The Future of TMVR Therapy

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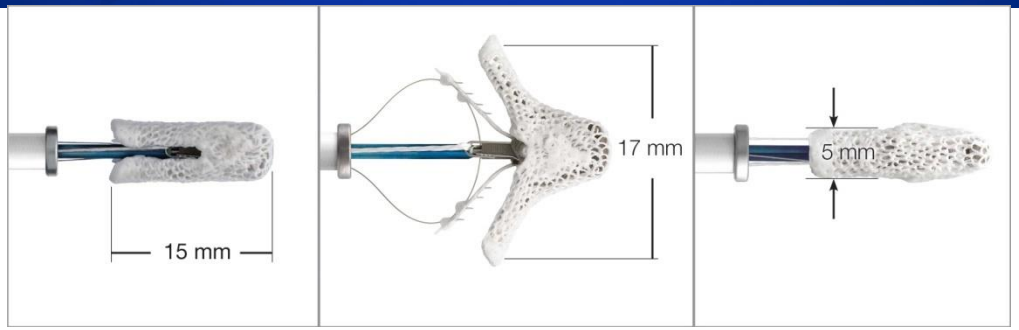
Conflict of Interest

- *Procotor/advisory board*: Abbott Vascular, WL Gore, St Jude Medical, Symetis
- *Research grant*: Abbott Vascular, Medtronic
- *Consultant*: NuHeart

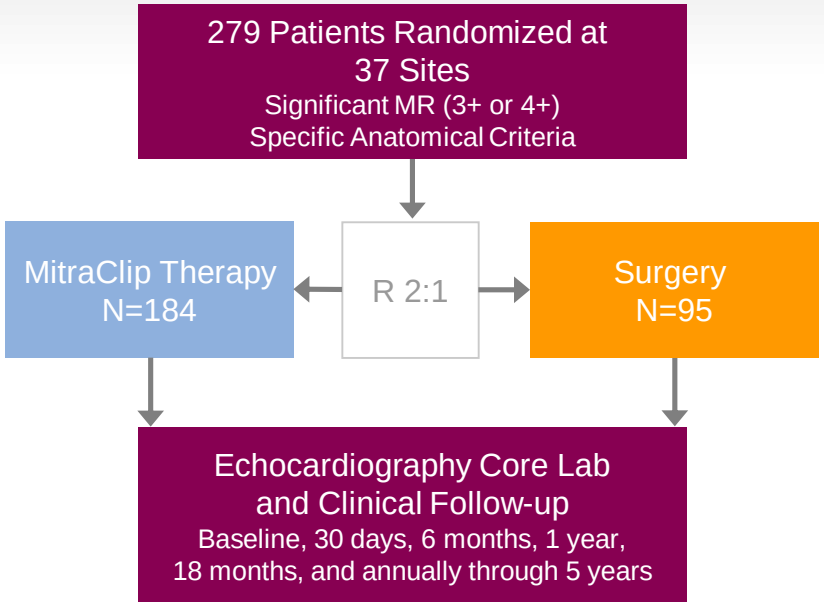
Agenda

- MitraClip Trial Update
- MitraClip NT
- Tendyne Transcatheter Mitral Valve

The MitraClip system



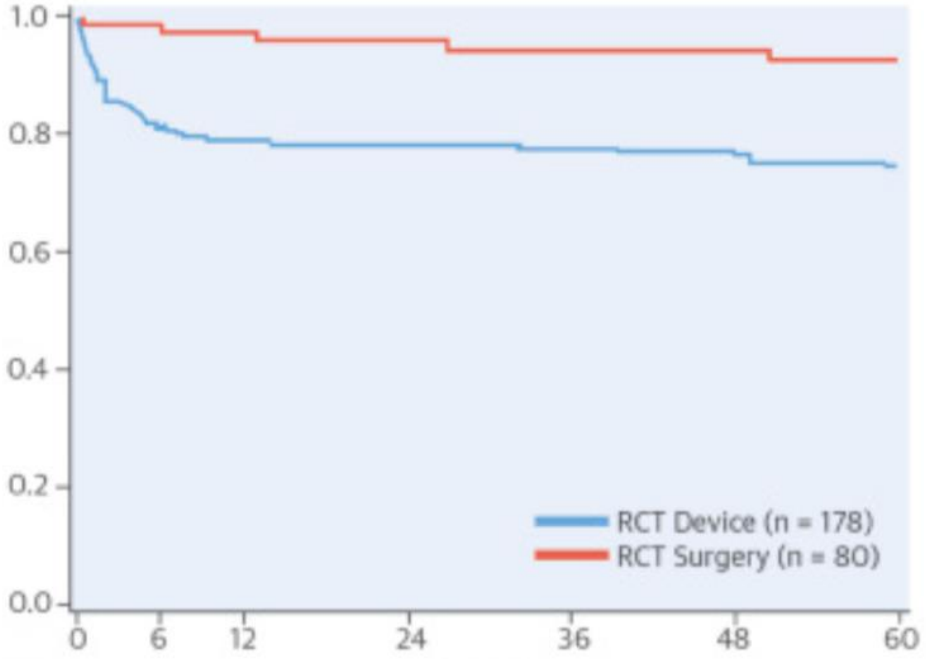
EVEREST II



Patient Demographics	MitraClip Therapy (n=184)	Surgery (n=95)	P-value
Age (mean)	67 years	66 years	0.32
Male	63%	66%	0.60
History of CHF	91%	78%	0.005
Degenerative MR Etiology	74%	73%	0.81
Functional MR Etiology	26%	27%	0.81
Mean Ejection Fraction	60%	61%	0.65
Previous Coronary Artery Bypass Grafting (CBAG)	21%	19%	0.54
NYHA Functional Class III/IV	51%	48%	0.61
Atrial Fibrillation	34%	39%	0.42

