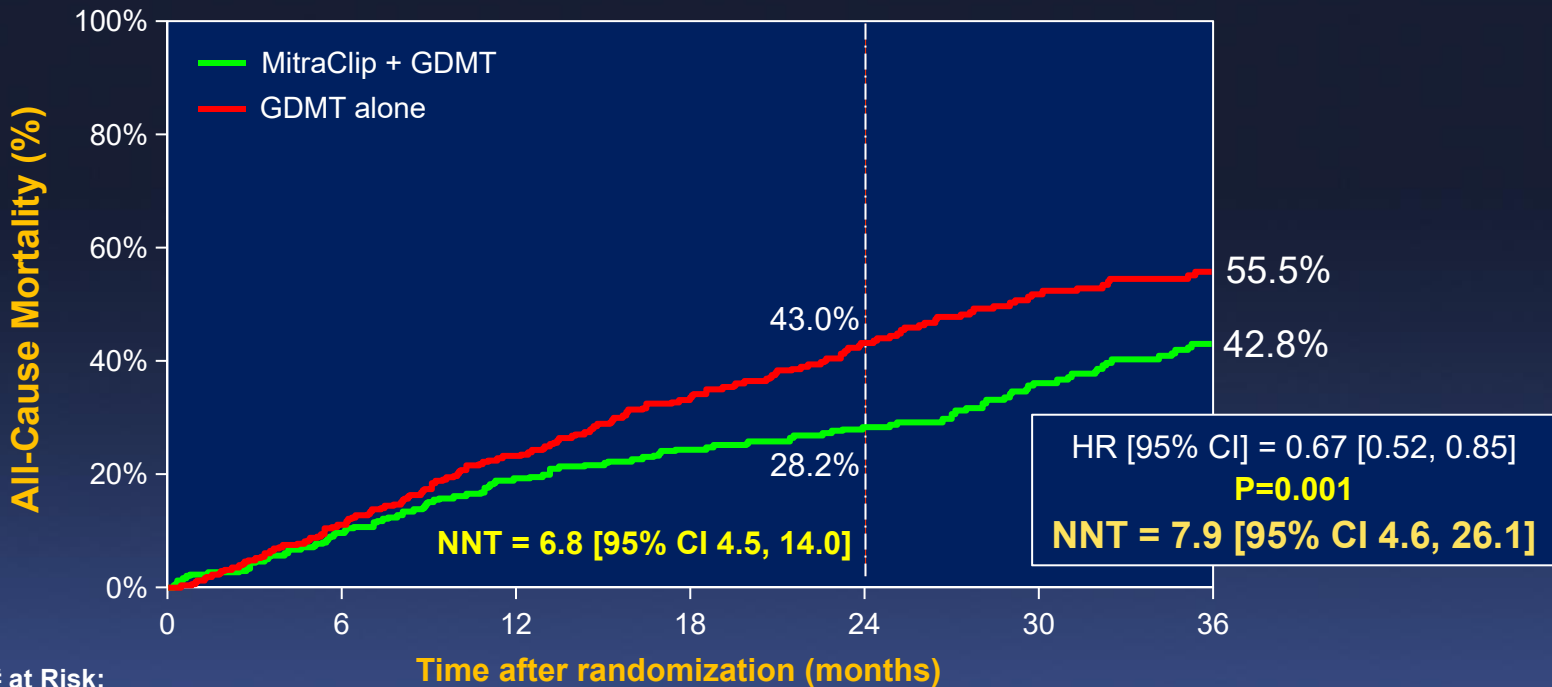


at Risk:

	0	6	12	18	24
MitraClip + GDMT	302	269	238	219	189
GDMT alone	312	272	223	186	145

All-Cause Mortality

All patients, ITT, including crossovers

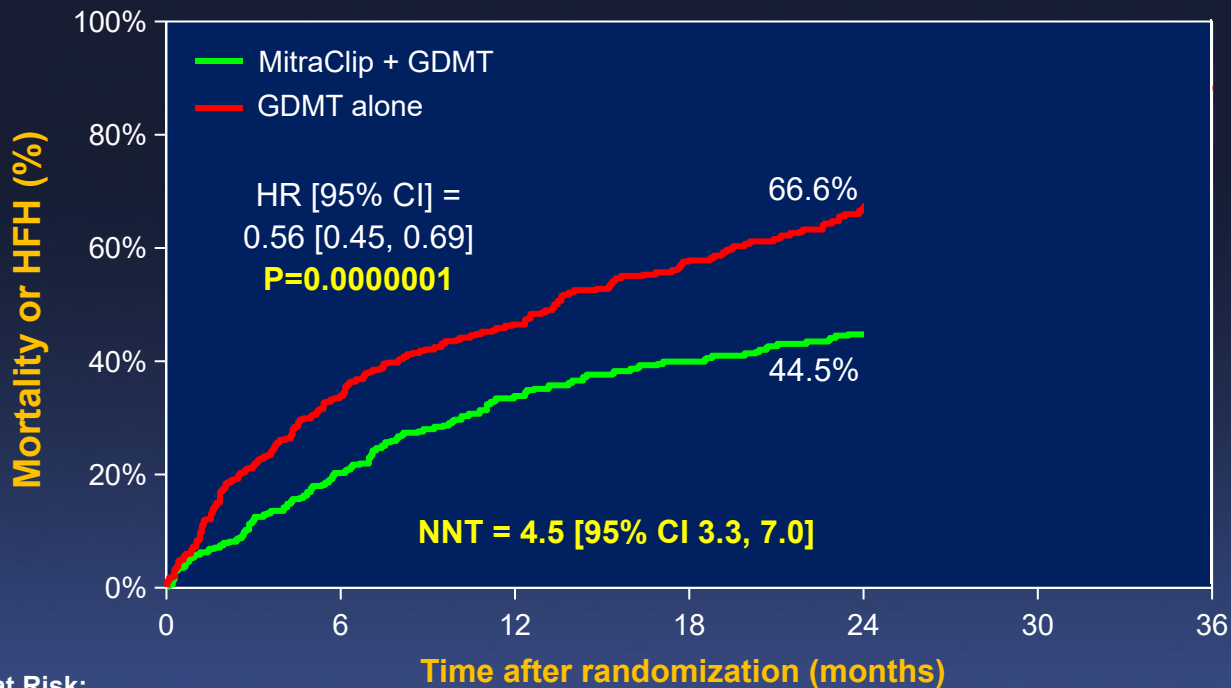


at Risk:

	0	6	12	18	24	30	36
MitraClip + GDMT	302	269	238	219	189	128	93
GDMT alone	312	272	223	186	145	91	70

