TEER vs. TMVR for Severe MR: The State of the Art in 2024

Luca Testa, MD, PhD,

Professor of Cardiology, «Vita e Salute Univ.» San Raffaele Hospital, Milan

Interventional Cardiology, IRCCS Pol. S. Donato, Milan

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.

Affiliation/Financial Relationship	Company
• Grant/Research Support	Medtronic, Philips, Abbott, Boston Scientific, Cardionovum, Meril, Concept Medical
• Consulting Fees/Honoraria	Medtronic, Philips, Abbott, Boston Scientific, Cardionovum, Meril, Concept Medical
• Proctoring Activity	Abbott, Boston Scientific, Cardionovum, Meril, Concept Medical

Expanding portfolio of transcatheter mitral repair and replacement

NeoChord

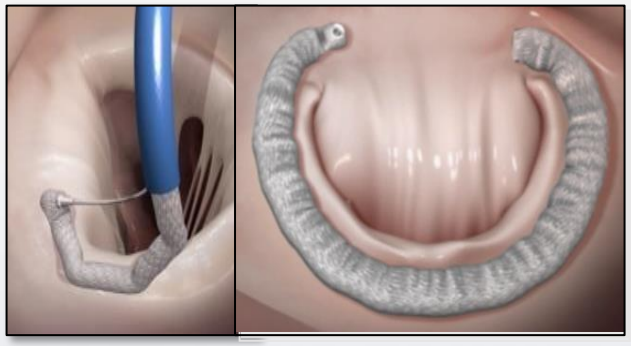
Harpoon

Chordal Replacement
NeoChord
Harpoon

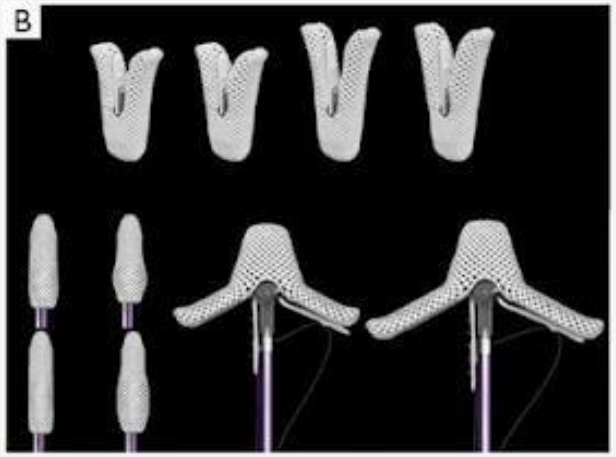
Leaflet Repair
MitraClip
PASCAL

Combo procedures

Annuloplasty
Cardioband
Carillon



Cardioband

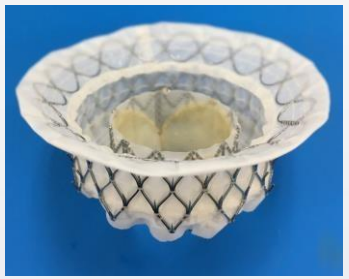


MitraClip XTR/W & NTR/W

PASCAL

Replacement
Tendyne, Intrepid, Tiara, Cardiovalve, HighLife, etc.

Tendyne



Intrepid

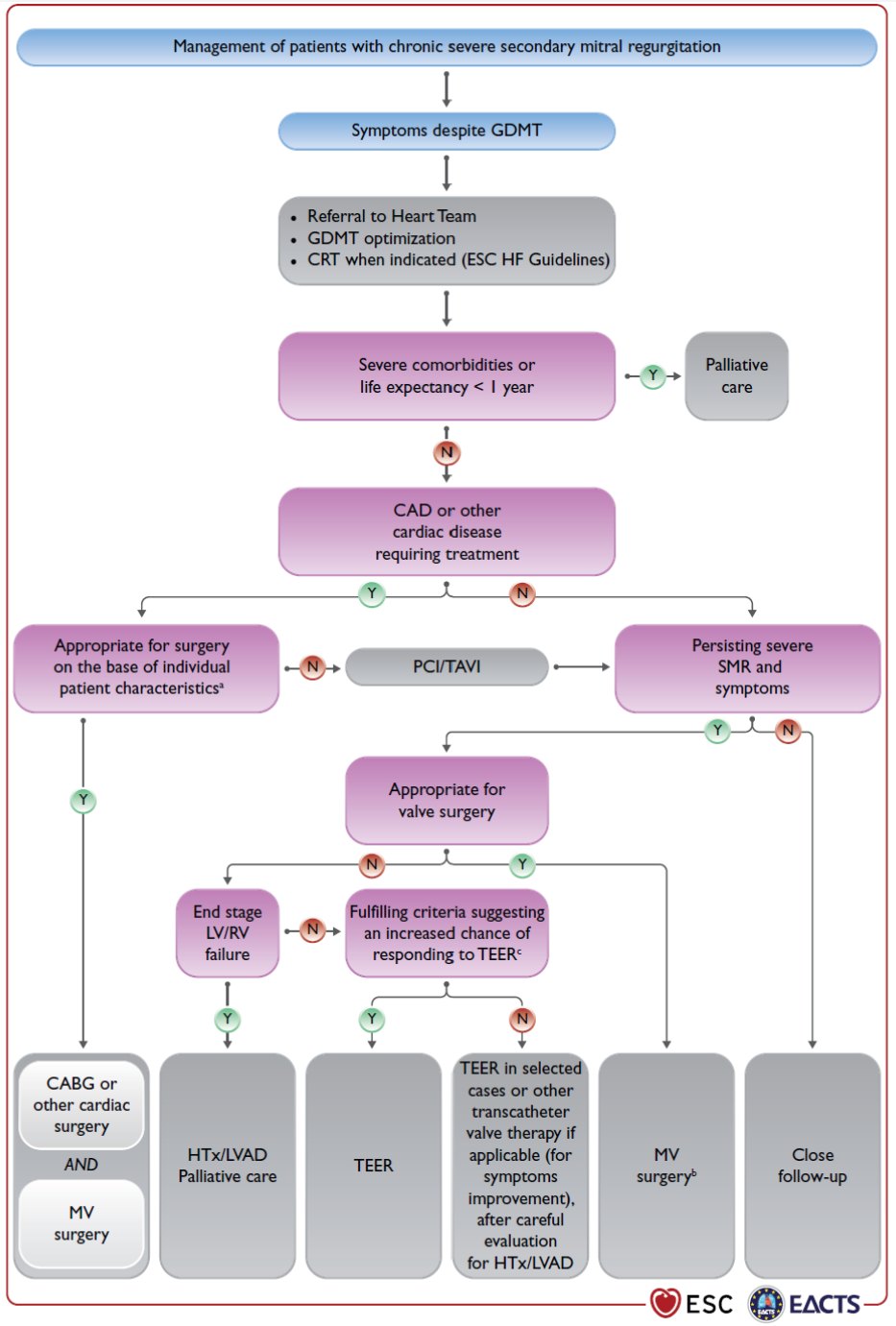
ESC European Society of Cardiology

European Heart Journal (2021) **00**, 1–72
doi:10.1093/eurheartj/ehab395

ESC/EACTS GUIDELINES

2021 ESC/EACTS Guidelines for the management of valvular heart disease

Developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)



16+ Years Dedicated to the Treatment of Valvular Regurgitation

$0.5B+
CLINICAL STUDY SPEND OVER SH LIFETIME

30K+
PATIENTS STUDIED

100K+
PATIENTS TREATED

MITRACLIP FIRST IN MAN

EVEREST I
Feasibility Study
55 Patients Enrolled
2003-2006

EVEREST II
RCT
279 Patients Enrolled
2005-2008

EVEREST II HIGH RISK STUDY
Single-Arm Study
78 Patients Enrolled
2007-2008

MITRACLIP™ CE MARK APPROVAL

EVEREST II REALISM
Continued Access
965 Patients Enrolled
2009-2014

ACCESS EUROPE
Single-Arm Study
567 Commercial Patients Enrolled
2009-2012

COAPT™
RCT
614 Patients Enrolled
2013-2017

MITRACLIP FDA APPROVAL FOR PMR

MITRACLIP PAS
Prohibitive Risk Primary MR
Commercial Registry
1998 Patients Enrolled
2013-2016

MITRACLIP AVAILABLE IN CANADA

MITRA.FR*
RCT
304 Patients Enrolled
2014-2017

MATTERHORN* & RESHAPE-HF2*
RCT
Currently Enrolling
2015-Present

MITRACLIP™ JAPAN
Single-Arm Study
30 Patients
2015-2016

COAPT CAS
Continued Access
Currently Enrolling
2017-Present

MITRACLIP AVAILABLE IN JAPAN

EXPAND STUDY
Observational Study
Core Lab/CEC Adjudication
Enrollment complete
1040 Patients

MITRACLIP JAPAN PMS
Post-Market Surveillance
Enrollment complete
500 Patients

COAPT Data Release at TCT

MITRACLIP PAS
Secondary MR
Commercial Registry
5000 Patients

MITRACLIP FDA APPROVAL For SMR

GIOTTO EHJ

EXPAND-G4 STUDY
Observational Study
Core Lab/CEC Adjudication
Currently Enrolling
1000 Patients

