MitraClip for Functional Mitral Regurgitation

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Disclosure Statement of Financial Interest
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Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support	• Abbott Vascular, Boston Scientific, Gore Medical, CardioKentix, St Jude Medical
• Consulting Fees/Honoraria	• Abbott Vascular, Boston Scientific, Gore Medical, Coherex
• Other Financial Benefit	• Coherex, Biosensors International

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Mitral Regurgitation (MR)

Primary Disorder of the Mitral Valve Apparatus (annulus, leaflets, chords, papillary muscle

Valve makes the Ventricle Sick

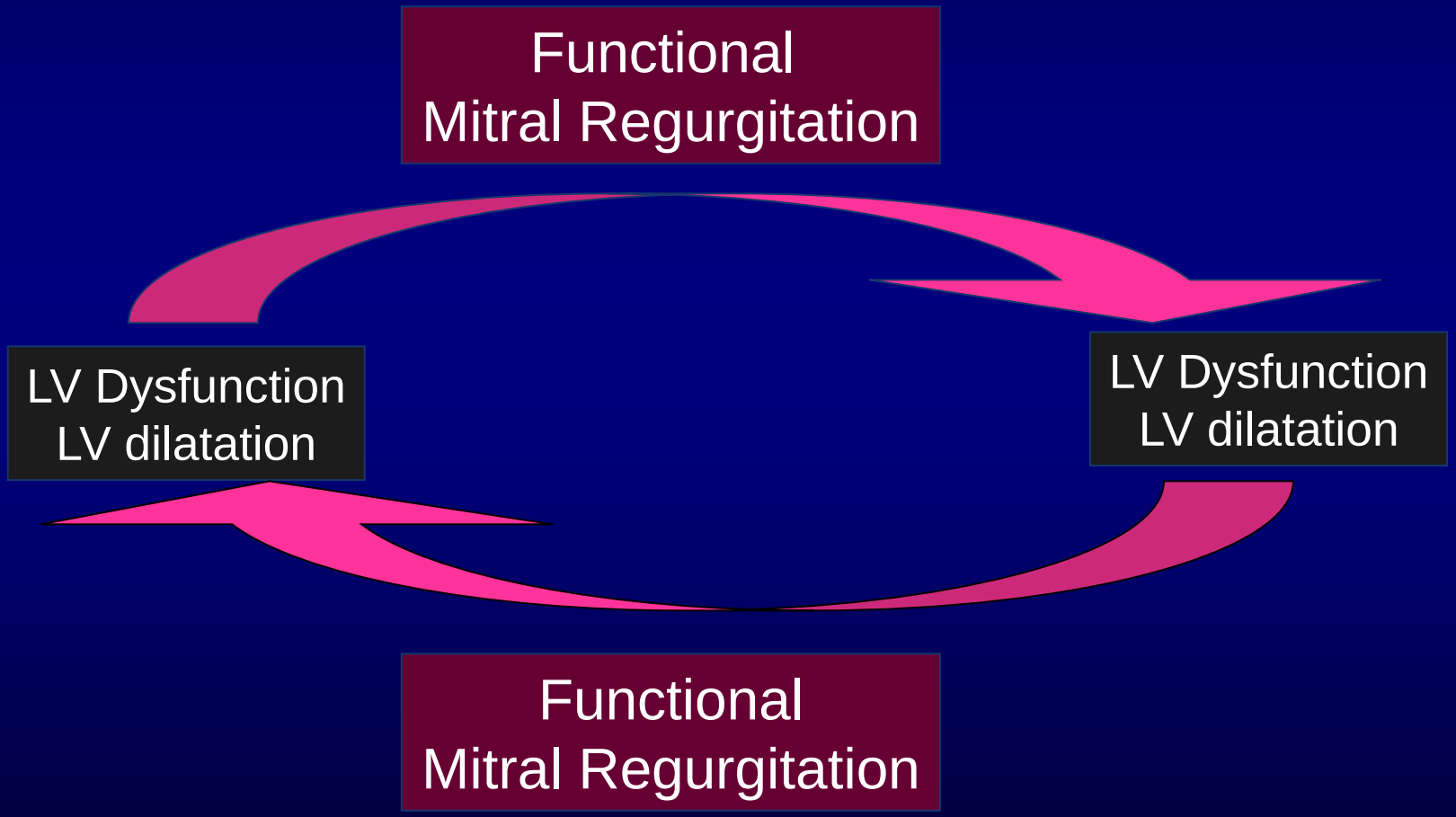
Mechanical Solution: Open Surgical /Transcatheter repair/replacement

Functional MR: Leaflets appear normal, MR due to abnormal LV geometry

Ventricle makes the Valve Sick

Question:
Treat the muscle
Or Treat the Valve

FMR and LV dysfunction



Treatment of FMR

- Medical treatment is the mainstay
- The role of surgery is controversial
  - Often high risk since patients have low EF
  - Symptomatic improvement
  - High recurrence
  - No mortality benefit
  - No census whether repair is better than replacement