All-Cause Mortality or HF Hospitalization

All patients, ITT, including crossovers

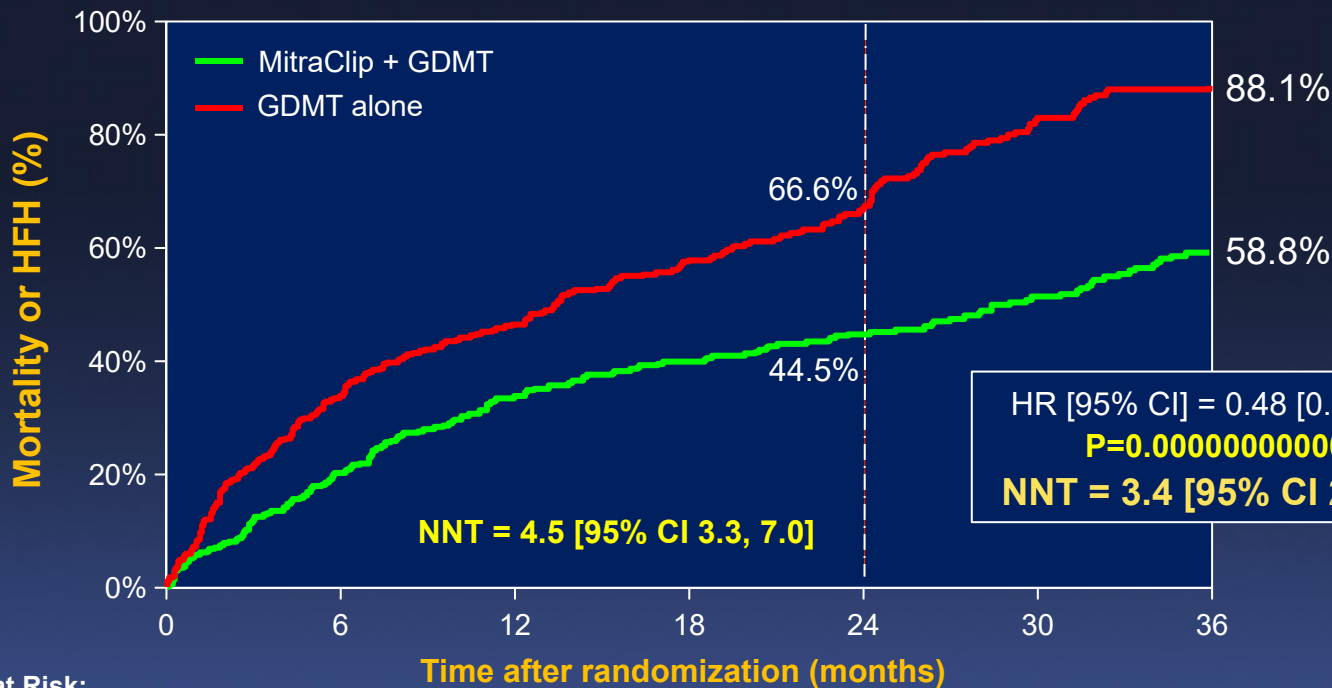


at Risk:

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

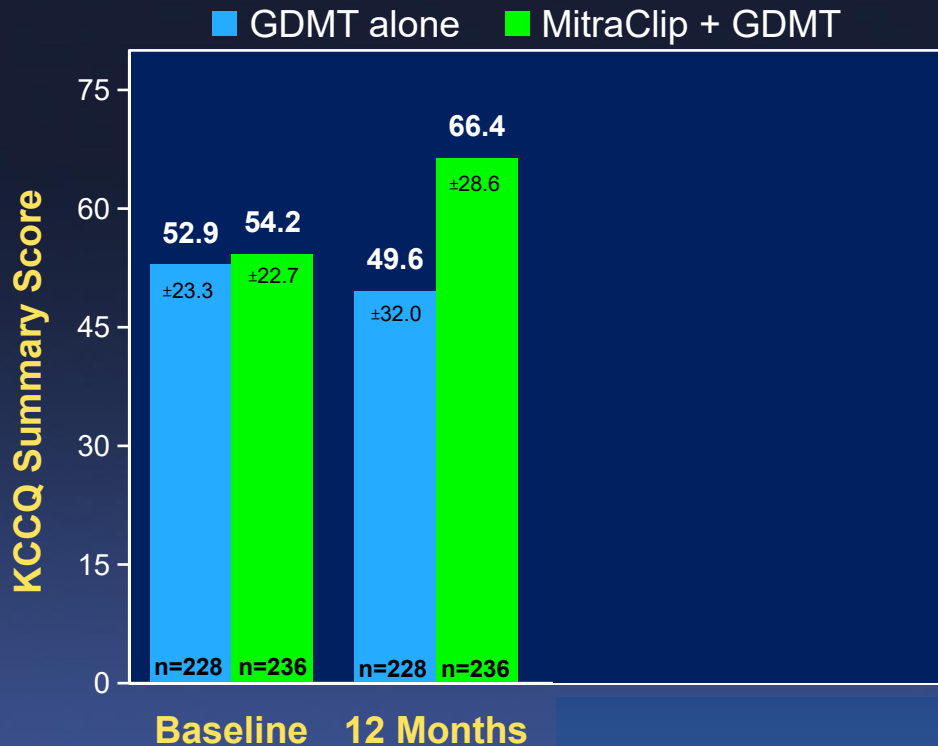


at Risk:

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

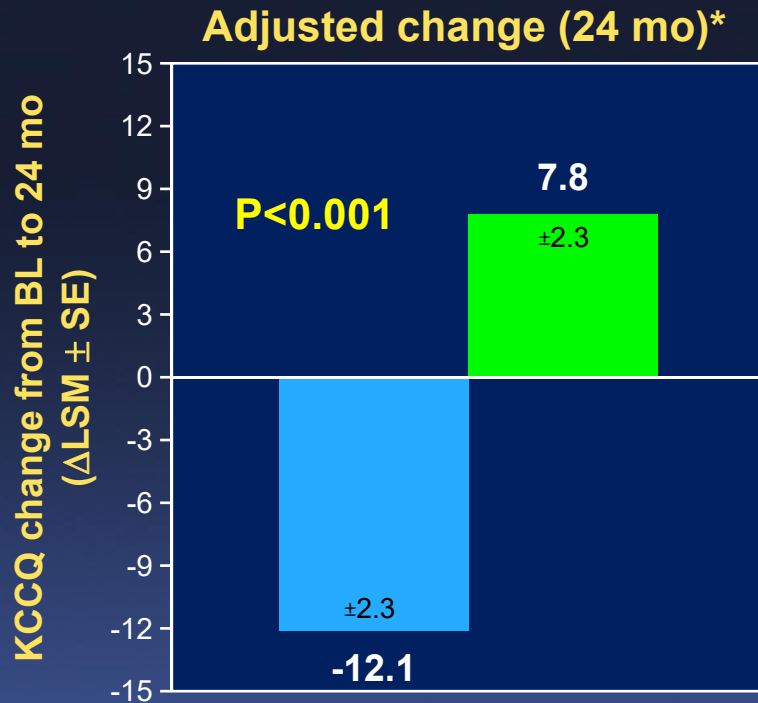
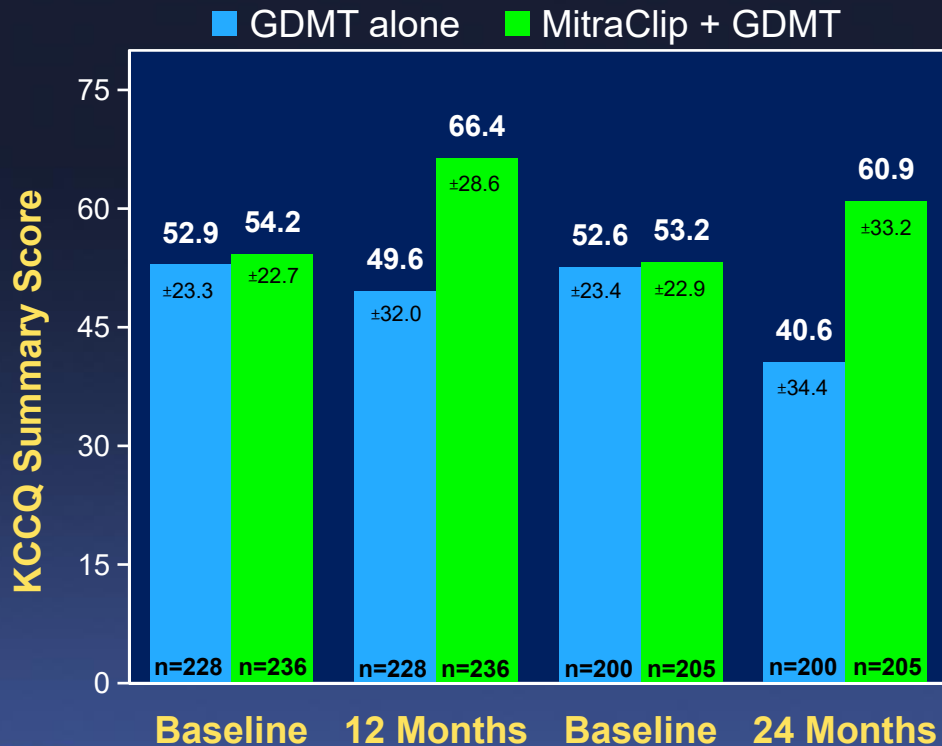
KCCQ Summary Score