REPAIR MR
Multi-Center RCT – IDE Trial
Enrollment Starts
500-600 Patients

MITRACLIP KOREA PMS
Post-Market Surveillance
600 Patients / 4 Years

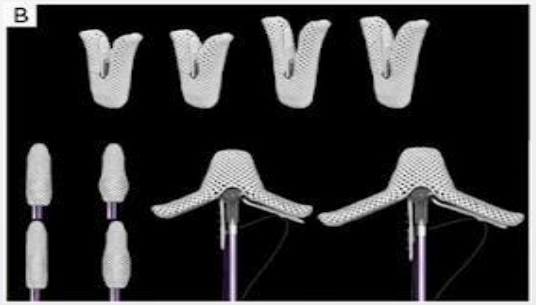
MITRACLIP RUSSIA FEASIBILITY
Single-Arm StudY
Currently Enrolling
16 Patients

MITRACLIP INDIA PMS
Post-Market Surveillance
Enrollment Starts
30-50 Patients

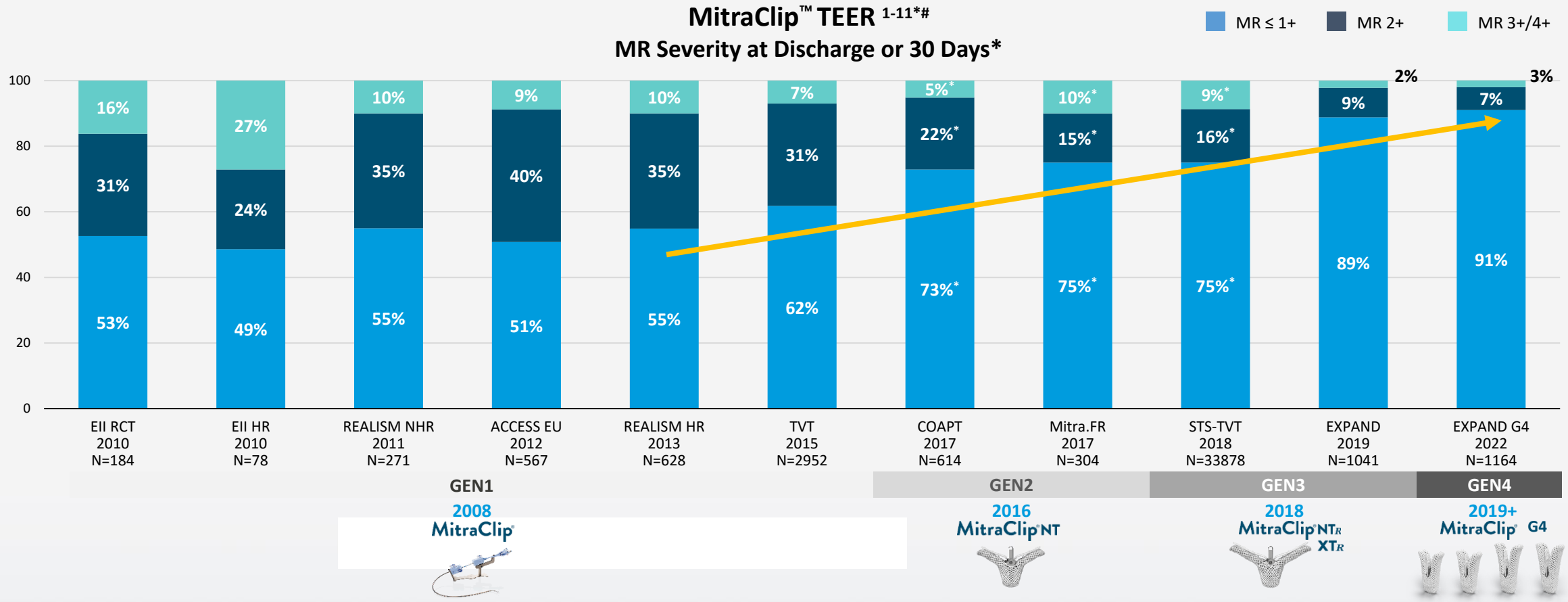
MITRACLIP CHINA PMS
Post-Market Surveillance
Ongoing 2020
60-100 Patients

2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 **2022**

Commercial approvals
Clinical Study



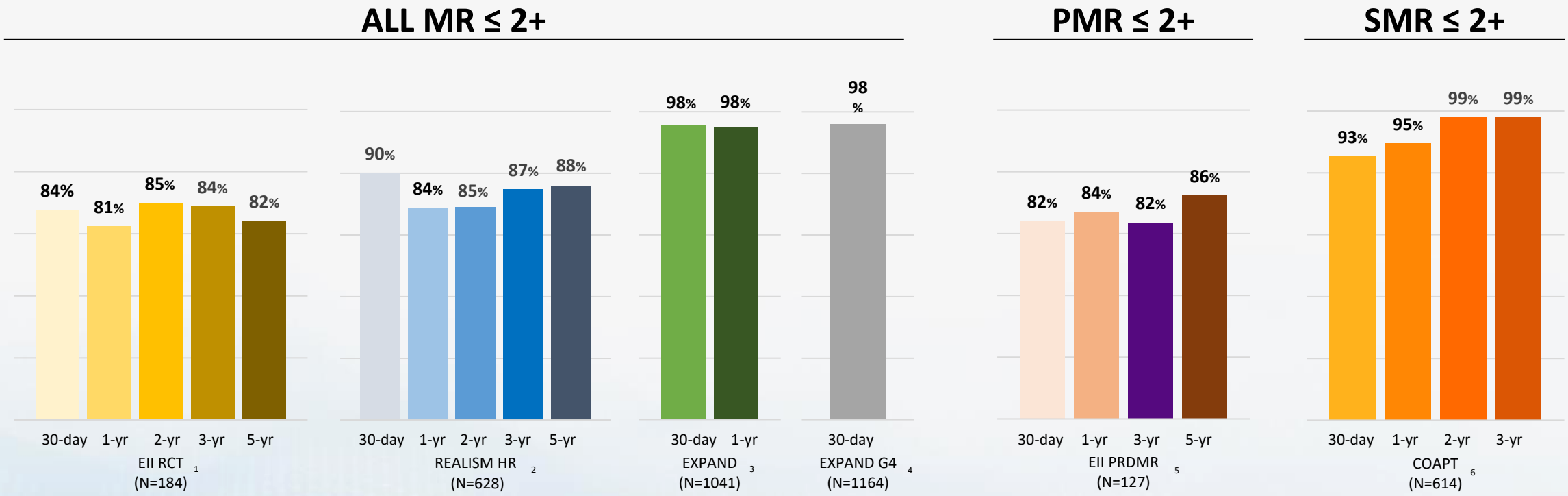
Proven clinical results show significant MR reduction



*Discharge rate was used if 30-day data not available. Mack et. al. did not report MR≤1+, rate assumed from Mitra.FR, > Sorajja TVT 2017. # all study years based on end of enrollment (trials), analysis period (TVT, STS registries), or publication year. Note: Data not from head-to-head studies. Data are provided for informational purposes only.

References 1-11: Please see slide 31

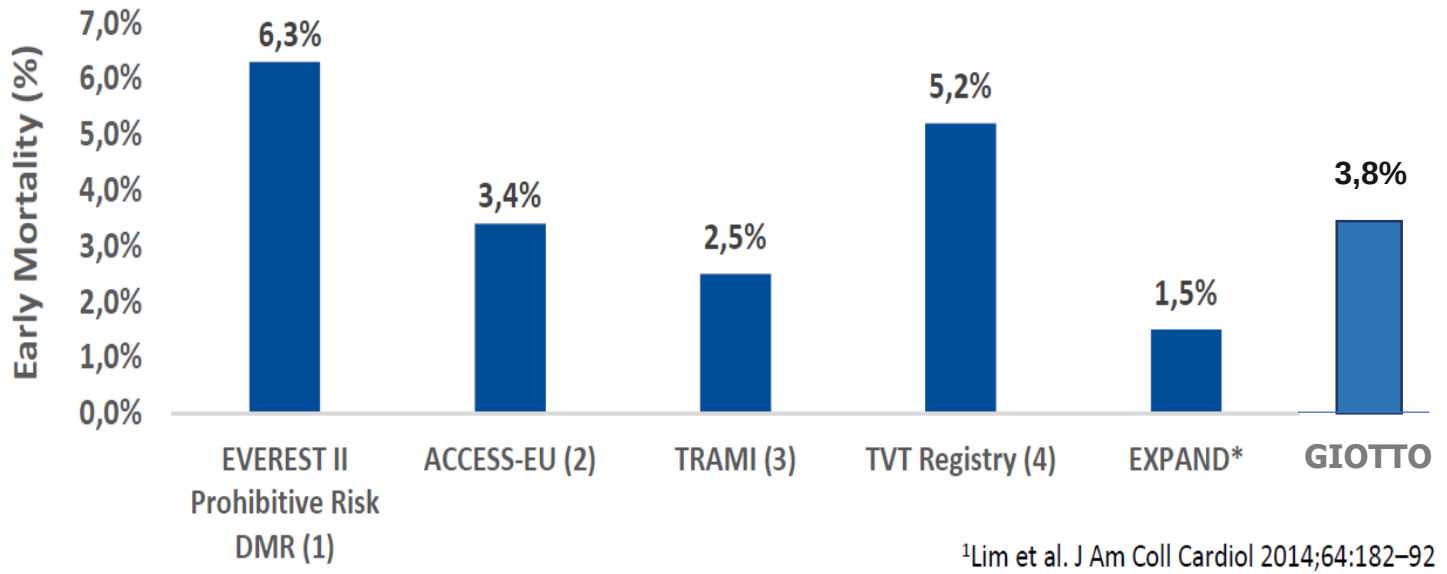
Durable MR reduction up to five years in a broad range of anatomies