Feldman et al NEJM 2011
Mauri et al JACC 2013
Feldman JACC 2015

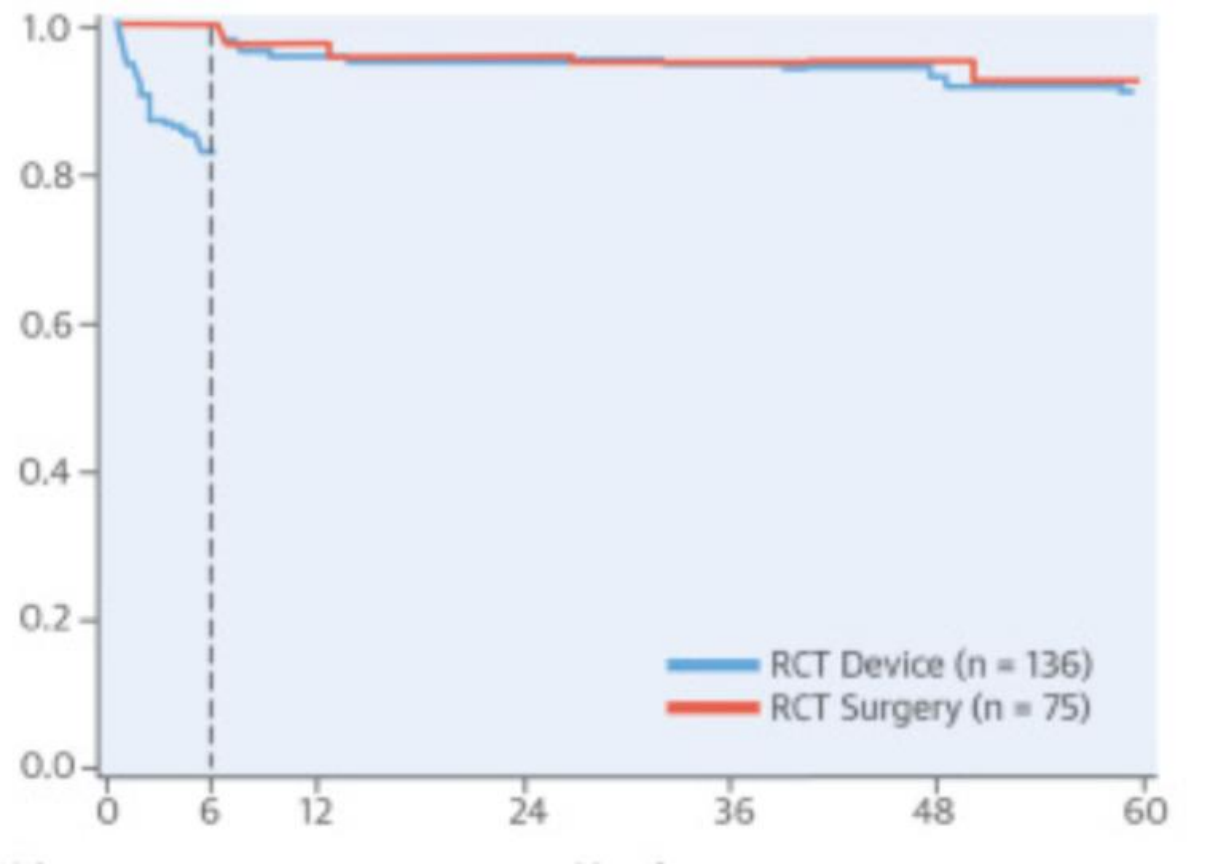
Effectiveness endpoint at 5y



Patients At Risk							
Device Group	178	136	128	117	109	98	45
Control Group	80	75	69	63	54	49	21