All patients, ITT, 24 months



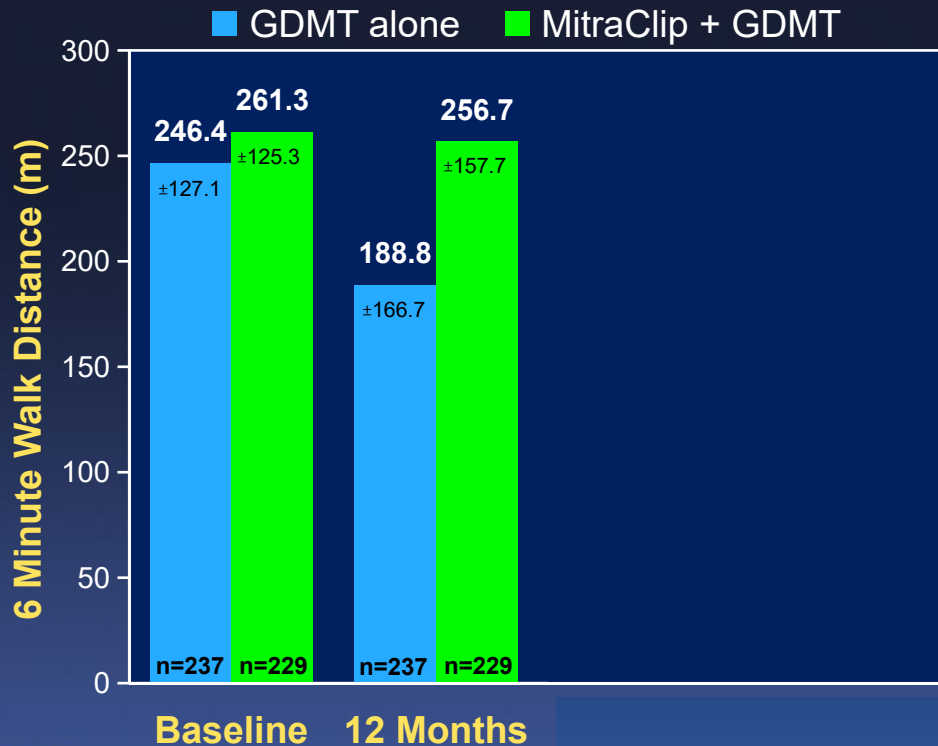
KCCQ Summary Score

All patients, ITT, 24 months



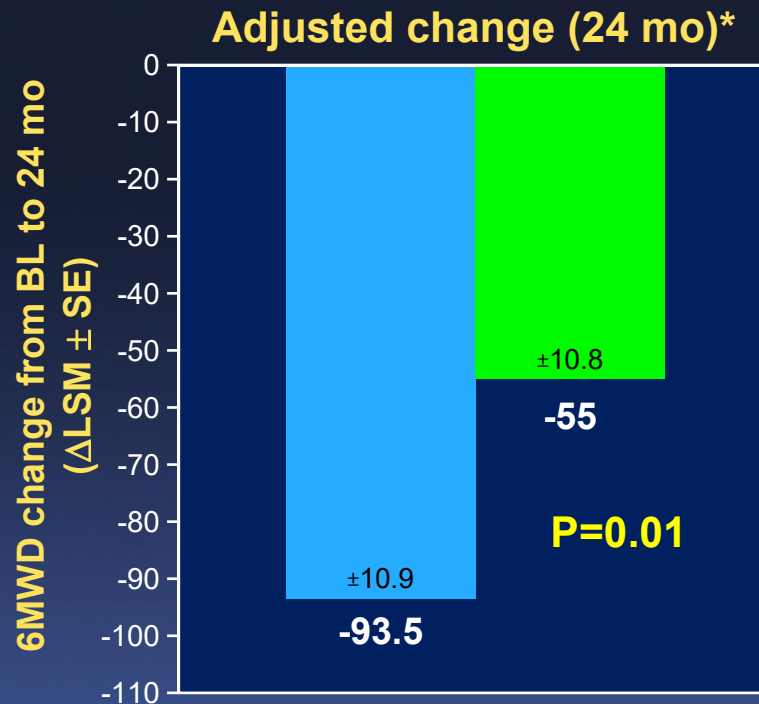
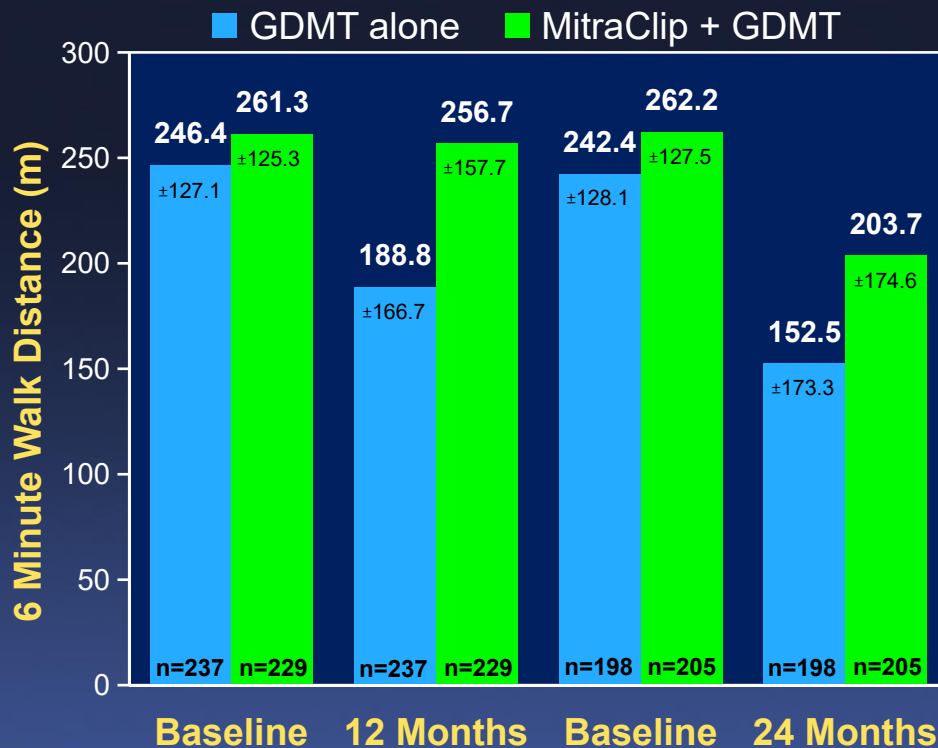
6MWD Outcomes

All patients, ITT, 24 months



6MWD Outcomes

All patients, ITT, 24 months



Adverse Event Rates (i)