Percutaneous Mitral Valve Repair

MitraClip® System

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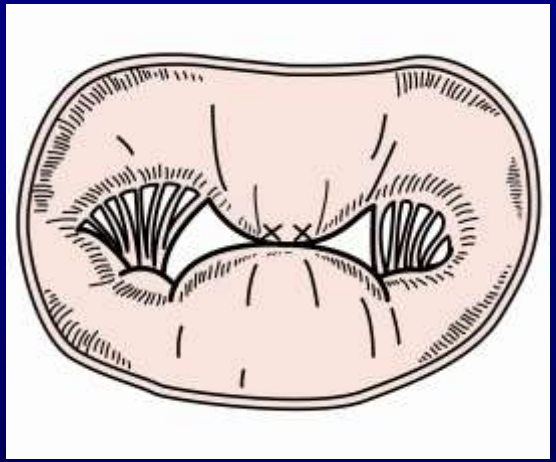
MitraClip Concepts

- **Coaptation of Leaflets**
  - **Reduces MR**
- **Creates tissue bridge**
  - **Limits dilatation of annulus**
  - **Septal-lateral (A-P) dimension**
  - **Supports durability of repair**
- **Restrains LV wall**
  - **Limits LV dilatation**



Clinical Summary: MitraClip

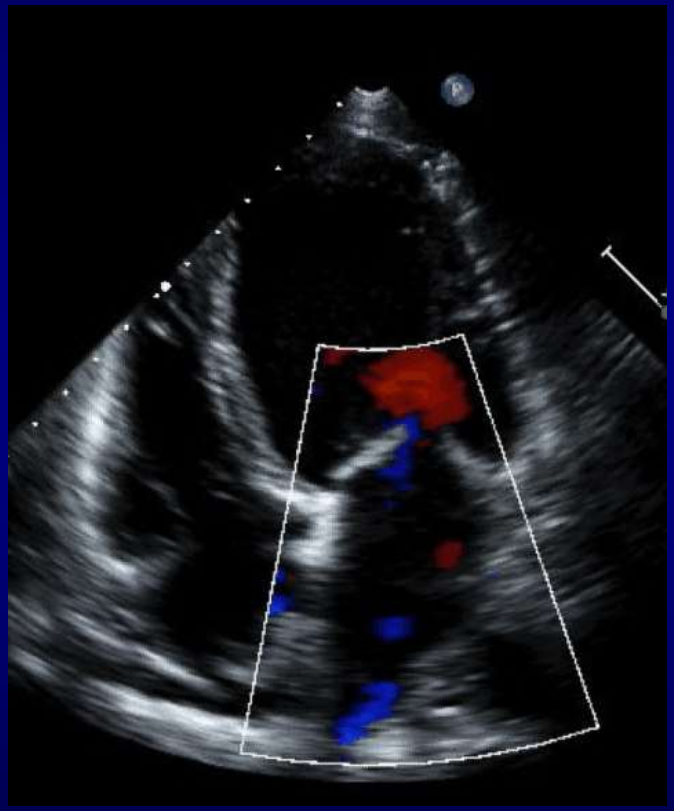
- > 20,000 patients treated worldwide
- >2000 patients in prospective clinical trials
- FDA approved for high risk primary MR
- Majority of patients (> 12,000 cases) worldwide are high risk functional MR patients
- Safe, durable and effective
- No randomized trial data supporting indication for FMR

MitraClip for FMR

- Data from registries and EVERES II high risk Cohort
- Safe even in high risk patients
- Modest reduction of MR that persists beyond 1 year
- Improvement of functional class
- Reduction of re-hospitalization from CHF
- Evidence of LV remodelling at 1 year

77 yr old lady with severe FMR underwent MitraClip on 6/14/07: NYHA II at 5 yrs

Baseline



LVEDD 63 mm
LVESD 57 mm
EF 20 %

At 5 years

LVEDD 51 mm
LVESD 41 mm
EF 25 %

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The EVEREST II High Surgical Risk Cohort:

Effectiveness of Transcatheter Reduction of Significant Functional Mitral Regurgitation in High Surgical Risk Patients