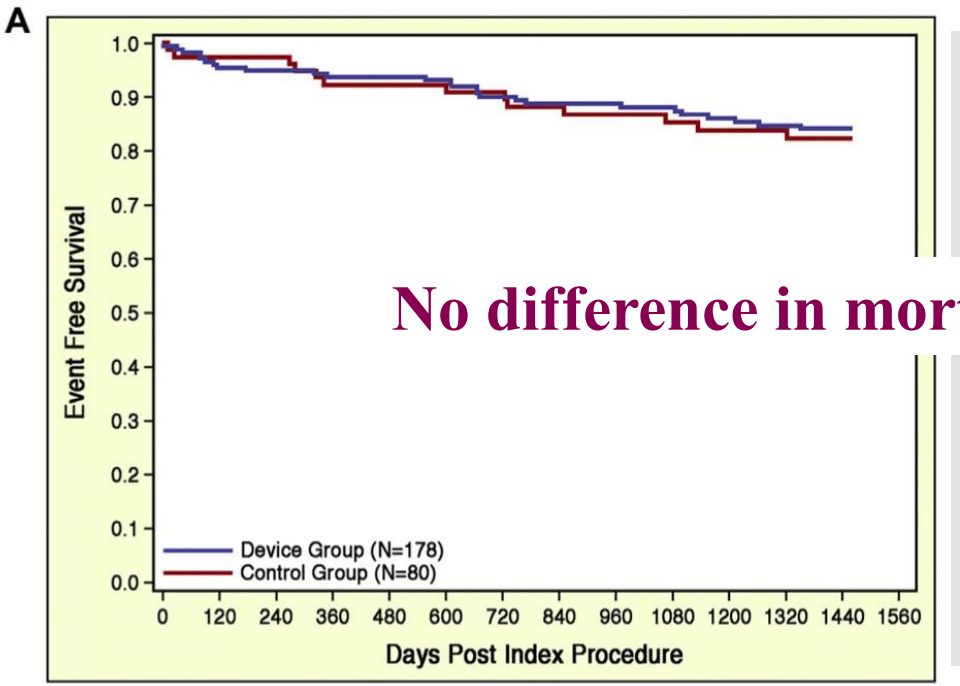
Feldman JACC 2015

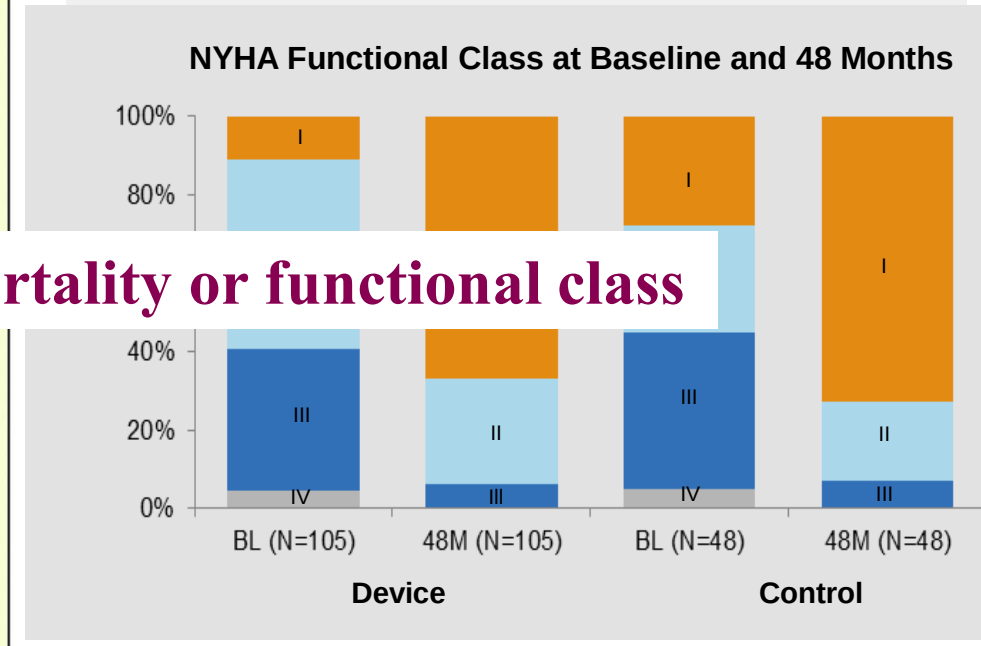
Landmark Analysis



Feldman JACC 2015

Mortality and NYHA class at 5 y





No difference in mortality or functional class

Feldman JACC 2015

Subgroup analysis

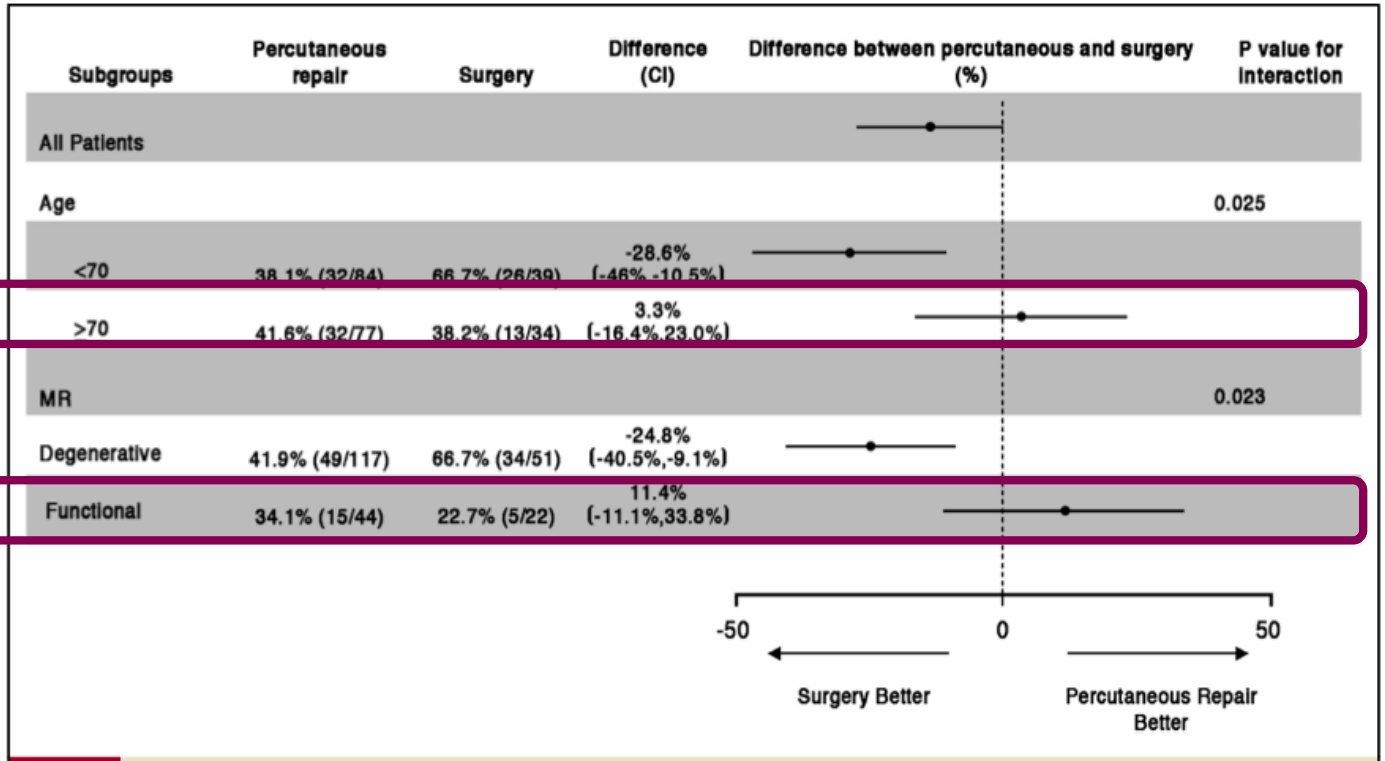


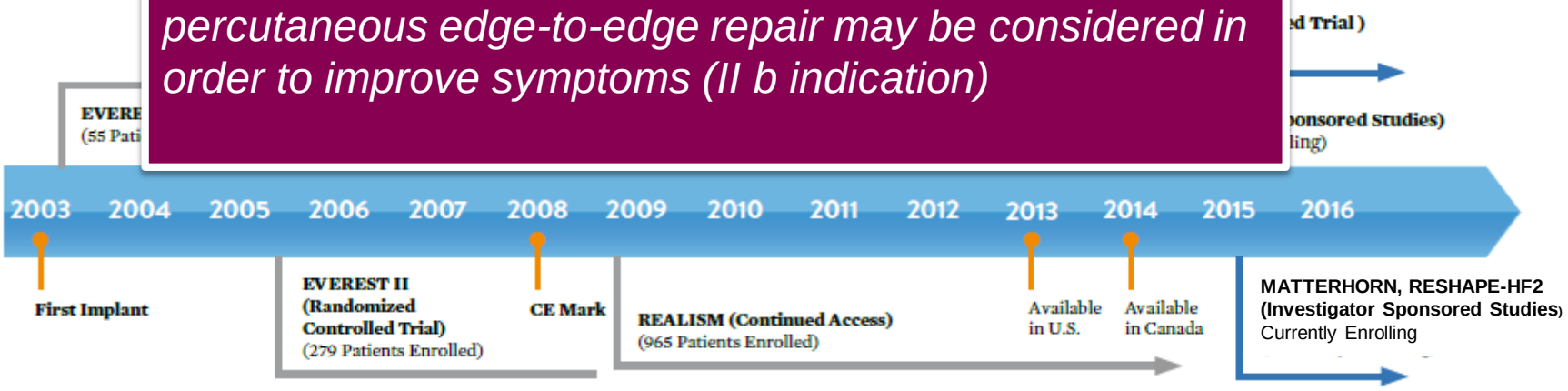
Figure 5 Subgroup Analyses of Efficacy Endpoint at 4 Years

Shown are the differences in rates of the efficacy endpoint (freedom from death, from mitral valve surgery, and from grade 3+ or 4+ mitral regurgitation [MR]) between patients in the percutaneous repair group and patients in the surgery group for all patients and for those in 2 subgroups (age and MR etiology). CI = confidence interval.