1. EII RCT Final Report 2014, Table 33, paired results out to 5-years. 2. REALISM HR 2018 Final Report on file. 3. Kar, EXPAND 1-year, TCT2020. 4. Bardeleben et al. Contemporary Clinical and Echocardiographic Outcomes of 1000+ Patients Treated with MitraClip™ G4: Results from the EXPAND G4 Post Approval Study presented at TCT 2022. 5. Lim DS, PR DMR 5y, ACC2018.
6. Mack M, et. al., JACC 77(8), (2021 Supplemental App).
Note: Only residual MR ≤ 2+ reported; data on residual MR ≤ 1+ is limited. Data not from head-to-head studies. Data provided for informational purposes only.

Complication Rate across the Trials

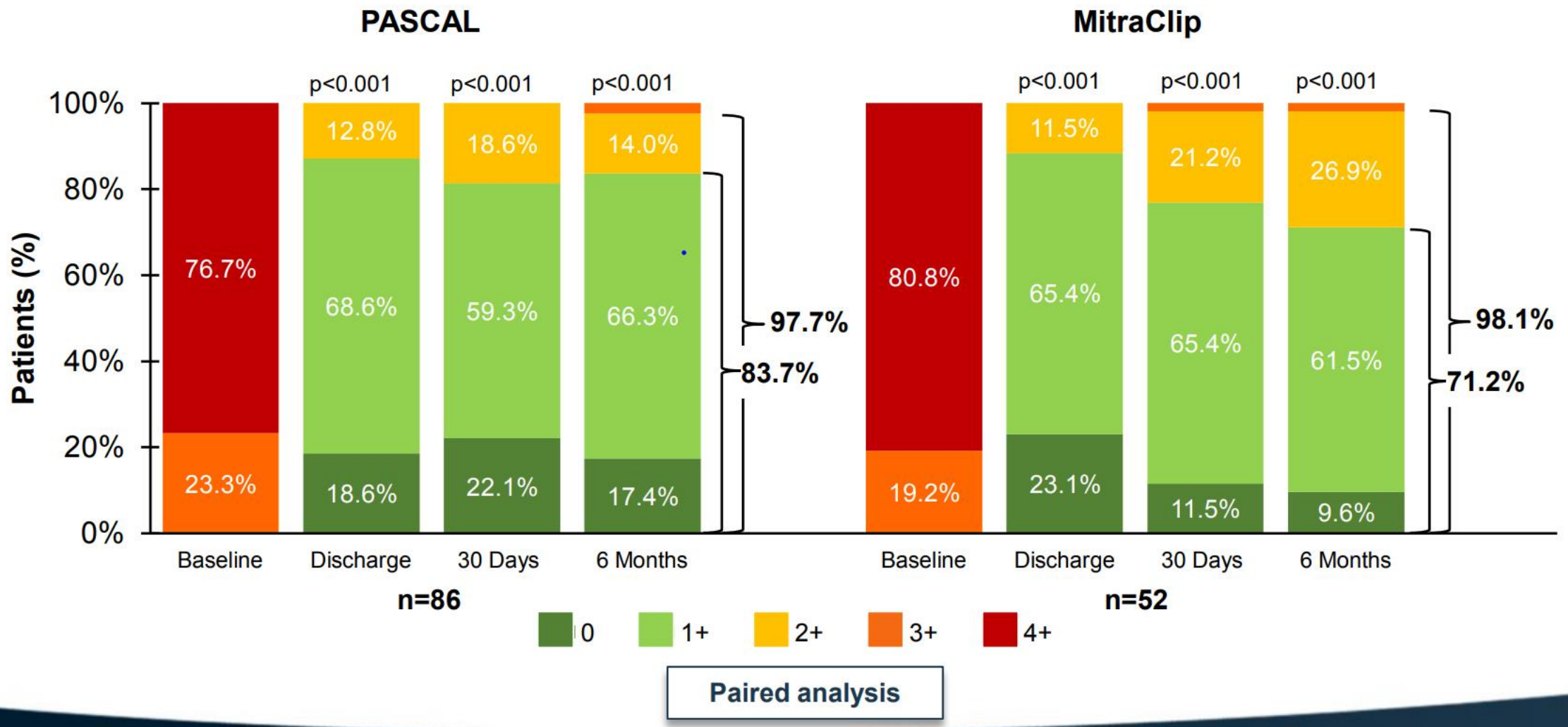
- The low mortality rate in EXPAND compared to prior registries is an indicator of current clinical outcomes at experienced, high volume MitraClip centers



[1]Lim et al. J Am Coll Cardiol 2014;64:182–92
[2]Maisano et al. J Am Coll Cardiol 2013;62:1052–61
[3]Baldus et al. Eur J Heart Fail. 2012 Sep;14(9):1050-5
[4]Sorajja et al. J Am Coll Cardiol 2017;70:2315–27)

MR Reduction by Core Lab[1]

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



Graph shows paired analysis and p values relative to baseline were calculated using the Wilcoxon signed rank test. [1]Echocardiographic core lab: Atlantic Health System Morristown Medical Center, Morristown, NJ, USA. MR severity assessed by transthoracic echocardiography (TTE).

TMVR in Functional MR
Different pts → different results

	GIOTTO (n= 890)	Mitra.FR (n= 152) Percutaneous repair group	COAPT (n=302) Percutaneous repair group	Mitraclip Expand (n= 1041)
Age	73 ± 8	70,1 ± 10,1	71,1 ± 11,8	77.3 ± 9.7*
Male	637 (71.6%)	120 (78,9%)	201 (66,6%)	571 (54.9%) *
NYHA I	5 (0.6%)	-	1 (0,3%)	2.8%*
NYHA II	138 (15.5)	56 (36,8%)	129 (42,7%)	18.7%*
NYHA III	650 (73.0%)	82 (53,9%)	154 (51,0%)	67.2%*
NYHA IV	97 (10.9%)	14 (9,2%)	18 (6,0%)	11.3%*
LVEF (%)	33 ± 10	33,3 ± 6.5	31.3 ± 9.1	38.6 ± 13.3
LVEDVi (mL/m²mean, SD)	**98 ± 35**	**135 ± 35**	**101 ± 34***	**97.8 ± 43**
EROA (mm²)	**35 ± 14**	**31 ± 10**	**41 ± 15**	**47 ± 24***
MR 2+	12 (2.3%)	-	-	7.9%
MR 3+	213 (23.9%)	-	148 (49,0%)	29.2%
MR 4+	665 (74.7%)	-	154 (51,0%)	62.8%
ICD	423 (47.5%)	90 (59,2%)	91 (30,1%)	18.7%*

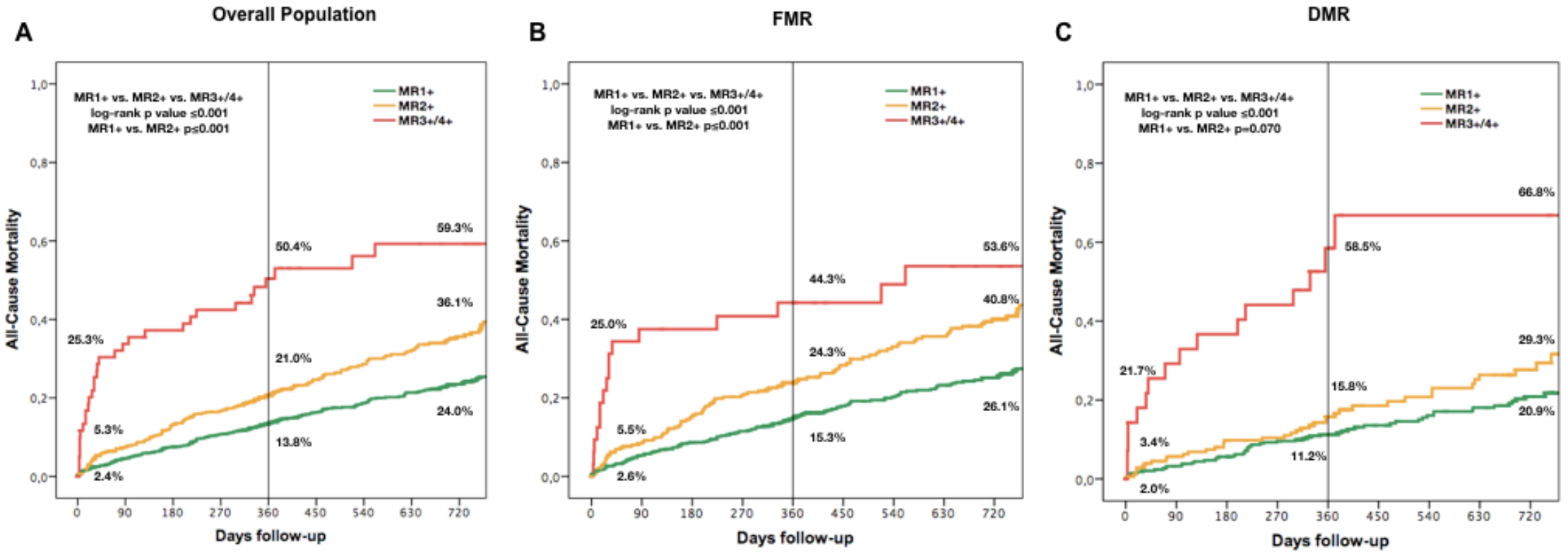
Mortality according to post-procedural MR