All patients, ITT, 36 months

	MitraClip + GDMT (n=302)	GDMT alone (n=312)	HR [95% CI]	P-value
Death, all-cause	42.8%	55.5%	0.67 [0.52, 0.85]	0.001
- CV	36.0%	47.4%	0.65 [0.49, 0.85]	0.002
- HF-related	21.6%	34.7%	0.51 [0.35, 0.74]	0.004
- Non-HF-related	18.4%	19.8%	0.88 [0.58, 1.34]	0.55
- Non-CV	10.6%	15.5%	0.74 [0.43, 1.27]	0.27
Hospitalization, all-cause	77.7%	93.3%	0.70 [0.58, 0.84]	<0.001
- CV	64.6%	86.7%	0.58 [0.48, 0.72]	<0.001
- HF-related	46.5%	81.5%	0.43 [0.34, 0.54]	<0.001
- Non-HF-related	40.8%	40.6%	0.98 [0.73, 1.31]	0.87
- Non-CV	56.9%	62.3%	0.89 [0.71, 1.12]	0.31
Death or HF hospitalization	59.0%	88.0%	0.48 [0.39, 0.59]	<0.001
CV Death or HF hospitalization	54.6%	85.1%	0.47 [0.38, 0.58]	<0.001

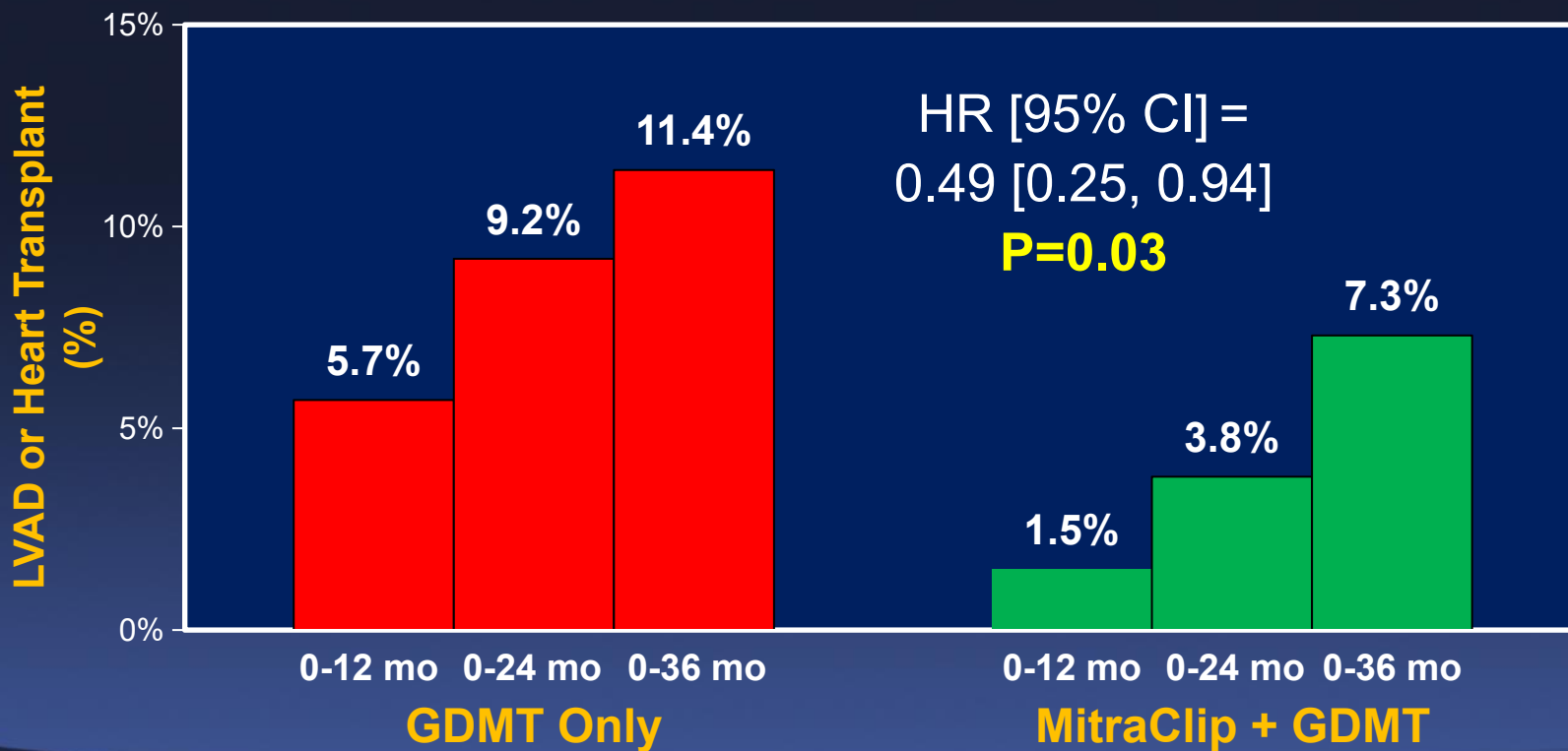
Adverse Event Rates (ii)

All patients, ITT, 36 months

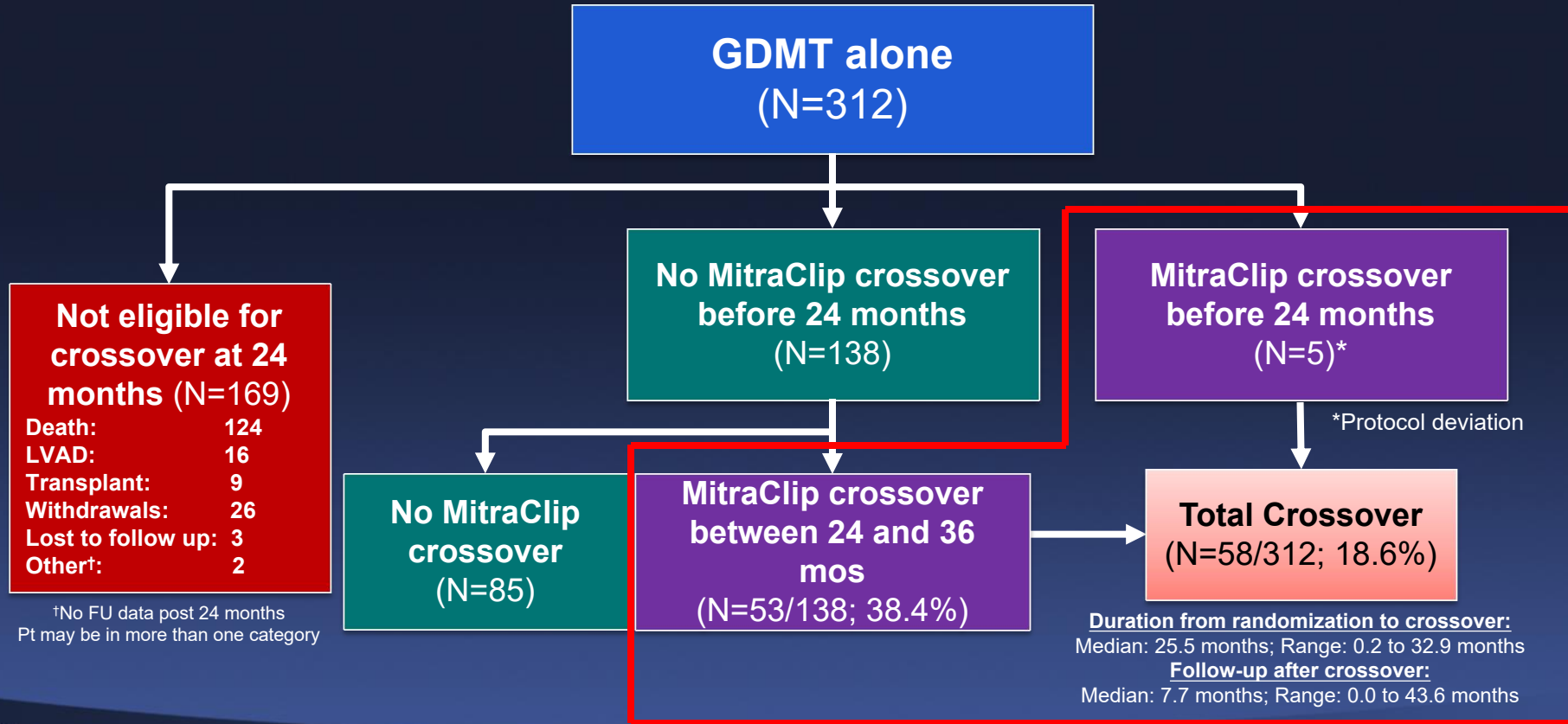
	MitraClip + GDMT (n=302)	GDMT alone (n=312)	HR [95% CI]	P-value
MV intervention or surgery*	3.8%	49.2%	0.10 [0.05, 0.20]	<0.001
- MitraClip*	3.5%	47.1%	0.10 [0.05, 0.20]	<0.001
- Mitral valve surgery	0.4%	3.3%	0.12 [0.02, 0.97]	0.05
PCI or CABG	4.0%	4.9%	0.70 [0.29, 1.66]	0.42
- PCI	4.0%	4.3%	0.83 [0.34, 2.05]	0.69
- CABG	0.0%	0.7%	-	1.0
Stroke	7.7%	9.8%	0.80 [0.41, 1.57]	0.51
MI	7.7%	13.3%	0.65 [0.35, 1.23]	0.19
New CRT implant	3.4%	3.1%	0.96 [0.36, 2.56]	0.93
LVAD or heart transplant	7.3%	11.4%	0.49 [0.25, 0.94]	0.03
- LVAD	5.4%	8.6%	0.48 [0.22, 1.04]	0.06
- Heart transplant	2.6%	4.9%	0.45 [0.15, 1.30]	0.14