WORLDWIDE CLINICAL EXPERIENCE

- Over 40 000 patients have been treated with the MitraClip Therapy worldwide.[1]
  - 75% are considered high risk* for mitral valve surgery
  - 67% h
  - 97% I
- The us gram.[1]

ESC guidelines 2012:
In patients with significant MR judged inoperable or at a unacceptably high surgical risk, percutaneous edge-to-edge repair may be considered in order to improve symptoms (II b indication)



1. Data as of November 2016. Source: Abbott Vascular.
* Determination of high surgical risk based on: logistic EuroSCORE ≥ 20%, or STS calculated mortality ≥ 12%, or pre-specified high surgical risk co-morbidities specified in EVEREST II High Risk Study protocol.

	COAPT	RESHAPE-HF-2
N patients, sites	430 @ 75 US sites	420 @ 50 EU sites
Control arm	GDMT ± CRT	GDMT ± CRT
FMR grade	≥3+ (EROA ≥30 mm² and/or Rvol >45 mL by ECL)	≥3+ (EROA ≥30 mm² and/or Rvol >45 mL by ECL)
NYHA class	II, III, or ambulatory IV	III or ambulatory IV
Other inclusion criteria	HF hosp within 12 months or BNP ≥300 pg/ml or nT-proBNP ≥1500 pg/ml within 12 months; MV surgery is not local standard of care	HF hosp within 12 months or BNP ≥350 pg/ml or nT-proBNP ≥1400 pg/ml within 90 days; not eligible for MV surgery
LVEF	≥20% - ≤50%	≥15% - ≤40%
LV volumes	LVESD ≤70 mm	LVEDD ≥55 mm
Primary efficacy endpoint	Recurrent HF hospitalization at 12 months	Death or recurrent HF hospitalization at 12 months
Primary safety endpoint	SLDA, device embolizations, endocarditis/MS/device-related complications requiring non-elective CV surgery, LVAD, OHT	All-cause mortality, stroke, MI, new renal replacement therapy, non-elective CV surgery for device related complications
Total follow-up	5 years	1 year
PIs	GW Stone, M Mack	P Ponikowski, S Anker

	MITRA-FR	MATTERHORN
N patients, sites	288 @ 22 French sites	210 @ 15 EU sites
Control arm	GDMT ± CRT	MV Surgery
FMR grade	Severe (EROA >20 mm² + Rvol >30 mL) by ECL	≥3+
NYHA class	II - IV	≥III
Other inclusion criteria	HF hosp within 12 months; not eligible for MV surgery	-
LVEF	≥15% - ≤40%	≥20% - ≤45%
LV volumes	-	-
Primary efficacy endpoint	Death or recurrent HF hospitalization at 12 months	Death, HF rehosp, reintervention, assist device implantation or stroke at 12 months
Primary safety endpoint	-	Major adverse events at 30 days
Total follow-up	2 years	1 year
PIs	JF Obadia	J Hausleiter

4 ongoing MitraClip RCTs in FMR

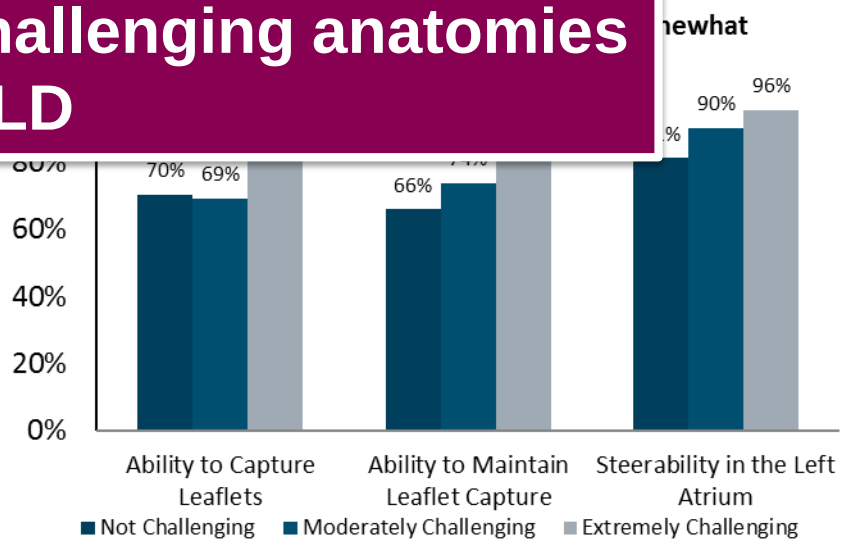
- COAPT 505/610 (83%)
- MITRA-FR 288/288 (100%)
- RESHAPE-HF-2 132/380 (35%)
- MATTERHORN 37/210 (31%)

Next generation MitraClip- MitraClip NT

- **Improved Leaflet Engagement**
- **Enhanced Steering Control**
- **Mitra… edural Chall…**