ESC European Society of Cardiology
European Journal of Heart Failure (2021)
doi:10.1002/ejhf.2159
RESEARCH ARTICLE

Italian Society of Interventional Cardiology (GIse) registry Of Transcatheter treatment of mitral valve regurgitaTiOn (GIOTTO): impact of valve disease aetiology and residual mitral regurgitation after MitraClip implantation

Francesco Bedogni[1†], Antonio Popolo Rubbio[1*†], Carmelo Grasso[2], Marianna Adamo[3], Paolo Denti[4], Arturo Giordano[5], Maurizio Tusa[1], Giovanni Bianchi[1], Federico De Marco[1], Antonio L. Bartorelli[6], Matteo Montorfano[7], Cosmo Godino[7], Rodolfo Citro[8], Francesco De Felice[9], Annalisa Mongiardo[10], Ida Monteforte[11], Emmanuel Villa[12], Cristina Giannini[13], Gabriele Crimi[14], Giuseppe Tarantini[15], Luca Testa[1†], and Corrado Tamburino[2]

p≤0.001



Number at risk

MR 1+	911	822	620	481	333
MR 2+	455	373	267	199	128
MR 3+/4+	60	39	23	14	10

Number at risk

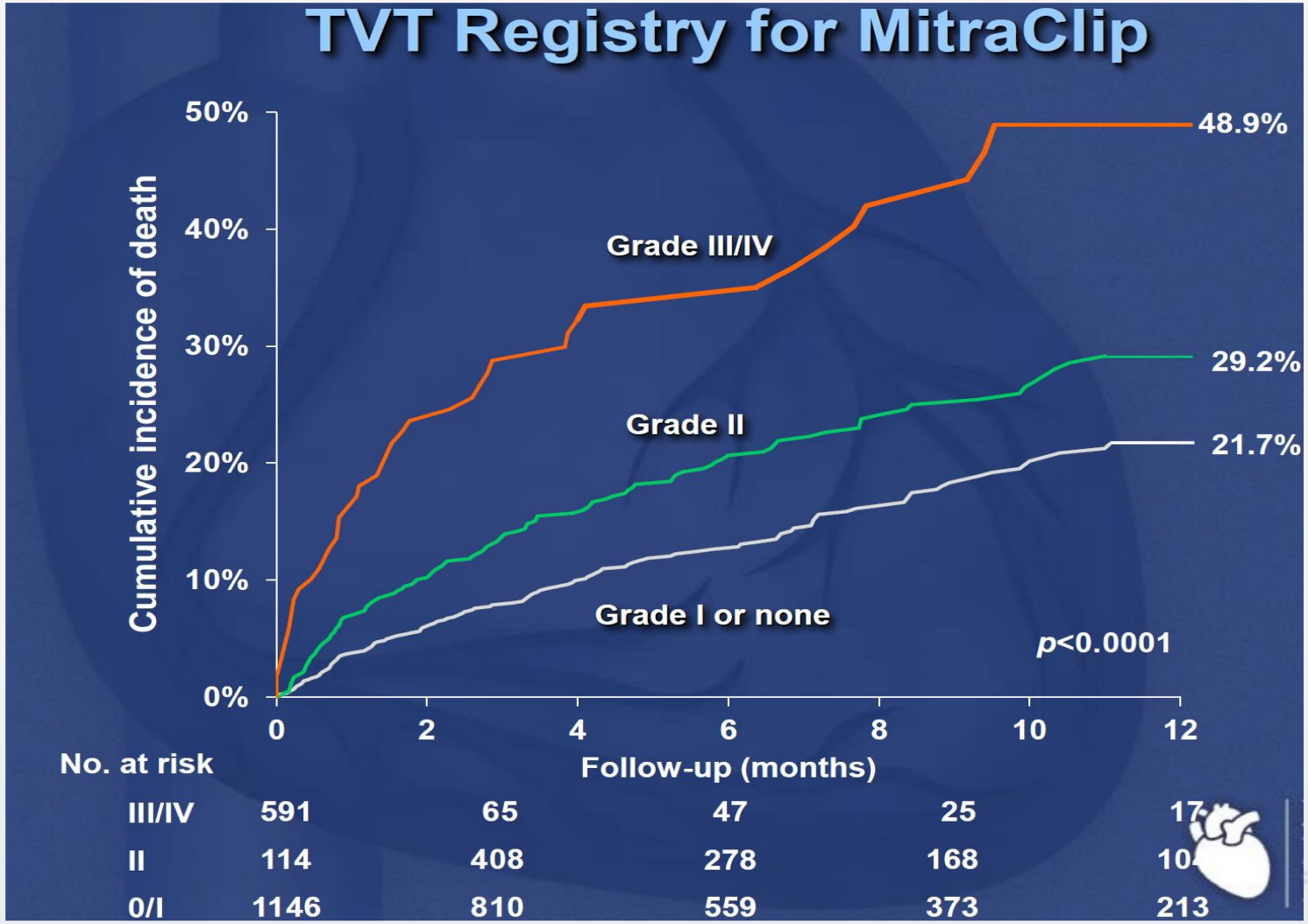
568	518	393	313	224
275	221	165	128	87
31	19	15	10	7

Number at risk

342	313	251	168	124
179	152	112	70	41
28	16	7	3	2

Post Procedural MR and Survival

STS/ACC TVT registry for Mitraclip



S.Lym TCT 2017

TEER Treatment Challenge | Treatment Efficacy

Many patients treated with TEER may not achieve MR grade ≤ mild at 30-days[1-6]

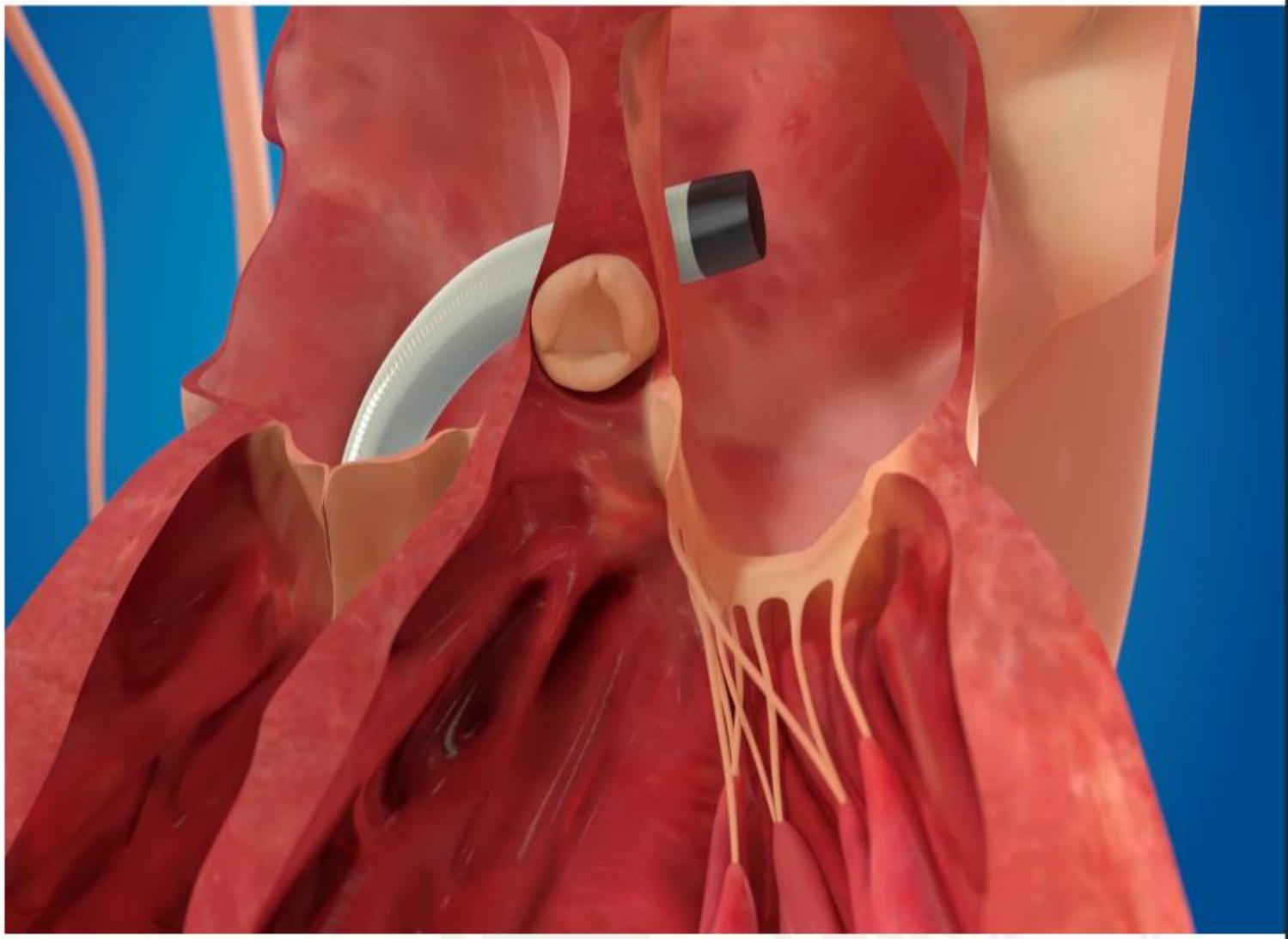
Device	Study	Study Date	Primary MR Etiology	Secondary MR Etiology	Study Cohort Size	MR ≤ Mild at 30-days
MitraClip[1]	Global EXPAND G4	2020-2022	41.6%	58.4%	1164	91%
MitraClip[2]	Global EXPAND	2018-2019	50.5%	49.5%	1041	89%
MitraClip[3]	STS/ACC TVT Registry	2014-2022	100%	0%	19,088	66%
MitraClip[4]	COAPT PAS	2019-2020	0%	100%	5000	62.5%
PASCAL[5]	CLASP IID	2018-2021	100%	0%	199	81%
PASCAL[6]	CLASP IID Registry	2019-2021	100%	0%	98	58%
PASCAL[7]	CLASP	2017-2020	31.5%	68.5%	124	77%