Baseline Demographics and Co-Morbidities

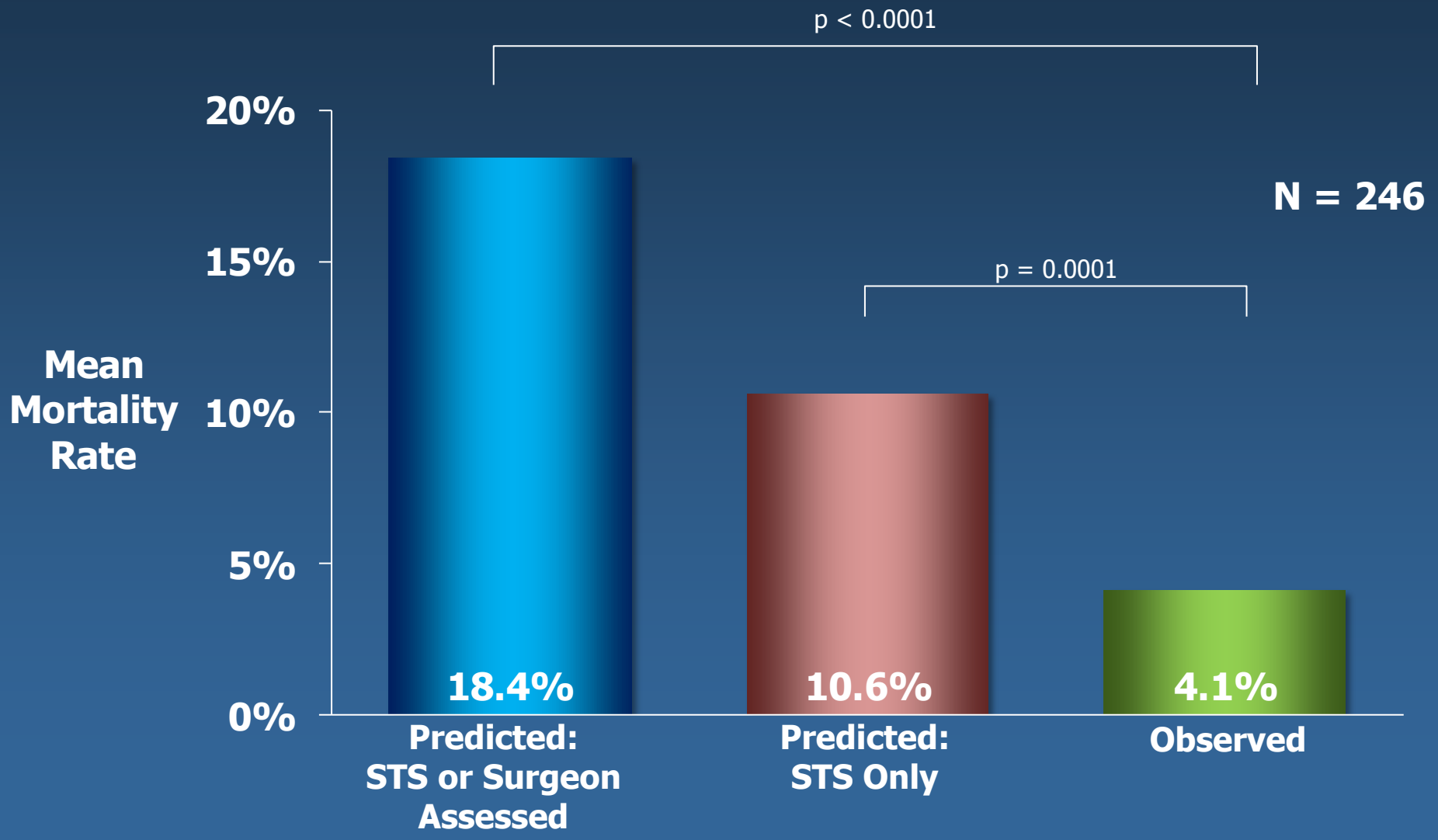
	EVEREST II High Surgical Risk Cohort
Demographics and Co-morbidities	FMR Patients (N=246)
Age ≥ 75 years	48%
Male	61%
History of CHF	98%
Coronary Artery Disease	85%
Prior Myocardial Infarction	60%
Prior Stroke	14%
Previous Cardiovascular Surgery	64%
Atrial Fibrillation	67%
COPD (with or without home O_2)	29%
Moderate to Severe Renal Disease	32%
Diabetes	44%
NYHA Functional Class III/IV	86%