LVAD or Heart Transplantation

All patients, ITT, including crossovers



MitraClip Crossovers in GDMT-Assigned Patients

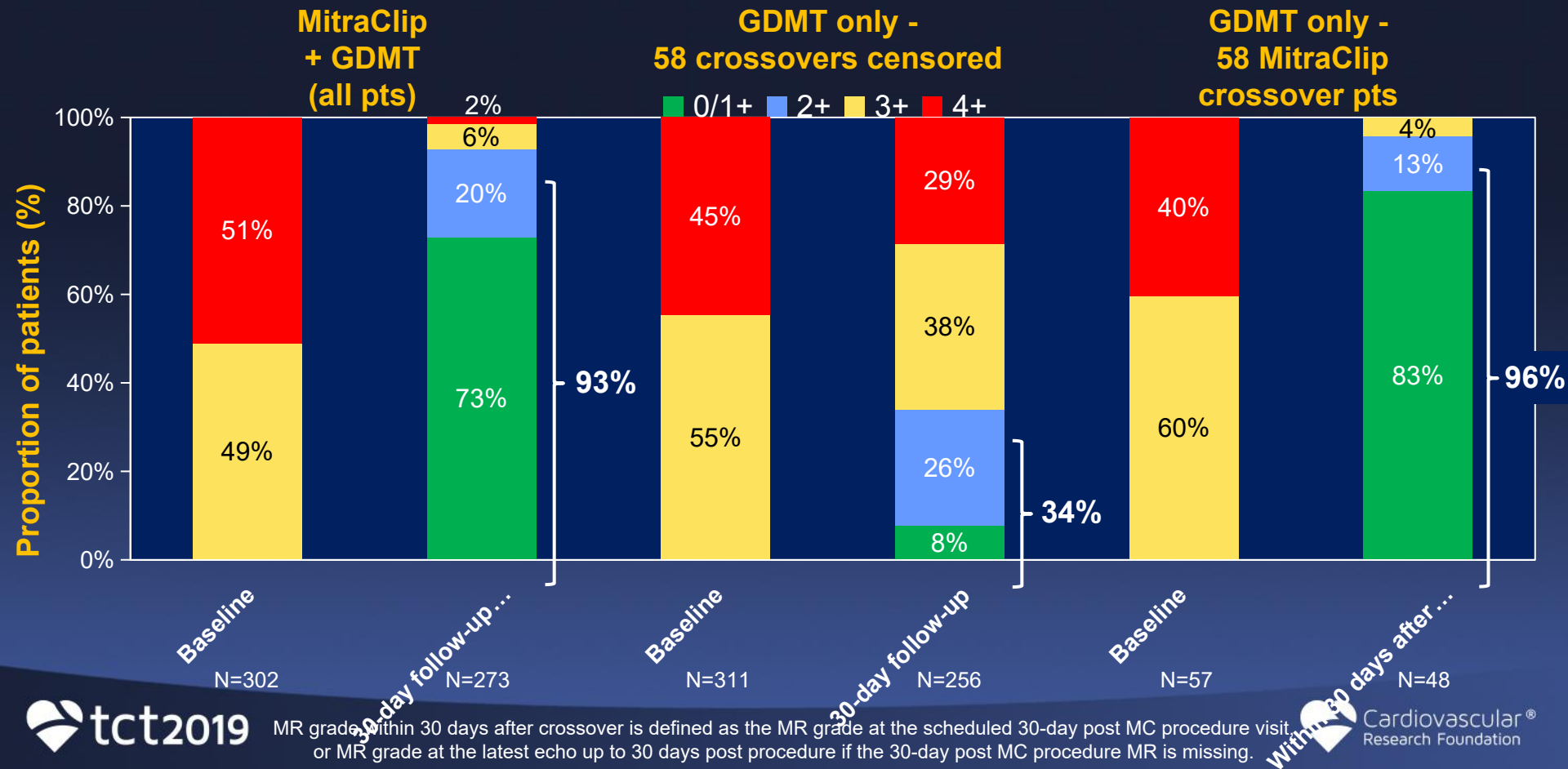


MitraClip Procedure Outcomes

(All pts undergoing a MitraClip procedure)