The data is not intended to be a comparison of these devices as there is no head-to-head clinical study, but rather is intended to summarize the clinical results of TEER therapies. Multiple factors contribute to clinical study outcomes and need to be considered in making any assessments across different devices.

The Dream of TMVR…

Design and Procedure Goals

- Ease of implantation
- Agnostic to etiology of MR
- Reliable elimination of MR
- Less recurrence of MR



Transcatheter Mitral Valve Replacement

CardioValve
Valtech (Edwards)

CardiAQ
Edwards

EVOQUE
Edwards

Sapien M3
Edwards

Fortis
Edwards

EPYGON
Affluent Medical

AccuFit
SINOMED

MValve
Mvalve Tech

Tiara
Neovasc

HighLife
HighLife Medical

Mi-thos
Shanghai NewMed

Caisson
Livanoval

Corona
Valcare

Permavalve
Micro Interventional

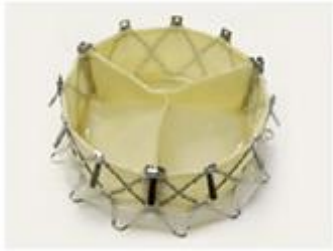
SATURN
InnovHeart

Intrepid
Medtronic

AltaValve
4C Medical

CEPHEA
Abbott

Tendyne
Abbott

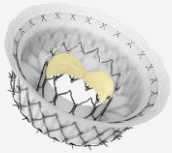


NaviGate
NCSI

Scotti et al. Vessel Plus 2021;5:6 I http://dx.doi.org/10.20517/2574-1209.2020.68

Current TMVR Clinical Pivotal Trial Landscape

TMVR clinical trials are earlier in development compared with TEER, with only one RCT currently enrolling.



	Tendyne SUMMIT Trial	Intrepid APOLLO Trial	SAPIEN M3 ENCIRCLE Trial
Sponsor	Abbott	Medtronic	Edwards Lifesciences
Population	≥Mod-severe MR Grade III-IV	≥Mod-Severe MR	≥3+ MR
Design	Randomized and non-randomized arms	Non-randomized	Non-randomized
Treatment	1:1 against TEER w/MAC cohort	Single-Arm w/MAC Cohort	Single-Arm
Primary Endpoint	Survival free of HFH at 1 year	All-cause mortality or HFH post-30 days or KCCQ improvement <10 composite	Non-hierarchical composite of death and HFH at 1 year
Patients (Est)	958	1350	500
Trial Start	June-15-2018	Oct-23-2017	Nov-12-2020

Table data from clinicaltrials.gov

Current TMVR Clinical Early Feasibility Trials

The TMVR early feasibility trial landscape continues to evolve and grow with the introduction of new devices.