Baseline Demographics and Co-Morbidities

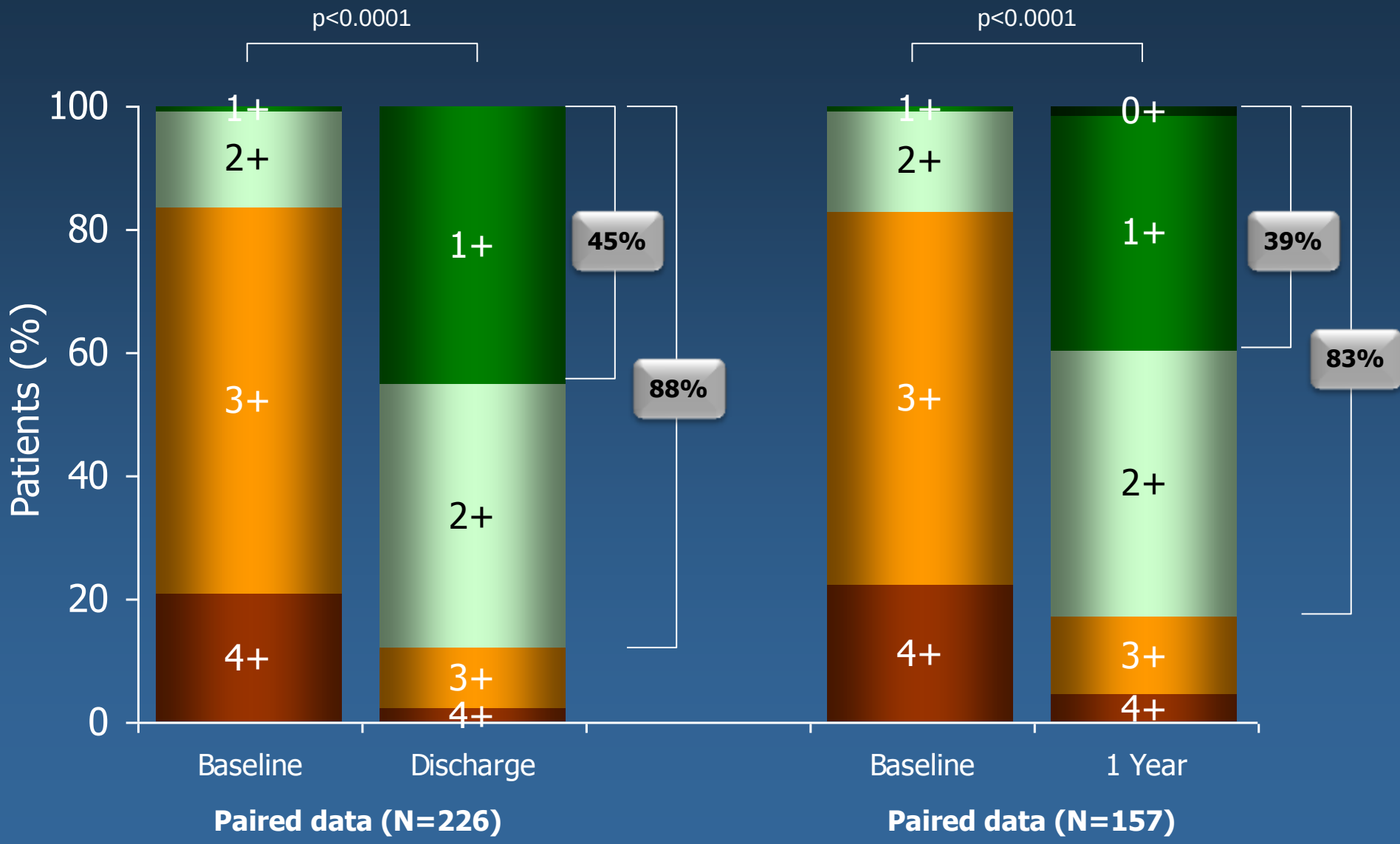
Demographics and Co-morbidities	EVEREST II High Surgical Risk Cohort FMR Patients (N=246)
Left Ventricular Ejection Fraction, (%) (means ± SD)	41.7±11.5
Left Ventricular Internal Diameter, systole, (cm) (means ± SD)	4.7±1.0

Primary Safety Endpoint – FMR Patients

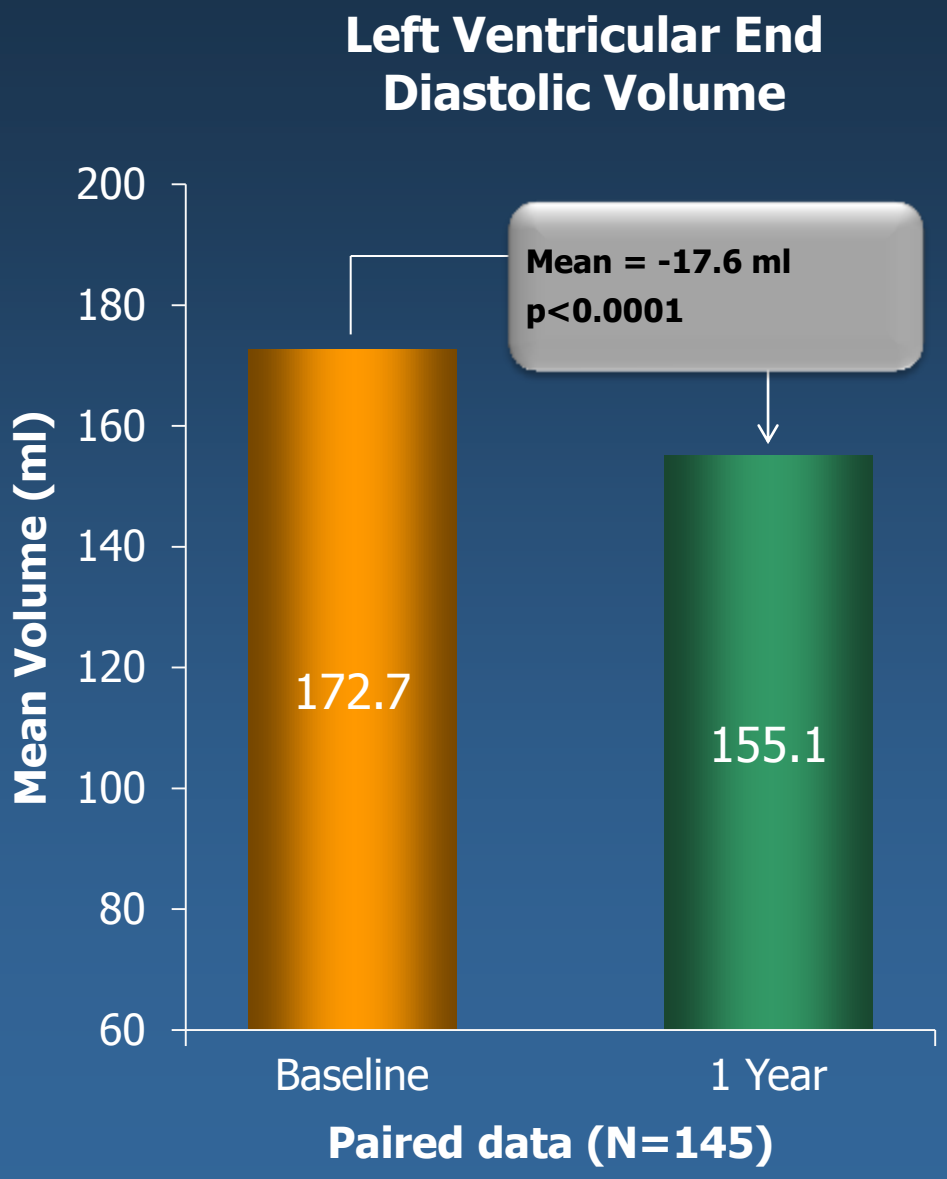
30-day Observed Mortality Lower than Predicted