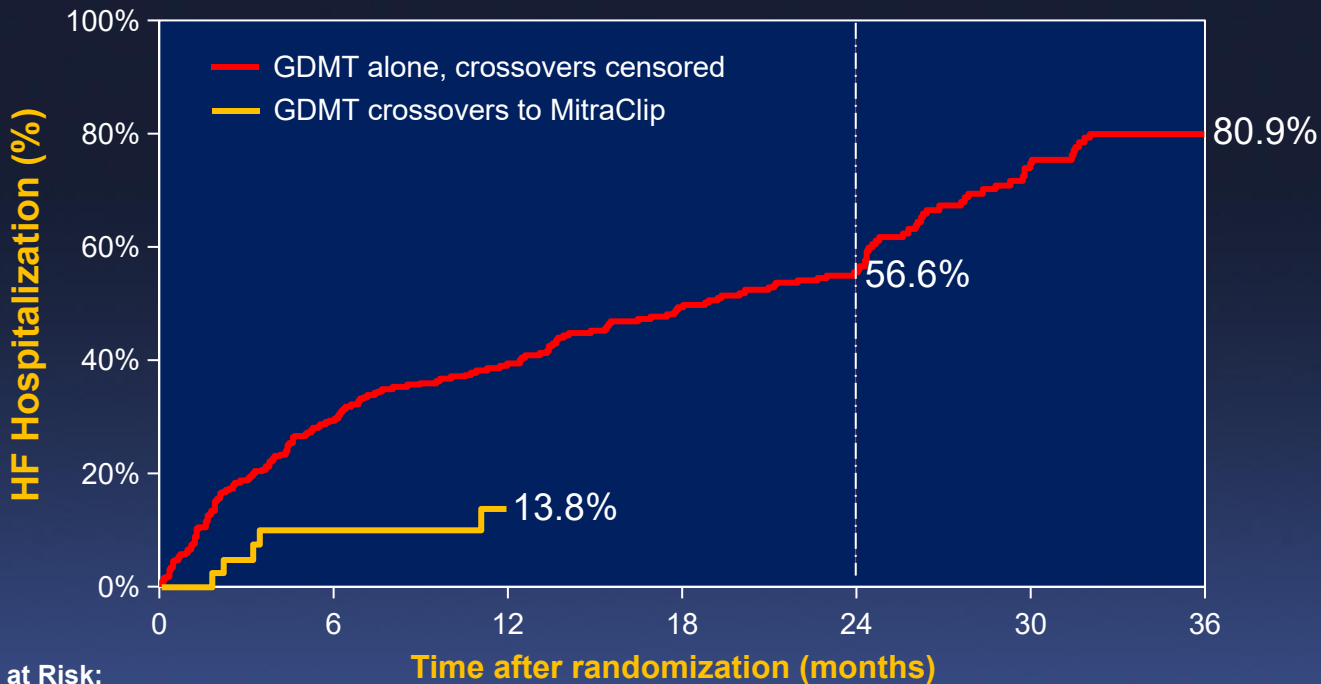
	MitraClip + GDMT (N=302)	GDMT alone, MitraClip crossovers (N=58)	P-value
MitraClip procedure attempted	293/302 (97.0%)	58/58 (100%)	
Clip implanted (MitraClip procedure attempted)	287/293 (98.0%)	55/58 (94.8%)	0.17
Clip implanted (all patients)	287/302 (95.0%)	55/58 (94.8%)	
Mean # of clips implanted	1.7 ± 0.7 (n=293)	1.6 ± 0.7 (n=58)	0.56
- 0 clips implanted	6 (2.0%)	3 (5.2%)	0.17
- 1 clip implanted	106 (36.2%)	22 (37.9%)	0.80
- 2 clips implanted	157 (53.6%)	27 (46.6%)	0.33
- 3 clips implanted	23 (7.9%)	6 (10.3%)	0.60
- 4 clips implanted	1 (0.3%)	0 (0.0%)	1.00
Procedure duration (mins)	162.9 ± 118.1 (293)	132.9 ± 50.0 (57)	0.002
- Device procedure time (mins)	118.9 ± 63.5	97.5 ± 46.2 (59)	0.004
- Device time (mins)	82.7 ± 80.8	60.3 ± 34.8 (56)	<0.001
- Fluoroscopy time (mins)	33.9 ± 23.2	30.0 ± 15.5 (51)	0.13

MR Grade at Baseline and 30 Days



First Heart Failure Hospitalization

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

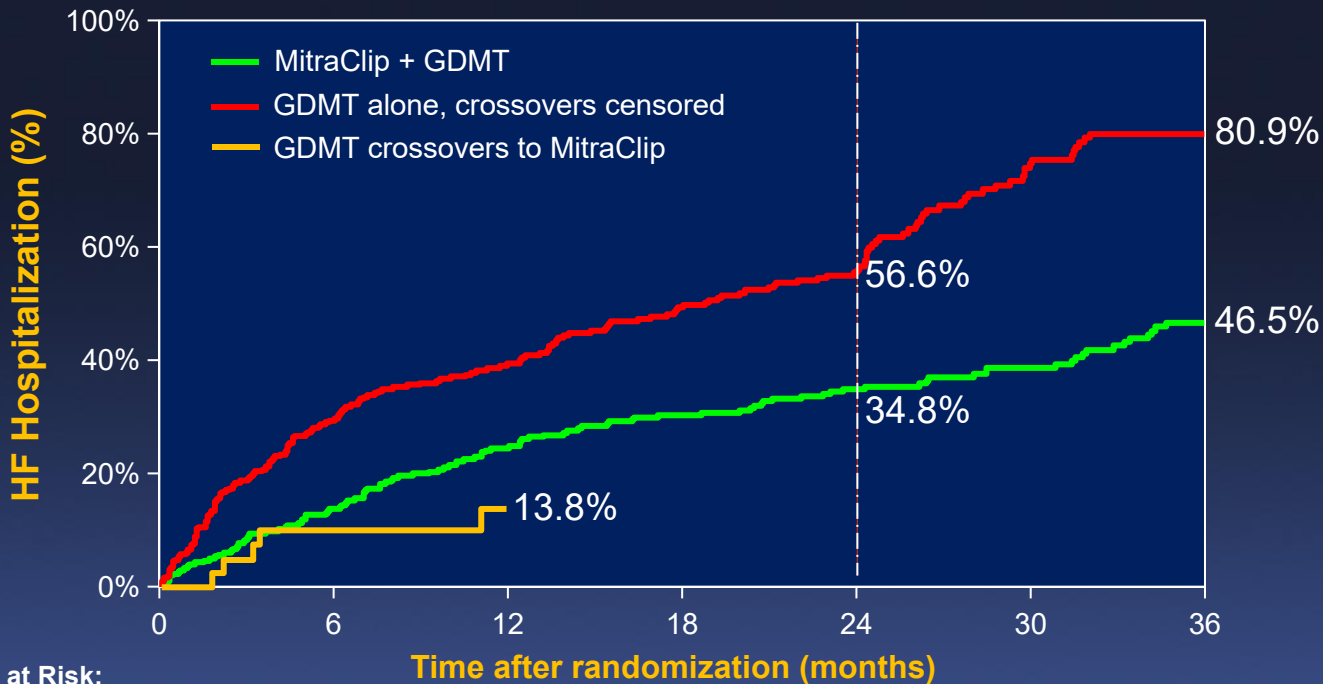


at Risk:

	0	6	12	18	24	30	36
GDMT only, crossovers censored	312	205	155	119	85	33	19
GDMT crossovers to MitraClip	58	30	22				

First Heart Failure 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				

Multivariable Predictors of First HFH Within 36 Months

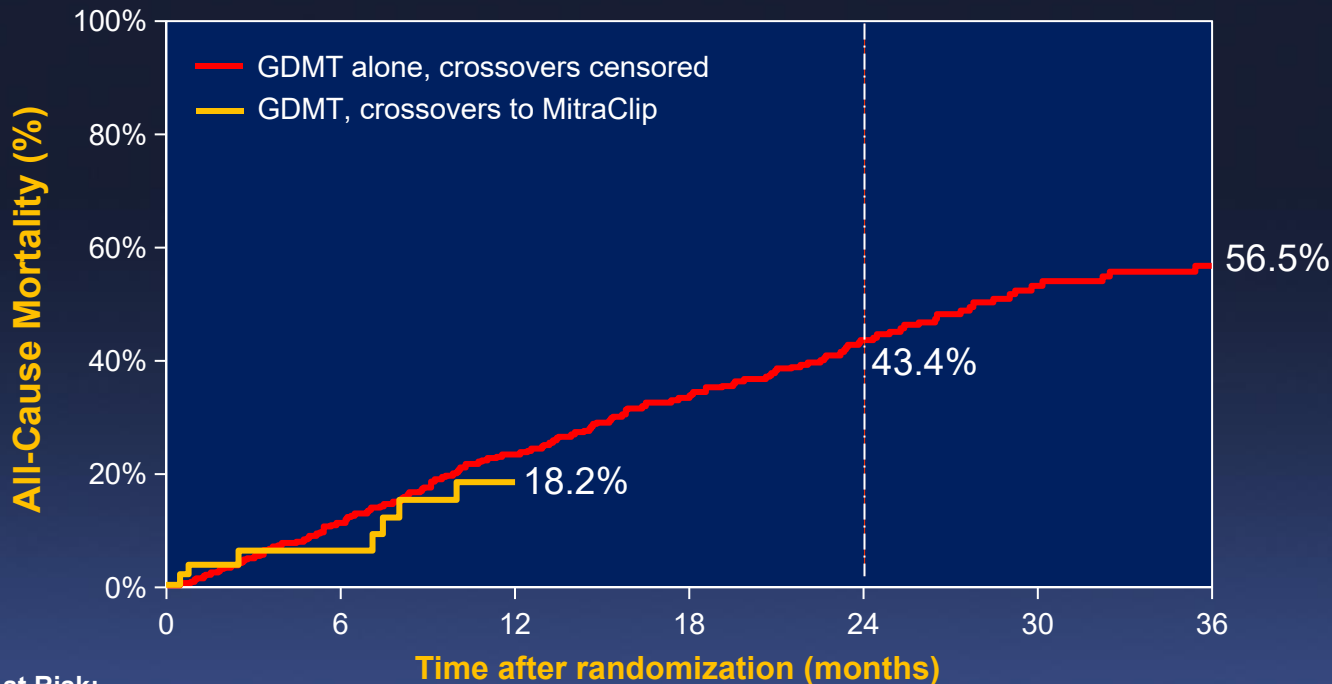
GDMT only group with MitraClip crossover as a time-adjusted covariate