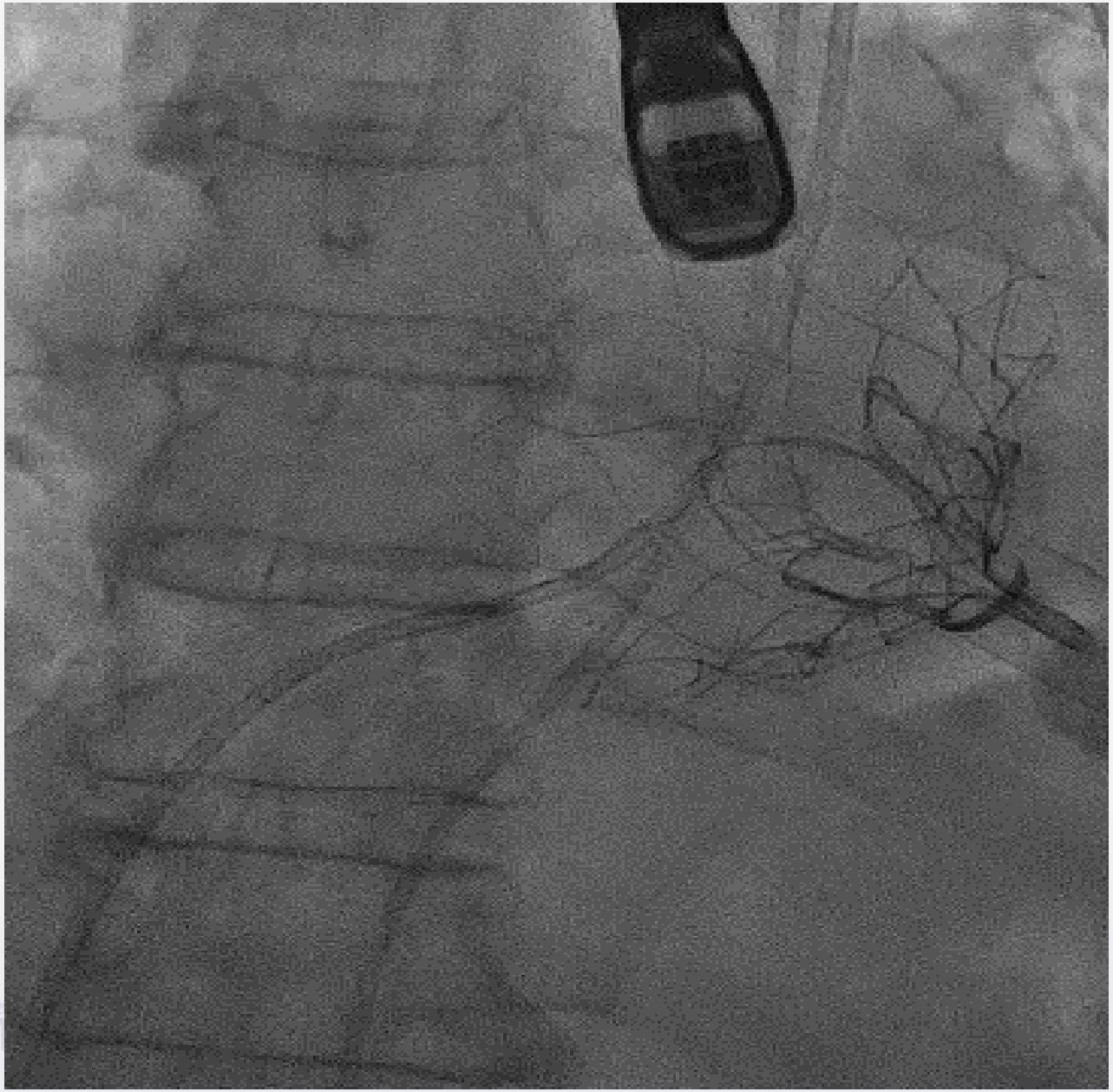


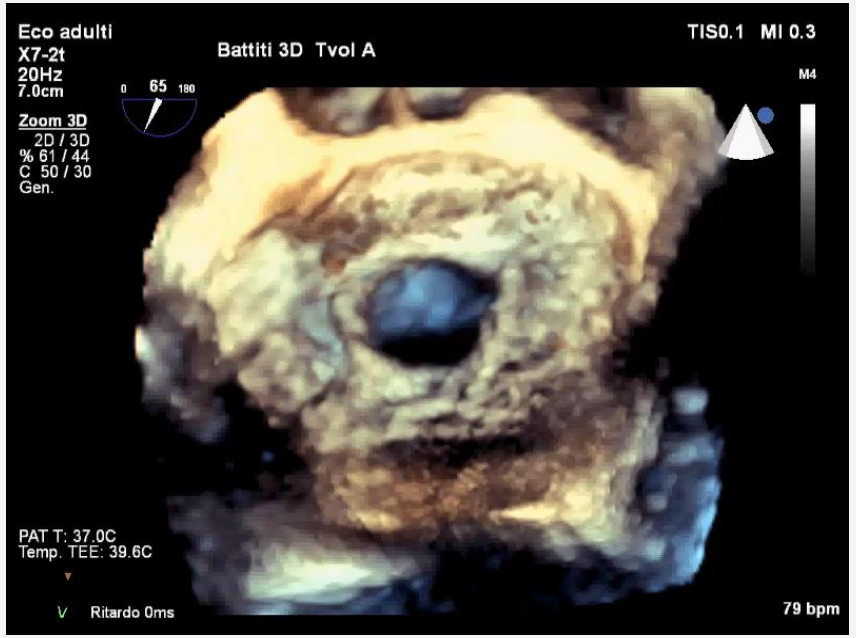


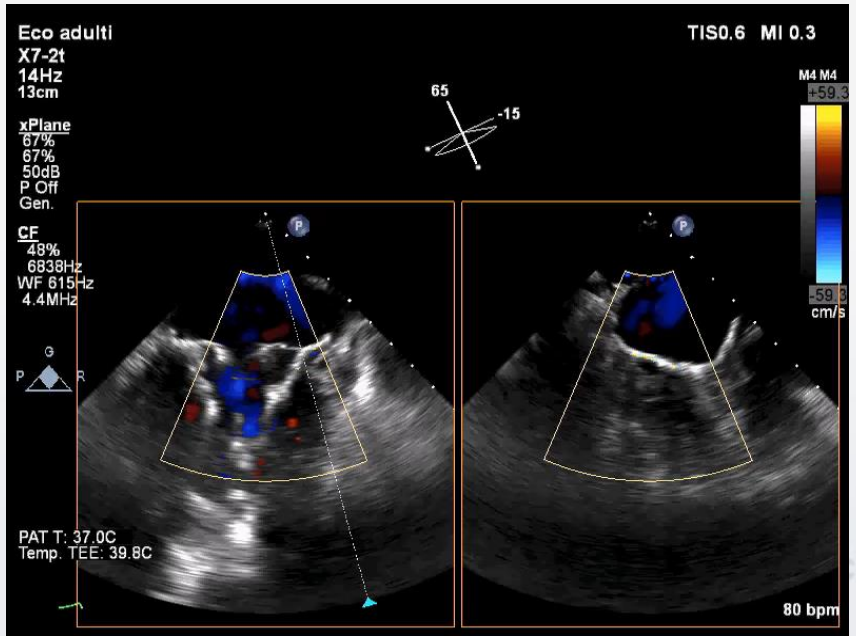
	Highlife Feasibility Study	AltaValve Feasibility Study	Cephea Feasibility Study	CardioValve AHEAD Trial	EVOQUE MiSCEND Study
Sponsor	HighLife Medical	4C Medical Technologies	Abbott	Cardiovalve Ltd.	Edwards Lifesciences
Population	Severe MR	Mod to severe or severe MR	MR ≥ Grade III	Severe MR, Grade 3-4+	Clinically significant, symptomatic MR
Design	Non-randomized	Non-randomized	Non-randomized	Non-randomized	Non-randomized
Treatment	Single-Arm	Single-arm	Single-arm	Single-arm	Single-arm
Primary Endpoint	Freedom from MAE at 30 day; continued intended performance of the bioprosthetic valve at 30 days; and technical success	Major adverse cardiac event at 30 days	Freedom from all-cause mortality at 30 days and proportion of subjects with MR <2+at 30 days	Freedom from all-cause mortality and MAE at 30 days, 6 months, 1 year, and 2 years	Composite MAE at 30 days
Patients (Est)	5 (actual)*	15	30	30	123
Trial Start	July-20-2017	Dec-4-2019	April-28-2022	April-23-2018	Feb-06-2015

Table data from clinicaltrials.gov

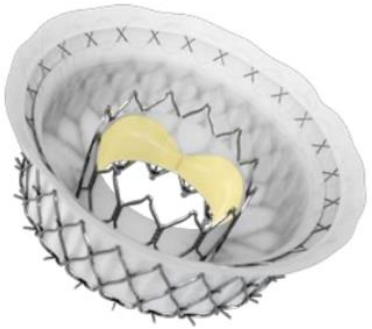
Deployment and release of a Tendyne







Next Generation Intrepid Transfemoral System



42 mm

48 mm

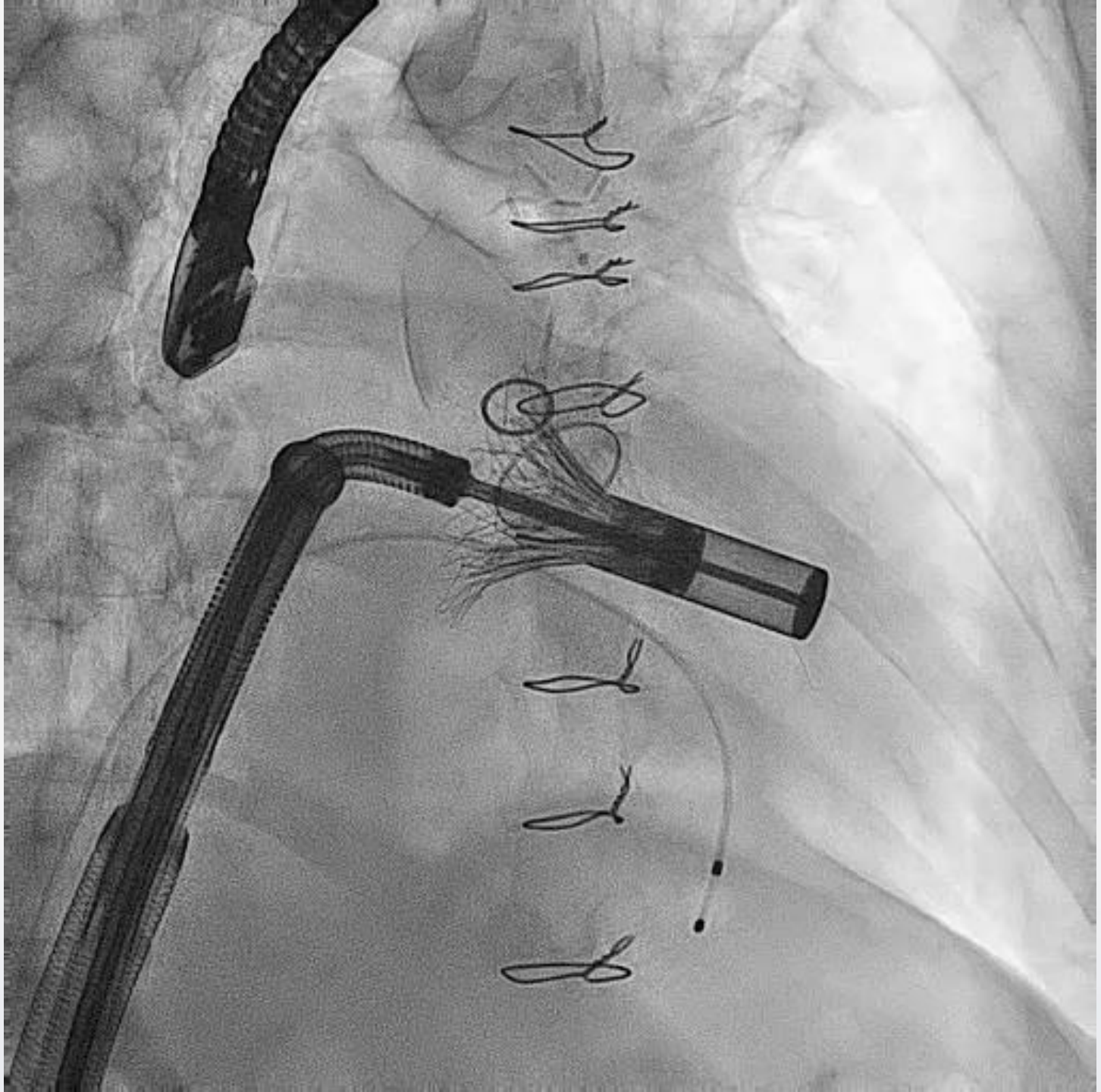
54 mm

Consistent Intrepid* Valve Design

- Optimized for 29Fr Profile & LVOT
- Increased Patient Eligibility with Larger Valve Size

