Supplementary Table 1: Comparison of COAPT and MITRA-FR trials.

	COAPT	MITRA-FR
Intervention arm	MitraClip + GDMT	MitraClip + GDMT
Control arm	GDMT	GDMT
Total No. of patients	614	420
No. of patients in interventional/control	302/312	152/152
Inclusion/exclusion criteria	US Guidelines	European Guidelines
Moderate to severe MR Definitions	EROA ≥30 mm^2 and/or RV >45 mL	EROA >20 mm^2 and/or RV >30 mL
LVESD (mm)	≤70 mm	
LV ejection fraction (%)	≥20 and ≤50	≥15 and ≤40
Symptomatic status	NYHA class: II, III, Iva (ambulatory)	NYHA class: II, III, IV
Primary endpoints	HF hospitalisation at 1 year	Death or HF hospitalisation at 1 year

CHF=congestive heart failure, LVESD=left ventricular end systolic dimension, PAP=pulmonary arterial pressure, CAD=coronary artery disease, COPD=chronic obstructive pulmonary disease, LVEF=left ventricular ejection fraction, LVEDV=left ventricular end diastolic volume

Supplementary Table 2: Summary of Transcatheter Mitral Valve Repair and Replacement Studies

Device	Trial	Study Type	Inclusion Criteria	Exclusion Criteria	n	Outcomes
TEER						
MitraClip	EVEREST I Feasibility (NCT00209339)	Single-arm, open-label	▪ Age ≥18 years ▪ Candidate for MV surgery ▪ Moderate to. Severe (3+) or severe (4+) MR ▪ Flail segment width <15mm and a regurgitant jet origin from within the central two-thirds of the line of leaflet coaptation	▪ AMI within 14 days ▪ Amy interventional or surgical procedure performed within 30days ▪ Prior median sternotomy ▪ Endocarditis ▪ Rheumatic heart disease ▪ EF <30% ▪ LVESD >55mm ▪ MV area <4.0cm^2	55	Mitral valve repair using the MitraClip system was shown to be feasible in patients at high surgical risk primarily determined by an adverse mitral valve morphology and/or severe LV dysfunction.
	EVEREST II Pivotal (NCT00209274)	Randomised, parallel assignment, open-label	• Age ≥18 years • Candidate for MV surgery • Moderate to severe (3+) or severe (4+) MR o Symptomatic ▪ EF >25% and ▪ LVESD ≤55mm o Asymptomatic with one or more of the following ▪ EF 25-60% ▪ LVESD ≥40mm ▪ New onset AF ▪ Pulmonary HTN	• AMI within 12weeks • Need for other cardiac surgery • Renal insufficiency (Cr>2.5) • Endocarditis • Rheumatic heart disease • MV anatomic exclusions o MV area <4.0cm^2 o Leaflet flail width (≥15mm) and gap (≥10mm) o Leaflet tethering/coaptation depth (>11mm) and length (<2mm)	279	MitraClip significantly reduced MR, improved clinical symptoms, and decreased LV dimensions at 12 months in this high-surgical-risk cohort.
	MITRA-FR (NCT01920698)	Randomised, parallel assignment, open-label	• Age ≥18 years • Severe SMR (European guidelines) • RVol>30 mL/beat or EROA>20 mm² • NYHA ≥ II • EF 15% to 40% • ≥1 HF hospitalisation within 12mo preceding randomisation • Optimal standard of care therapy for heart failure according to investigator. • Not eligible for a mitral surgery intervention according to the Heart Team.	• Eligible for a mitral surgery intervention according to the Heart Team. • Primary mitral regurgitation • MI, CABG, cardiac resynchronisation, cardioversion, TAVI, or stroke within 3mo prior to randomisation. • Need for any cardiovascular surgery (including registration on cardiac transplant list). • Coronary angioplasty within one month prior to randomisation. • Previous surgical mitral valve repair. • Renal replacement therapy. • Active infection requiring current antibiotic therapy. • Severe hepatic insufficiency. • Concurrent medical condition with a life expectancy of less than 12 months. • Uncontrolled arterial hypertension. • Hypersensitivity to nitinol. • Participation to another trial. • Pregnancy	420	Patients with severe secondary mitral regurgitation, the rate of death or unplanned hospitalisation for heart failure at 1 year did not differ significantly between patients who underwent percutaneous mitral-valve repair in addition to receiving medical therapy and those who received medical therapy alone.