	Hazard Ratio [95% CI]	P-Value
Treatment with MitraClip	0.42 [0.22, 0.80]	0.009
Vasodilator use (hydralazine or nitrates)	2.70 [1.90, 3.83]	<0.0001
BNP (per 100 pg/mL)	1.02 [1.01, 1.03]	0.0006
Beta-blocker use	0.52 [0.32, 0.83]	0.006
LVEF (per 10%)	0.79 [0.66, 0.95]	0.01

Variables entered the final model include: ACEi/ARB/ARNI use, age, beta-blocker use, BNP, body surface area, serum creatinine, treatment with MitraClip, vasodilator use (hydralazine or nitrates), KCCQ summary score, LVEDV, LVEF, renal disease, 6MWD, prior stroke, systolic BP, TR grade; other variables tested had $\alpha > 0.20$ in univariable analysis, were colinear with the present variables or had <90% values

All-Cause Mortality

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

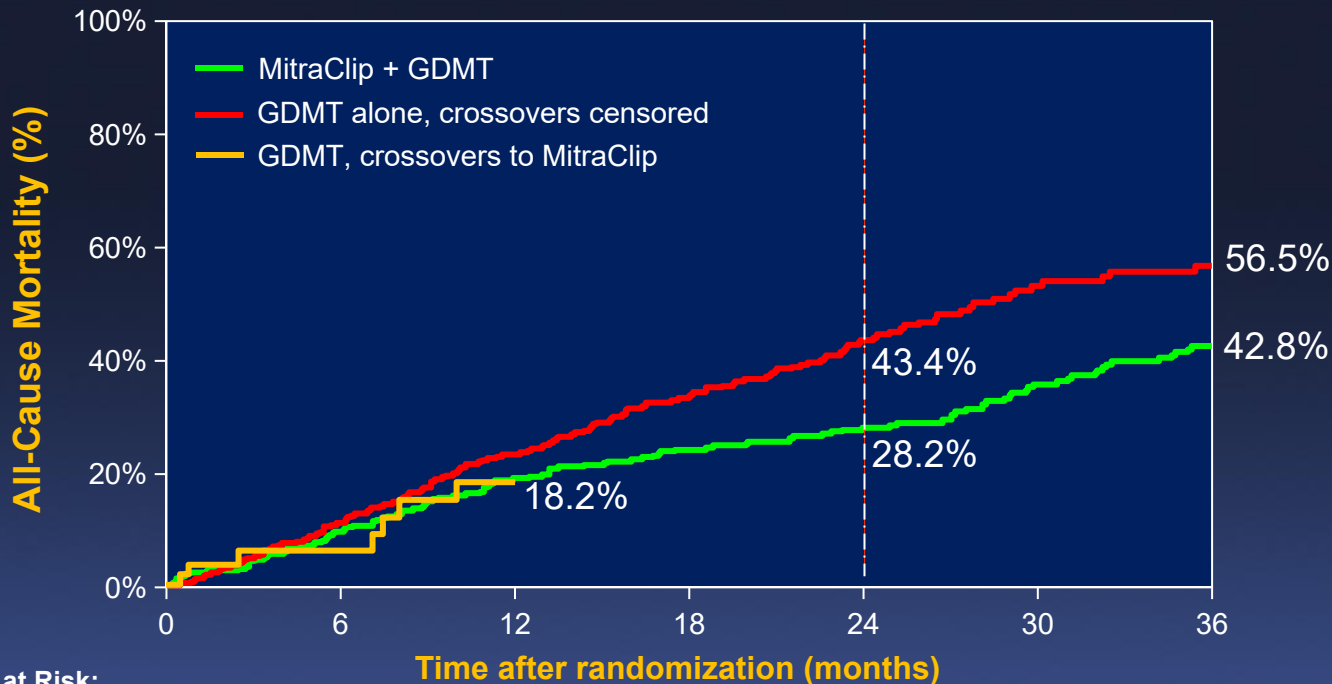


at Risk:

	0	6	12	18	24	30	36
GDMT only, crossovers censored	312	271	222	183	134	60	41
GDMT crossovers to MitraClip	58	33	24				

All-Cause Mortality

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



at Risk:

	0	6	12	18	24	30	36
MitraClip + GDMT	302	269	238	219	189	128	93
GDMT only, crossovers censored	312	271	222	183	134	60	41
GDMT crossovers to MitraClip	58	33	24				

Multivariable Predictors of Mortality Within 36 Months

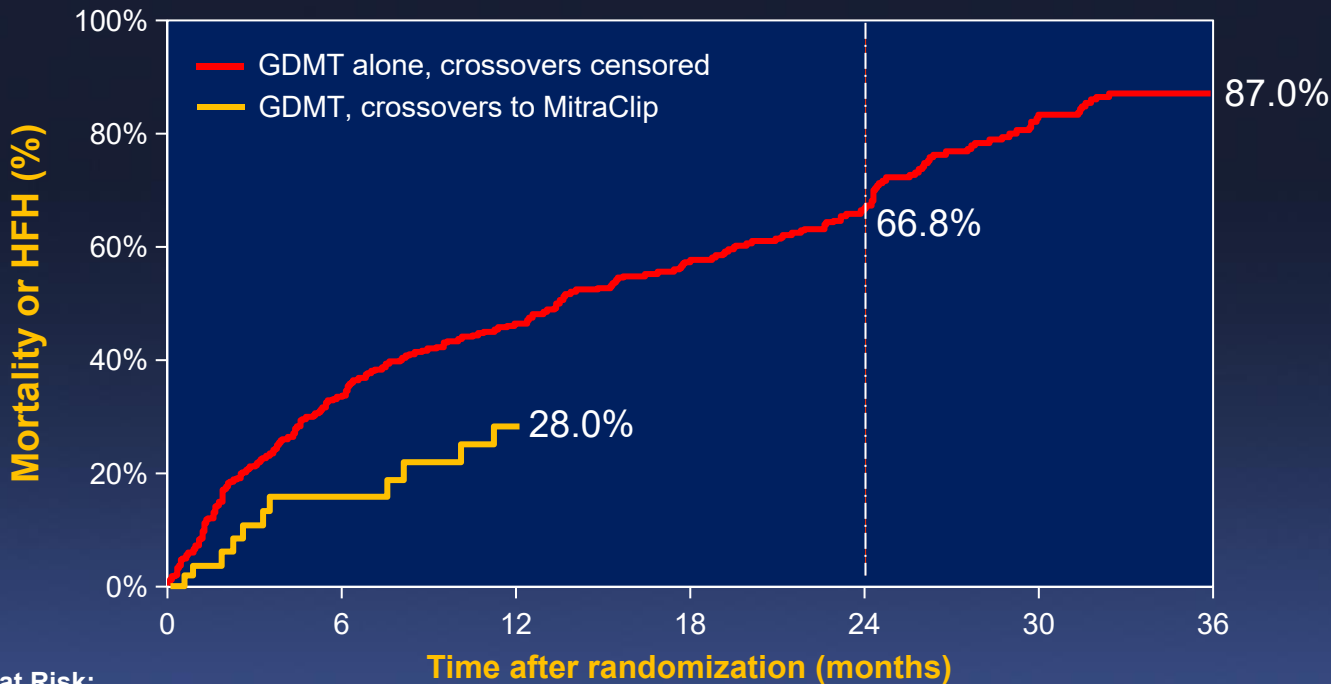
GDMT only group with MitraClip crossover as a time-adjusted covariate