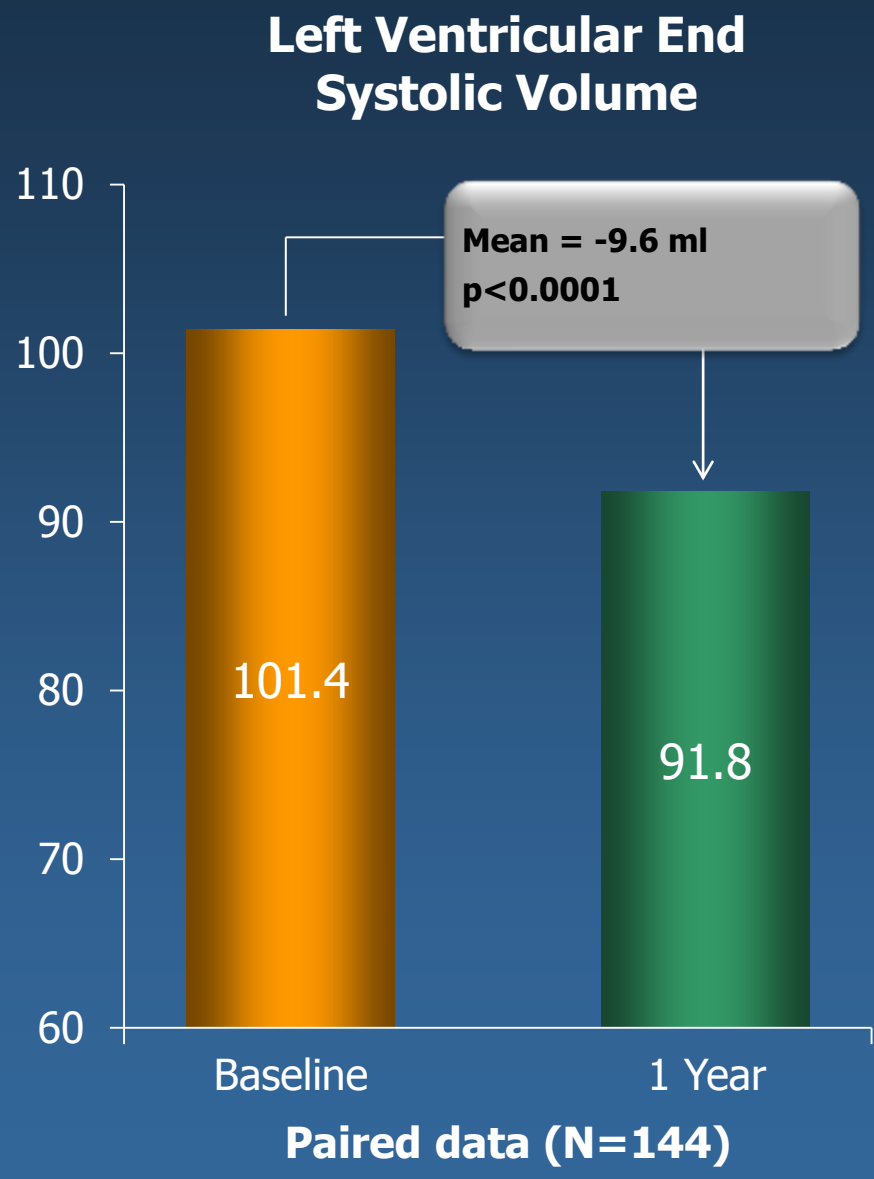


Mitral Regurgitation Grade

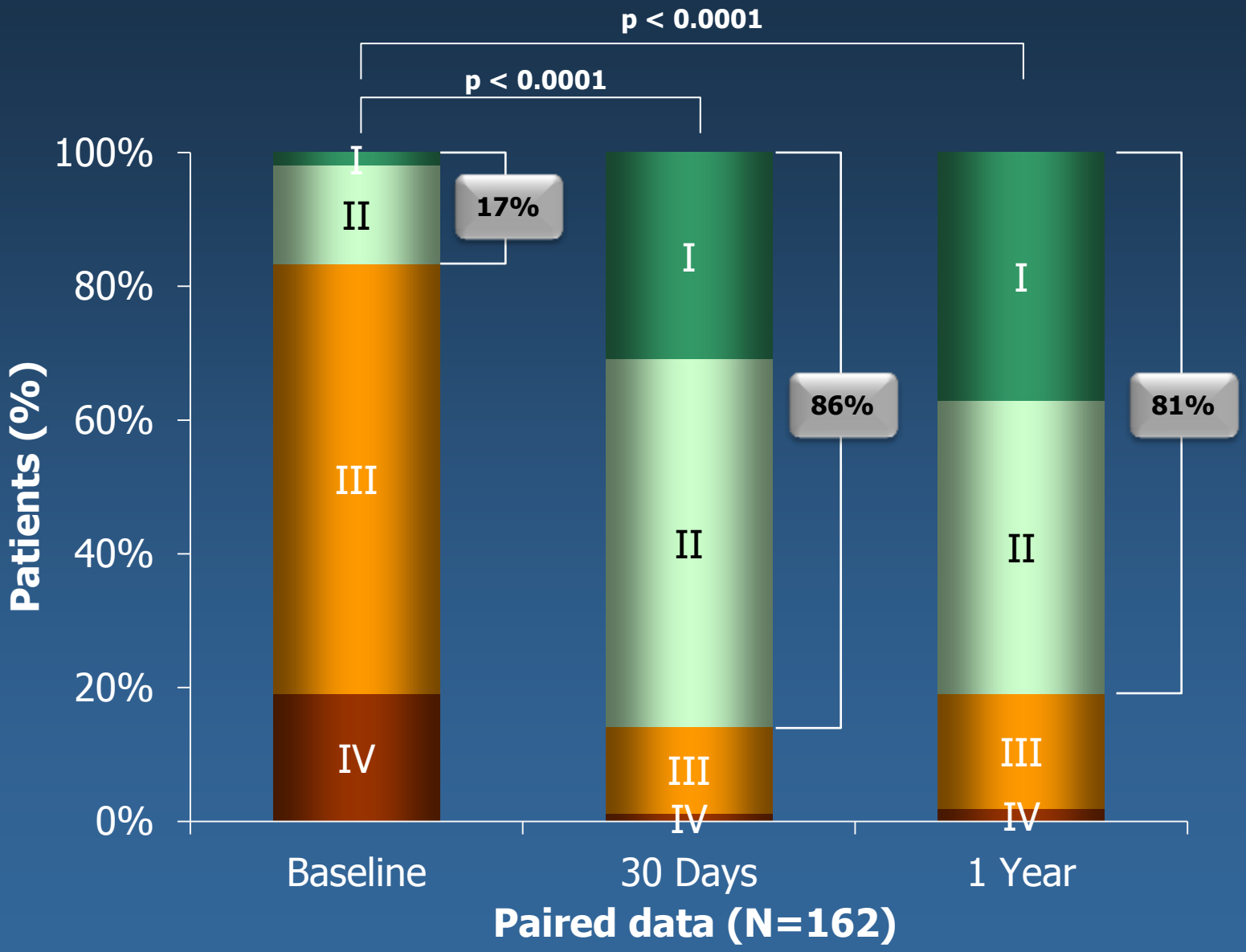


Left Ventricular Volumes

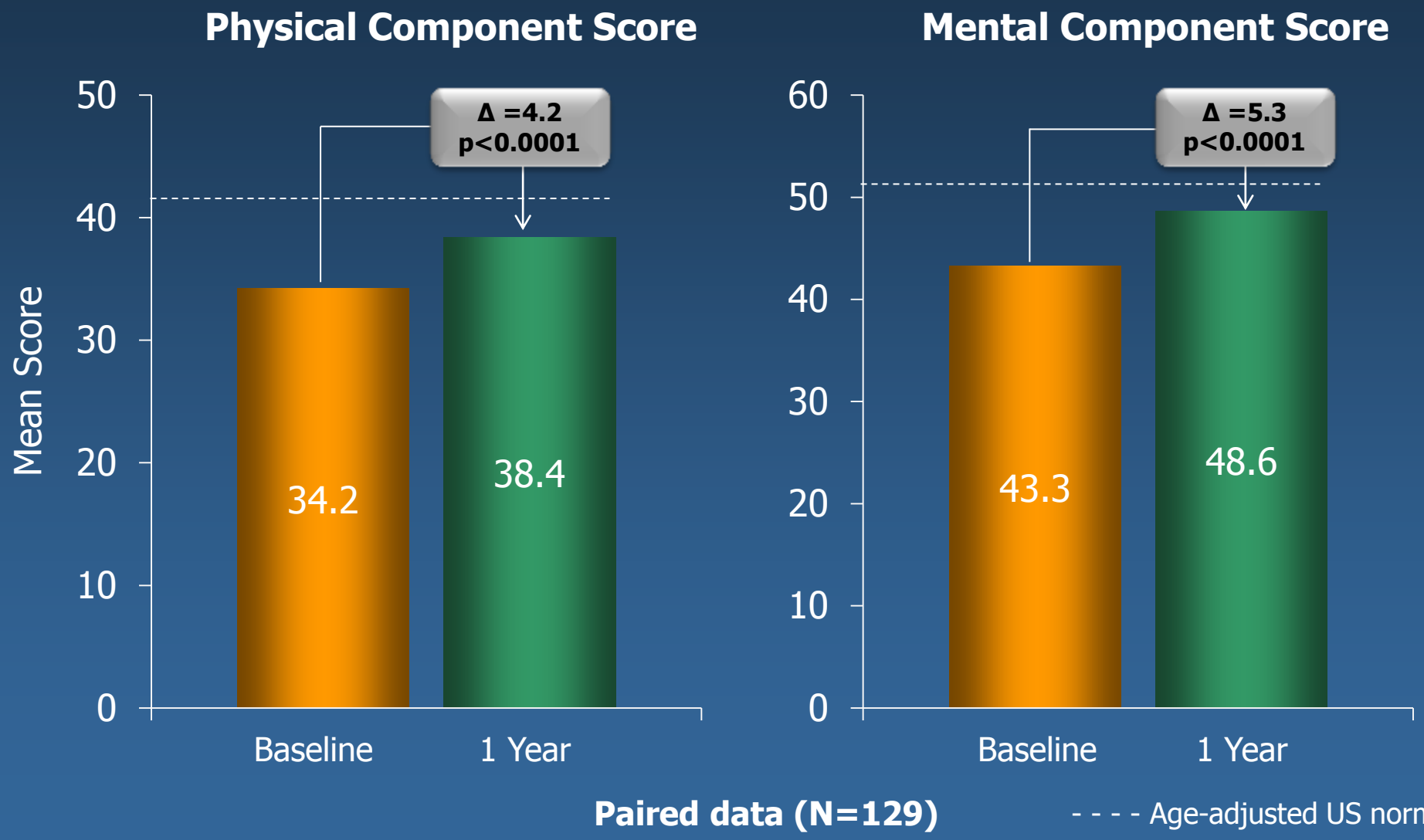




NYHA Functional Class



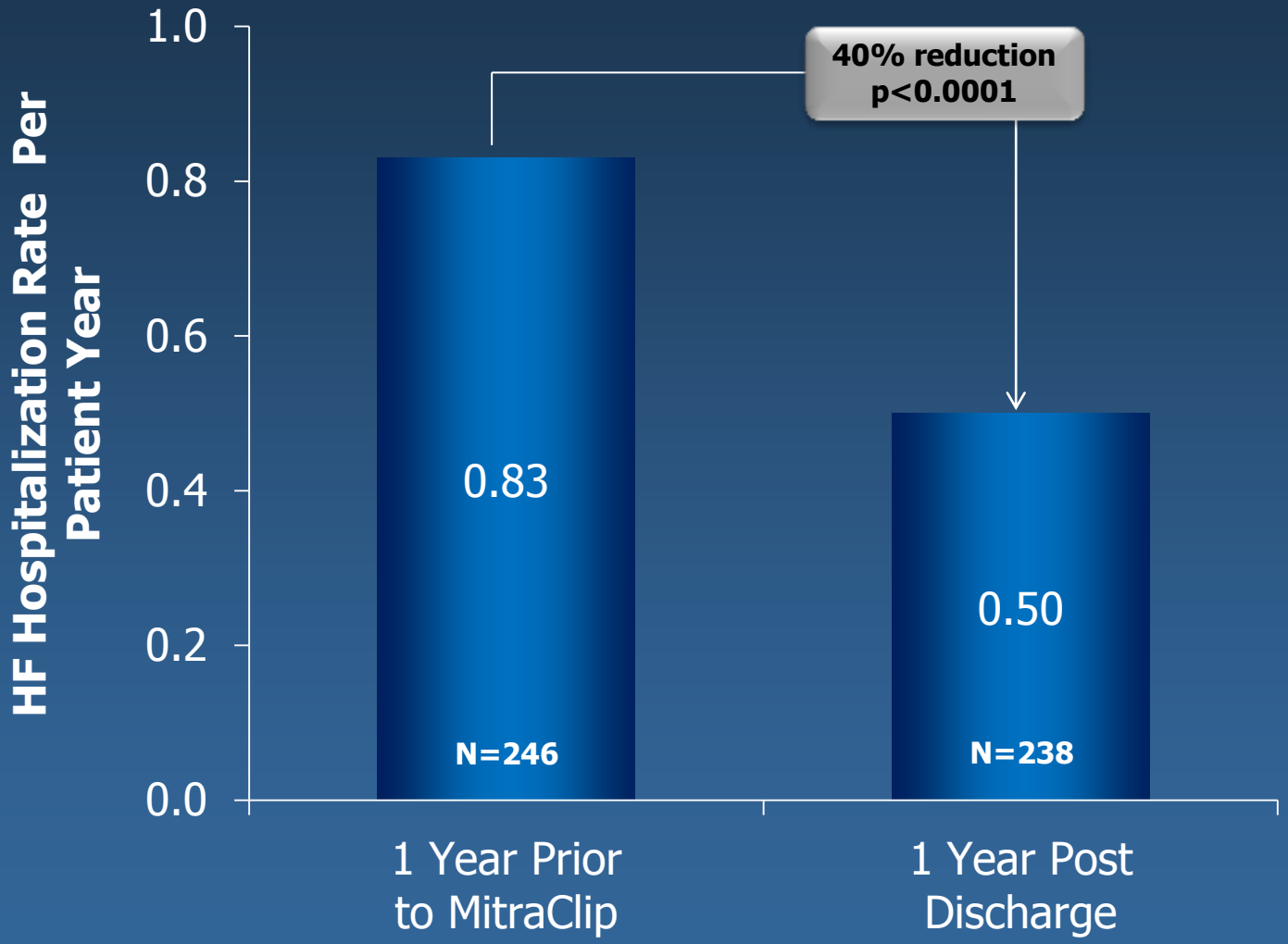
SF-36 Quality of Life Scores



Paired data (N=129)

- - - - Age-adjusted US norm

Hospitalizations for Heart Failure



Conclusion

- The MitraClip therapy provides an additional option for select patients with