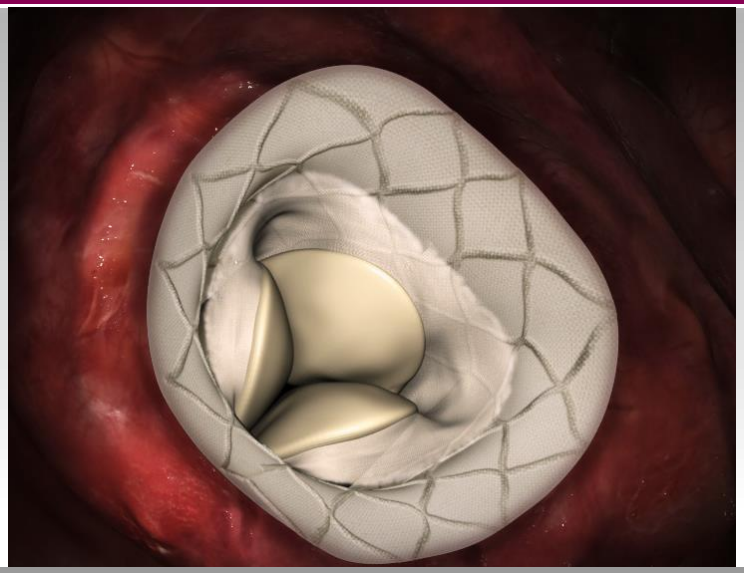
Has the potential to:

- **Speed up the procedure**
- **Able to treat more challenging anatomies**
- **Reduce the risk of SLD**



Data on File at Abbott Vascular

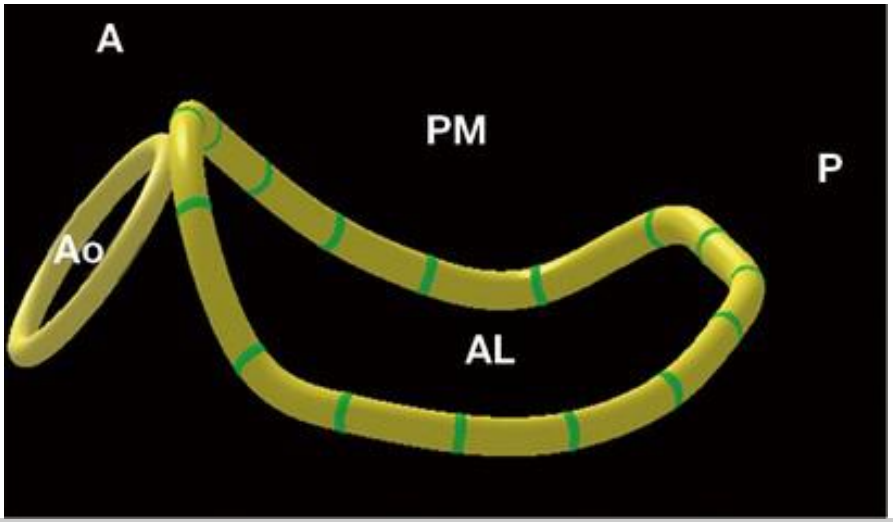
*Challenge as perceived by the users

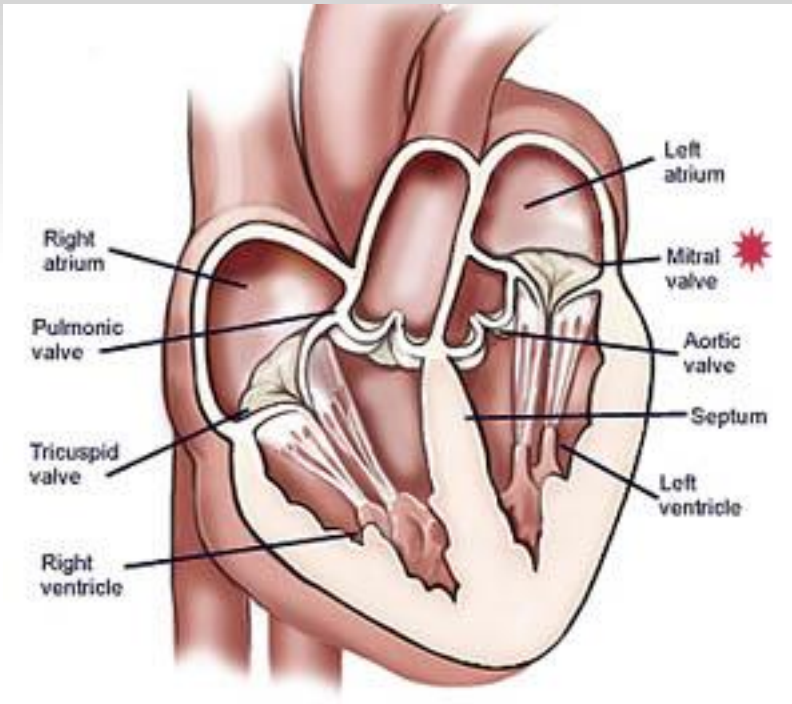


Tendyne Transcatheter Mitral Valve

Challenges for PMVR

- Saddle shape annulus
- Risk for LVOT obstruction and SAM
- Subvalvular apparatus needs to be preserved
- Needs to be able to treat a wide annulusrange