	Hazard Ratio [95% CI]	P-Value
Treatment with MitraClip	0.89 [0.43, 1.85]	0.76
BNP (per 100 pg/mL)	1.03 [1.02, 1.05]	< 0.0001
EROA (per 10 mm ²)	1.23 [1.10, 1.37]	0.0004
Systolic blood pressure (per 1 mmHg)	0.98 [0.97, 0.99]	0.004
Beta-blocker use	0.47 [0.28, 0.78]	0.004
STS replacement score (per 1 unit)	1.04 [1.01, 1.08]	0.005
6MWD (per 10 meters)	0.98 [0.96, 1.00]	0.01
Female sex	0.62 [0.41, 0.93]	0.02
Serum creatinine (per 1 mg/dL)	1.11 [1.01, 1.22]	0.03
Prior defibrillator implant	0.65 [0.44, 0.97]	0.03

Variables entered the final model include: ACEi/ARB/ARNI use, prior atrial fibrillation, age, aldosterone inhibitor use, history of anemia, beta-blocker use, BNP, serum creatinine, treatment with MitraClip, prior defibrillator implant, diabetes, diastolic BP, EROA, sex, hypertension, KCCQ summary score, prior PCI/CABG, PVD, renal disease, 6MWD, STS replacement score, systolic BP, TR grade, race; other variables tested had $\alpha > 0.20$ in univariable analysis, were colinear with the present variables, or had <90% values

All-Cause Mortality or HF Hospitalization

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

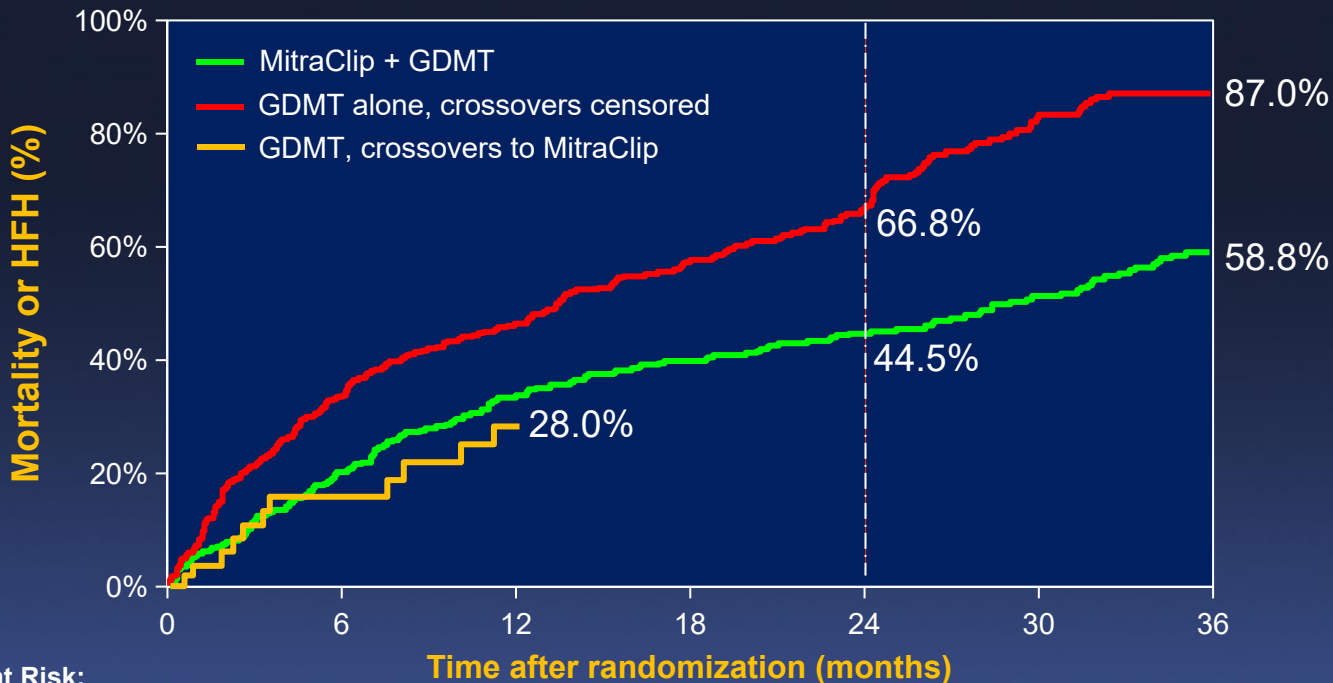


at Risk:

GDMT only, crossovers censored	312	205	155	119	85	33	19
GDMT crossovers to MitraClip	58	30	22				

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				

Multivariable Predictors of Death or HFH Within 36 Months

GDMT only group with MitraClip crossover as a time-adjusted covariate

	Hazard Ratio [95% CI]	P-Value
Treatment with MitraClip	0.43 [0.24, 0.78]	0.006
BNP (per 100 pg/mL)	1.02 [1.01, 1.03]	<0.0001
Vasodilator use (hydralazine or nitrates)	1.91 [1.37, 2.66]	0.0001
Systolic blood pressure (per 1 mmHg)	0.99 [0.98, 1.00]	0.004
STS replacement score (per 1 unit)	1.04 [1.01, 1.07]	0.005
Beta-blocker use	0.57 [0.37, 0.88]	0.01
LVEDV (per 10 mL)	1.02 [1.00, 1.04]	0.02

Variables entered the final model include: ACEi/ARB/ARNI use, aldosterone inhibitor use, history of anemia, beta-blocker use, BNP, serum creatinine, treatment with MitraClip, EROA, sex, vasodilators (hydralazine or nitrates), LVEDV, LVEF, prior PCI/CABG, renal disease, 6MWD, prior stroke, STS replacement score, SBP, TR grade; other variables tested had $\alpha > 0.20$ in univariable analysis, were colinear with the present variables or had <90% values

Conclusions

In pts with HF and 3+/4+ secondary MR who remained symptomatic despite maximally-tolerated GDMT:

- At 36 months transcatheter mitral leaflet approximation with the MitraClip was safe, provided durable reduction in MR, reduced the rate of HF hospitalizations, and improved survival, QOL and functional capacity compared to GDMT alone
- GDMT only-assigned pts who crossed-over and received a MitraClip experienced fewer HF hospitalizations and deaths or HFHs within 12 months than those who did not crossover, with rates comparable to pts originally assigned to the MitraClip