severe functional mitral regurgitation who are deemed too high risk for open mitral valve surgery.

Ongoing studies using MitraClip for FMR

- COAPT study (North America)
- RESHAPE study (Europe)

Trial design

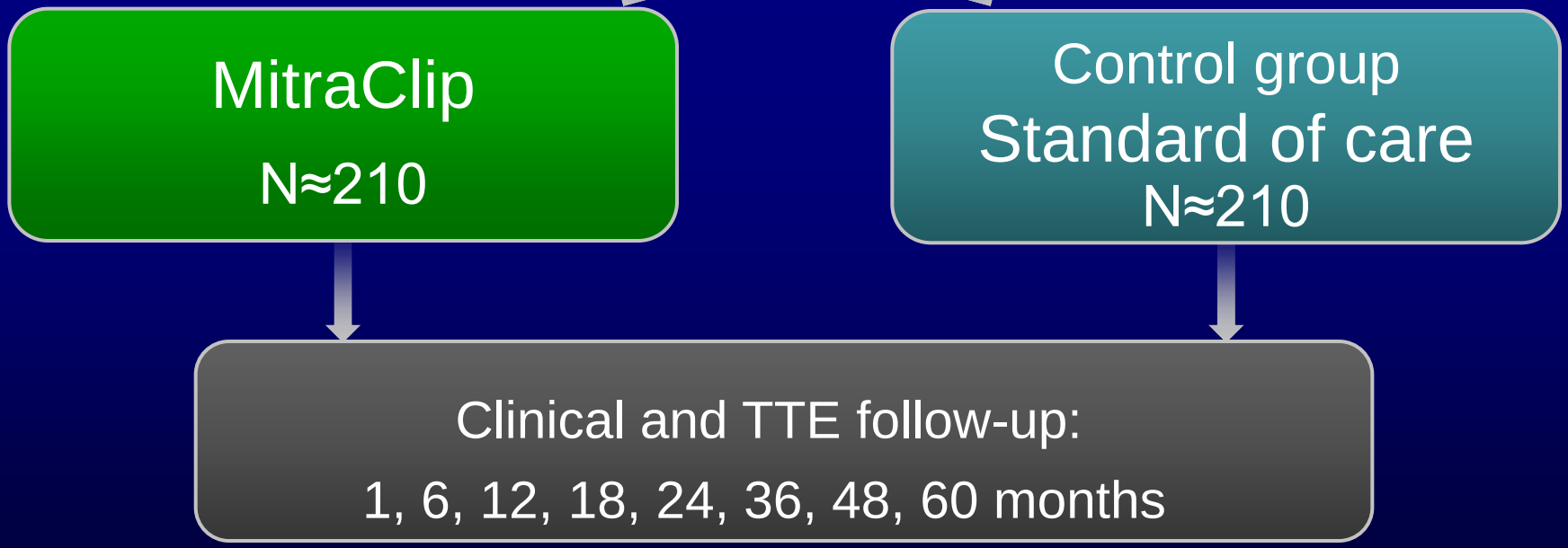
~450 patients enrolled at up to 75 US sites

Significant FMR (3+ - 4+ by core lab)

Not indicated for mitral valve surgery†

Specific anatomical criteria

Randomize 1:1



†Final definition to be determined in collaboration with FDA

Endpoints of COAPT

- **Primary efficacy endpoint**
  - Reduction of rate of recurrent heart failure
- **Primary Safety Endpoint**
  - Freedom from death(all-cause), stroke, worsening kidney dysfunction, LVAD, heart transplant
- Secondary efficacy endpoint
  - MR reduction, 6 minute walk test, QoL at 12 months

Status of COAPT study

- 202 patients have been enrolled
- Goal of completion of enrollment Dec 2015

Guidelines for FMR

- ACC guidelines
  - Approved for high surgical risk primary MR
- ESC guidelines
  - Approved for high risk primary and secondary MR

Conclusion

- Treatment of FMR is still a major challenge
- The MitraClip device in addition to optimal medical therapy is effective selected patients with significant FMR
  - Safe, improvement of NYHA class, reduction of re-hospitalization
- The ongoing COAPT study will provide additional supportive evidence of MitraClip in FMR