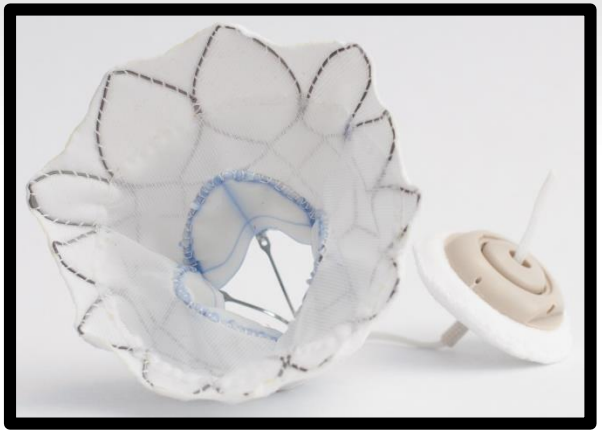


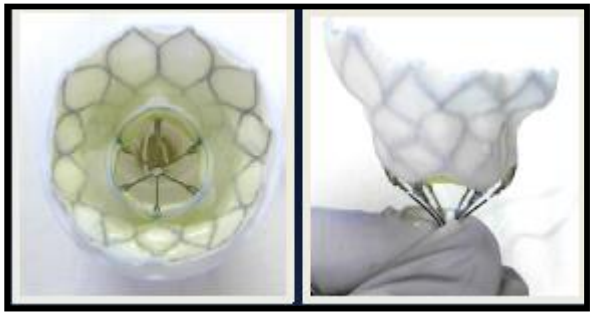
Tendyne product is currently in development at Abbott. Neither approved nor available for sale

Tendyne Transcatheter Mitral Valve

Tendyne Device

- D-Shaped Self-Expanding Nitinol Outer Frame
  - Designed to Conform to Native MV Anatomy
- Circular Self-Expanding Nitinol Inner Frame
  - Large Effective Orifice Area (>3.0cm2)
  - Larger EOA than any Surgical Valve
- Porcine Pericardial Tri-Leaflet Valve
- Large Valve Size Matrix to Treat Varying Anatomies
  - Outer Frame Sizes: 30-43mm AP x 34-50mm CC
- Valve Tether to Apex
  - Provides Valve Stability - Designed to Reduce PVL
- Apical Pad Assists in Access Closure





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The intervention

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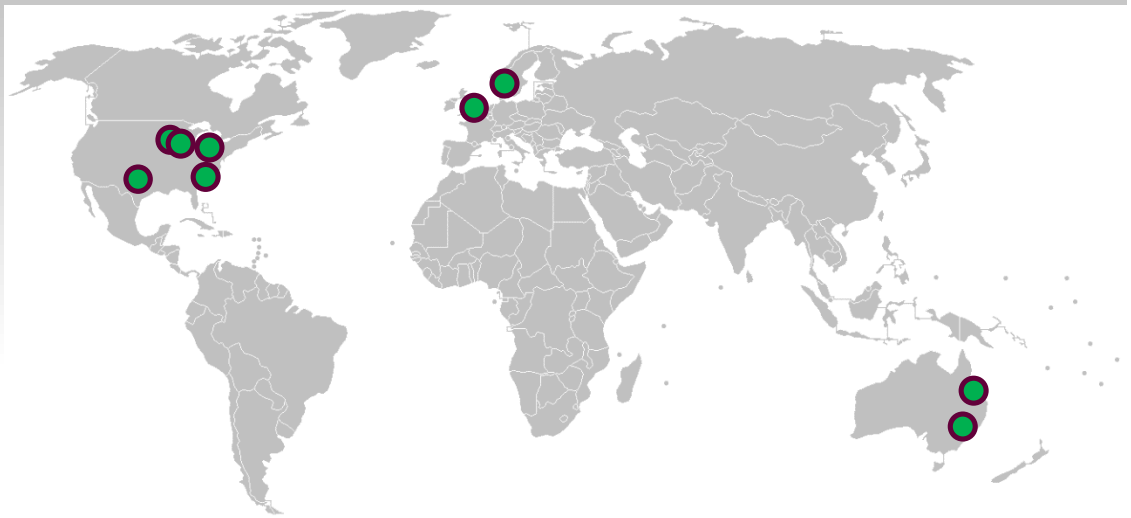
CE Mark/EFS Recent Experience

EFS SITES
St. Vincentt's
Prince Charles Hospital
Abbott
Cleveland Clinic
Baylor
Northshore
MedStar
Henry Ford Hospital
West Virgina University
Oslo University Hospital



- **Compassionate cases**
  - Royal Brompton Hospital
  - University Hospital Zurich
  - University of Bonn

Total experience to date: >50 cases, longest follow-up 2yrs

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Tendyne Global Feasibility Study

Inclusion criteria:

1. Severe mitral valve regurgitation of primary or secondary etiology
2. NYHA functional class II, III or ambulatory IV
3. Age ≥18yrs, able to provide informed consent
4. Not suitable candidate for cardiac surgery as determined by the Heart team (including Cardiologist and Cardiac Surgeon)

Exclusion criteria:

1. Severe mitral annular or valvular calcification/stenosis, vegetation or mass
2. Largest annular dimension <45mm, LVEDD >70mm
3. LVEF<30%, severe TR/RV dysfunction/pulmonary HT
4. Prior aortic or mitral valve surgery
5. Small neo-LVOT (echo, CT modeling, 3D printing)