Updated TF System

- 29Fr Profile
- Designed for Improved Steering
- Streamlined Accessories



JACC: CARDIOVASCULAR INTERVENTIONS VOL. ■, NO. ■
© 2024 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER

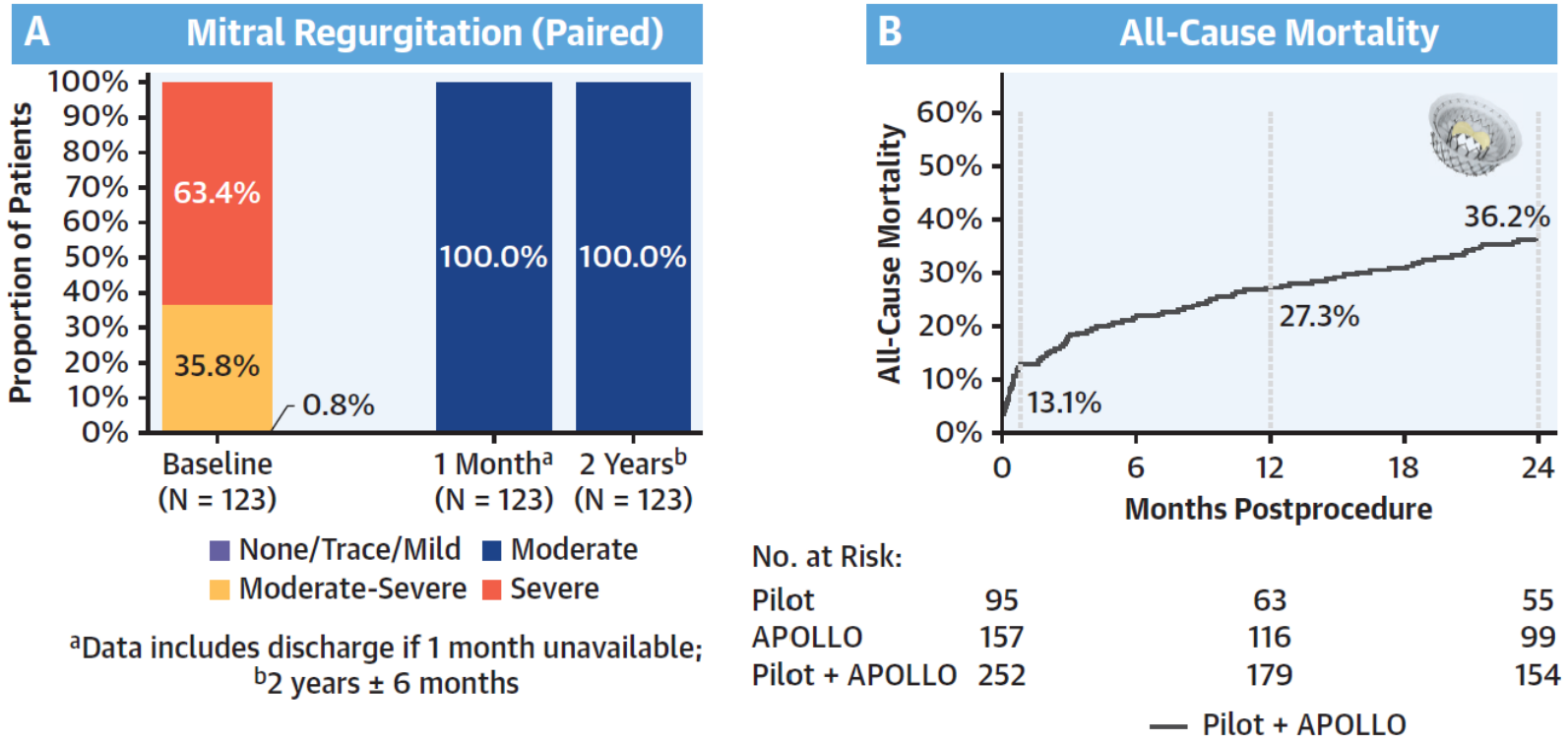
ORIGINAL RESEARCH

2-Year Clinical and Echocardiography Follow-Up of Transcatheter Mitral Valve Replacement With the Transapical Intrepid System

Vinayak Bapat, MBBS, MS, MCh,[a,b] Eric Weiss, MD,[c] Tanvir Bajwa, MD,[c] Vinod H. Thourani, MD,[d] Pradeep Yadav, MD,[d] Jeremy J. Thaden, MD,[e] D. Scott Lim, MD,[f] Michael Reardon, MD,[g] Sean Pinney, MD,[h] David H. Adams, MD,[h] Steven J. Yakubov, MD,[i] Thomas Modine, MD, PhD,[j] Simon R. Redwood, MD,[a] Antony Walton, MD,[k] Konstantinos Spargias, MD,[l] Angie Zhang, MS,[m] Michael Mack, MD,[n] Martin B. Leon, I

CENTRAL ILLUSTRATION 2-Year Results of Transapical Transcatheter Mitral Valve Replacement

2-Year Outcomes After Transcatheter Mitral Valve Replacement With the Transapical Intrepid System



[a]Data includes discharge if 1 month unavailable;
[b]2 years ± 6 months

- Marked and sustained reduction in mitral regurgitation over 2 years
- Significant early morbidity and mortality among this high-risk cohorta

Bapat V, et al. J Am Coll Cardiol Intv. 2024;■(■):■-■.

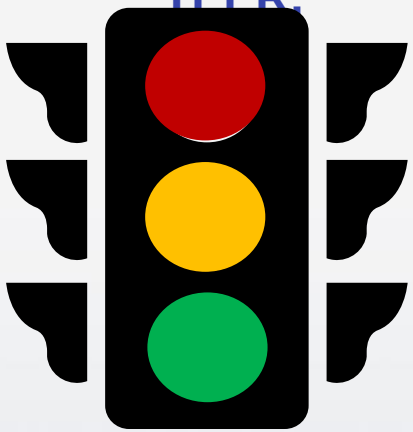
(A) Mitral regurgitation severity over time (paired). (B) Kaplan-Meier estimates for all-cause mortality (inset: Intrepid Valve).

TEER Treatment Suitability for Mitral Regurgitation

- TEER is a safe and effective treatment for MR and supported by the largest patient experience for any transcatheter intervention.
- However, there are potential challenges that suggest alternative therapeutic approaches are needed to address mitral valve complexities:

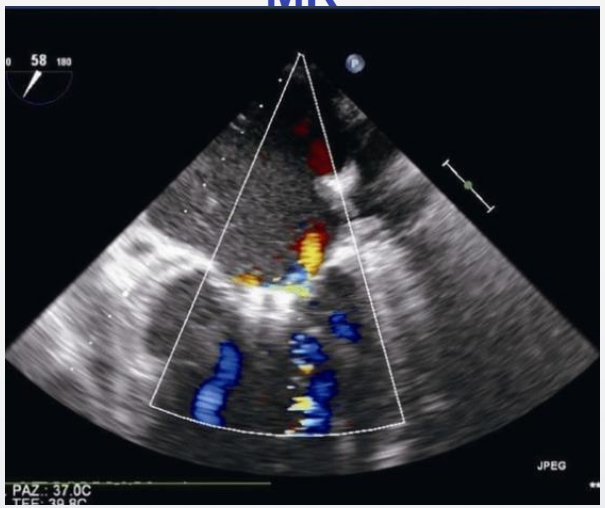
Anatomical Suitability

Numerous anatomies potentially unsuitable for TEER.



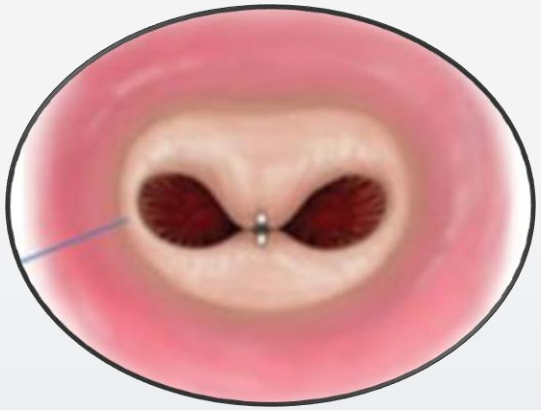
Treatment Efficacy

Patients Left with Residual MR



Treatment Durability

Risk of MR Recurrence



TEER Treatment Challenge | Anatomical Suitability

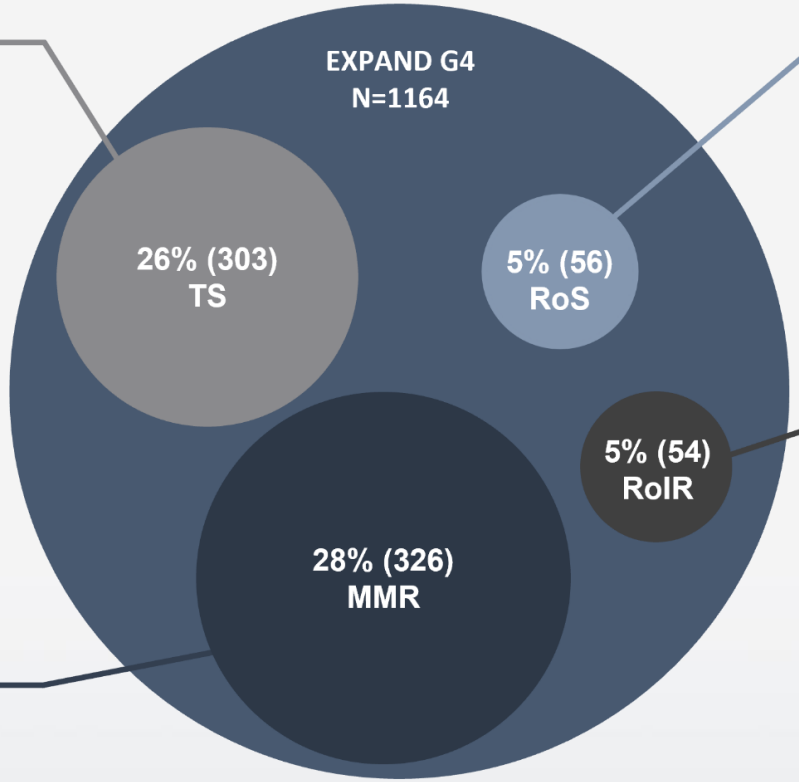
Only 26% of EXPAND G4 Study Population Classified as TEER Suitable[1].