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D. Muller, TCT 2016

Tendyne GFS: Patient Overview (n=30)

Baseline Mitral Valve pathology	
Primary MR	3 (10%)
Secondary MR	23 (76.7%)
Mixed pathology	4 (13.3%)
Baseline LV function	**N=29**
LVEF <30%	3 (10.3%)
LVEF 30-50%	14 (48.3%)
LVEF>50%	12 (41.4%)

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D. Muller, TCT 2016

Tendyne TMVI: D30 Outcomes

Outcome	N=30
Death (all cause)	1 (3.3%)
Cardiac	0 (0%)
Non-cardiac	1 (3.3%)
CVA	0 (0%)
MV surgery	0 (0%)
Re-hospitalisation	
Heart failure	4 (13.8%)
LVAD/transplant	0 (0%)
Other (ileus)	1 (3.3%)
Device-related	
Hemolysis, transfusion	1 (3.3%)
Leaflet thrombosis	1 (3.3%)

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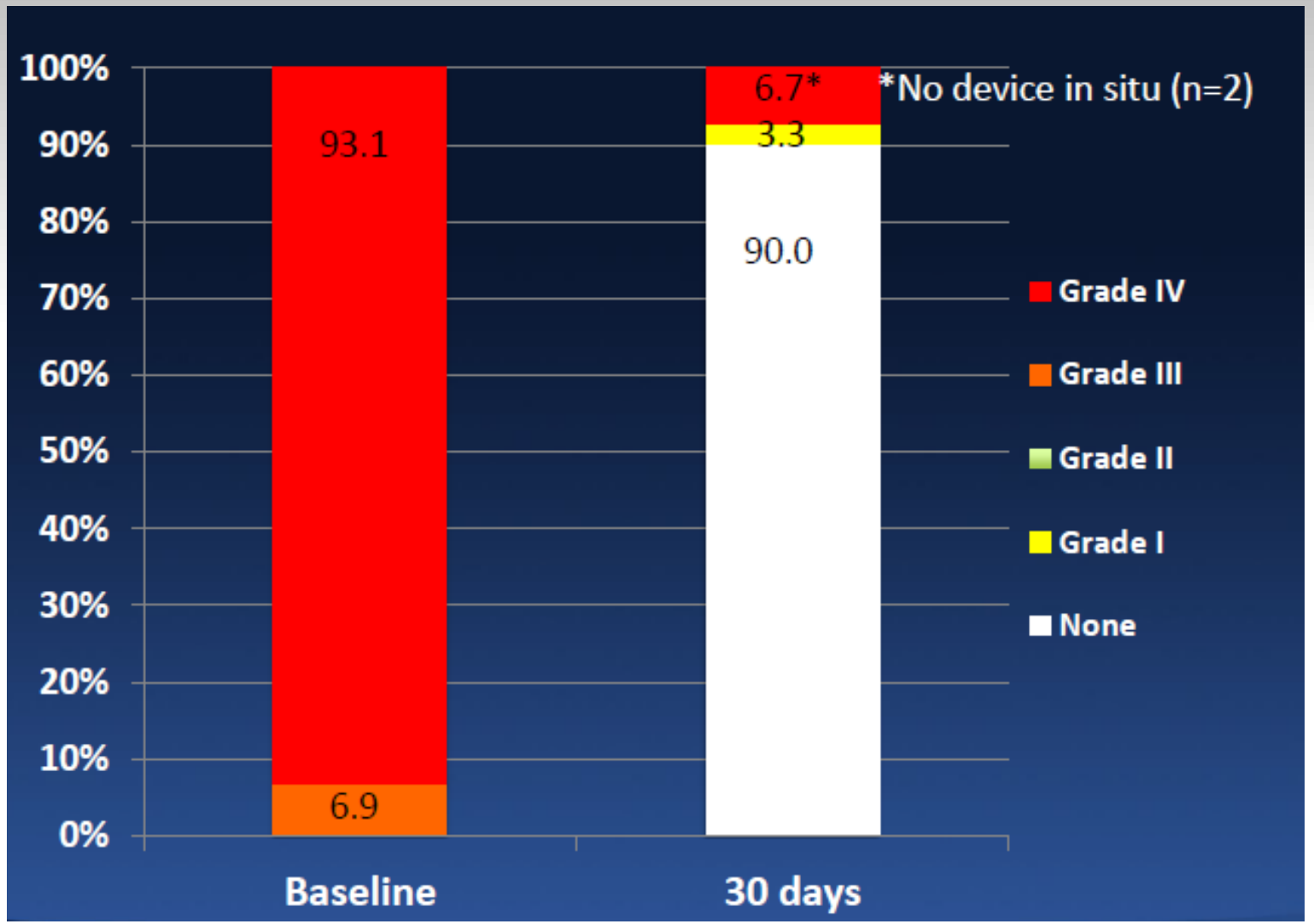
D. Muller, TCT 2016

MR severity post-TMVI (n=30)



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D. Muller, TCT 2016

The future for TMVR is so bright …

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