TEER SUITABLE

Baseline MR Severity 3+/4+
and ALL of the following:
- No Secondary Jet
- No Severe Mitral Annular Calcification
- No Severe Leaflet Calcification
- No Significant Cleft/Scallop
- MVA ≥ 3.5 cm^2
- No prior annuloplasty
- No Barlow's disease
- No bi-leaflet prolapse/flail
- No severe degenerative leaflets with large gaps
- No minimal leaflet tissue

BASELINE MODERATE MR OR LESS

Baseline MR Severity < 3+
assessed by Echo Core Lab per ASE guidelines



RISK OF STENOSIS

Baseline MR Severity 3+/4+
and at least ONE of the following:
- Severe Annular Calcification
- Severe Leaflet Calcification
- Prior Mitral Annuloplasty
- MVA < 3.5 cm^2

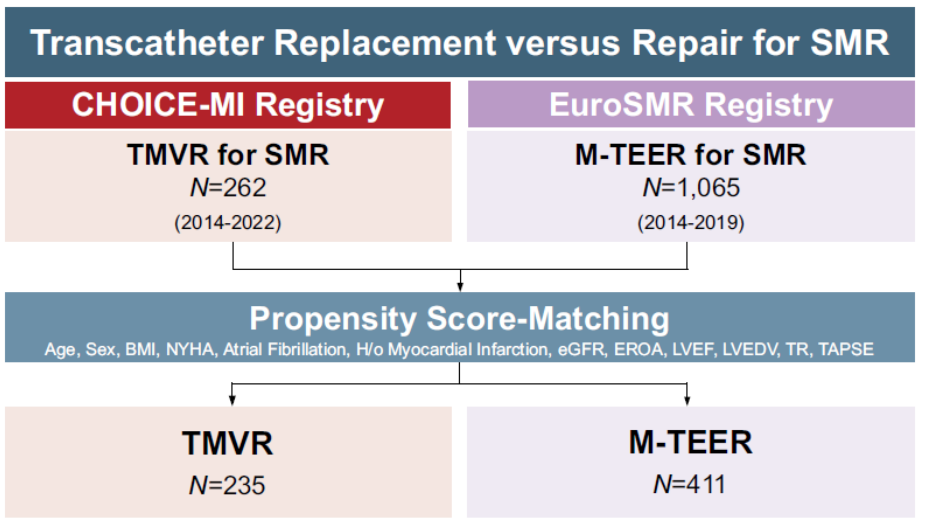
RISK OF INADEQUATE MR REDUCTION

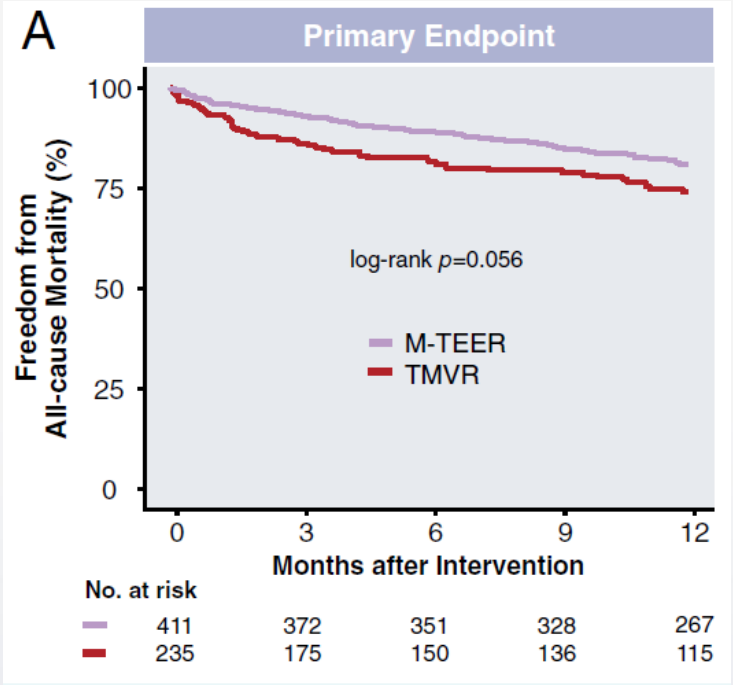
Baseline MR Severity 3+/4+
and at least ONE of the following:
- Barlow's disease
- Bi-leaflet flail/prolapse
- Significant secondary jet
- Severe leaflet degeneration with large gaps
- Minimal leaflet tissue
- Significant cleft or scallop

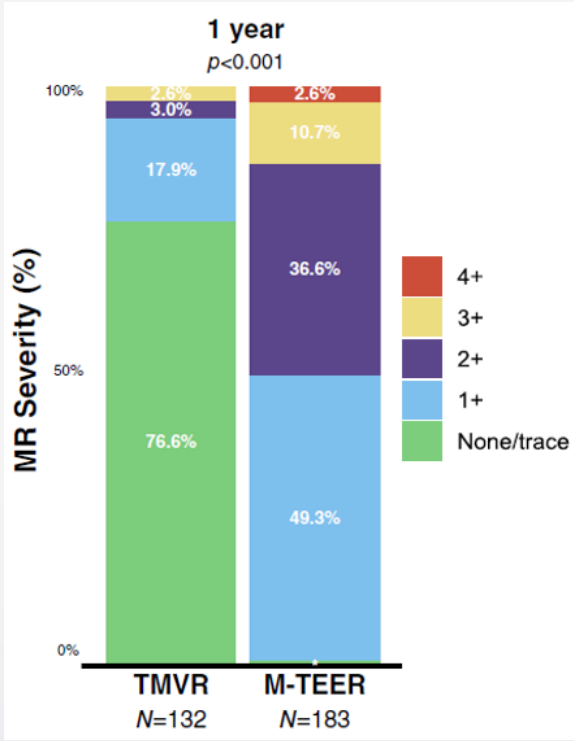
[1]Rogers, et al. JACC Intv. 2023 Jun 26;16(12):1474-1485

CHOICE-MI Registry: TEER vs TMVR

- Transcatheter mitral valve replacement (TMVR) is emerging as a viable option to manage MR, but there is a current evidence gap on whether it is comparable to the more established TEER therapy.
- A large PS-matched comparative analysis of secondary MR patients undergoing TMVR or TEER reported similar mortality between groups but better MR reduction with TMVR[1].
- TMVR results are encouraging, especially with the majority using a transapical approach[2].

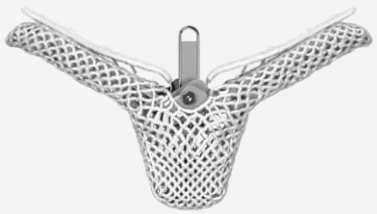






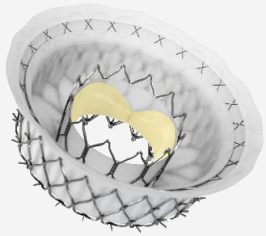
[1]Ludwig et al. *Eur J Heart Fail.* 2023 Mar;25(3):399-410; [2]Ludwig et al. *EuroIntervention*. 2023 Aug 21;19(6):512-525.

Head to Head

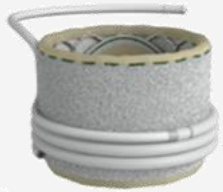


MitraClip

Pascal



Intrepid



Sapien M3

Tendyne

Highlife

TEER consistently demonstrates low all-cause mortality at 30-days (up to 1.8% in EXPAND G4)	Safety profile being established through early clinical experience: valve thrombosis?		**Safety**
~10-30% of patients do not receive optimal outcomes	Consistent, Predictable & Durable Elimination of MR		**Efficacy**
Leaflet grasping results in challenging imaging & procedure in complex anatomies & significant learning curve	Variable for each device		**Ease of use**
Prevents re-intervention on the Mitral Valve due to “bridge” across the valve (or requires complex procedure to remove the clip)	Should Enable Future Re-Intervention; anticoagulation?		**Lifetime**
Several anatomical restrictions, 15% scree out	Estimated 80% screen out rate: small LVOT!!		**Eligibility**

Conclusions

- A Toolbox of transcatheter mitral valve repair devices will likely be available in the future

- TEER is and will be the mainstream of TMVrepair in particulat for suitable anatomies and COAPT-like patients, at least until a reasonable TMV replacement platform will come…..