	COAPT (NCT01626079)	Randomised, parallel assignment, open-label	• Age ≥18 years • Symptomatic SMR (moderate-severe or greater, US guidelines) due to ischemic or non-ischemic cardiomyopathy • Adequately treated for coronary disease, LV dysfunction, MR, and heart failure • NYHA class II or greater • ≥1 HF hospitalisation in last year OR corrected BNP ≥ 300 pg/mL OR corrected NTproBNP ≥1500pg/mL • Local heart team has determined that MV surgery will not be offered as a treatment option • LVEF ≥ 20% and ≤ 50% • LVIDs ≤ 70mm • Primary MR jet is non-commissural, and implanting investigator deems Mitra Clip is feasible • CK-MB obtained within prior 14 days is normal • Transseptal catheterisation and femoral vein access is feasible per Mitra Clip investigator • Informed consent provided	• Untreated clinically significant coronary disease requiring revascularisation • CABG, PCI, TAVR, CVA, Carotid surgery or stenting within 30 days • Aortic or tricuspid valve requiring surgery or transcatheter intervention • COPD requiring continuous home oxygen therapy or chronic outpatient steroid use • Severe symptomatic carotid stenosis • ACC/AHA Stage D heart failure • Presence of any of the following: ○ Estimated PASP > 70 mmHg unless vasodilator therapy reduces PVR to < 3 Wood units or 3-4.5 Wood units with v wave less than twice the mean of PCWP ○ HCM, restrictive cardiomyopathy, constrictive pericarditis, or any other structural heart disease causing HF other than dilated cardiomyopathy of either ischemic or non-ischemic aetiology ○ Infiltrative cardiomyopathy • Hemodynamic instability or cardiogenic shock requiring inotropic support or mechanical assistance • Physical evidence of right-sided CHF evidence of moderate or severe RV dysfunction • Implant of CRT or CRT-D within 30 days • Mitral orifice area < 4.0cm2 • Leaflet anatomy which may preclude Mitra Clip implantation • Need for surgery within 12 months • Life expectancy < 1 year • Status 1 for cardiac transplant or history of cardiac transplant • Modified Rankin score ≥ 4 for disability • ECHO evidence of intracardiac mass, thrombus, or vegetation • Active infection requiring antibiotic therapy • Prior mitral valve surgery or prosthesis • TEE is contraindicated or high risk • Pregnant or planning pregnancy within 12 months • Known hypersensitivity or contraindication to procedural medications that cannot be adequately treated	614	Trial indicated that transcatheter mitral valve approximation using the MitraClip on a background of maximally tolerated GDMT was superior to GDMT alone in reducing HF hospitalisation and mortality in symptomatic HF patients with grade 3-4+ MR
PASCAL	CLASP (NCT03170349)	Single-arm, open-label	• Age ≥18 years	• TEE is contraindicated or high risk	124	Low complication rate and high survival, with

			• NYHA II-IVa despite OMT • Candidacy for surgical mitral valve repair or replacement determined by Heart Team evaluation • moderate-to-severe or severe MR • The primary regurgitant jet is non-commissural. If a secondary jet exists, it must be considered clinically insignificant. • MVA ≥ 4.0 cm² as measured by planimetry. If MVA by planimetry is not measurable, pressure half-time measurement is acceptable.	• Leaflet anatomy which may preclude PASCAL device implantation, proper device positioning on the leaflets, or sufficient reduction in mitral regurgitation. • MVA < 4.0 cm² as measured by planimetry (If MVA by planimetry is not measurable, PHT measurement is acceptable) • ECHO evidence of intracardiac mass, thrombus, or vegetation • Physical evidence of right sided CHF and ECHO evidence of severe RVD • Concurrent medical condition with a life expectancy of less than 12 months • Participation to another trial.		robust sustained MR reduction accompanied by significant improvements in functional status and quality of life at 1 year.
	CLAP IID/IIF (NCT03706833)	Randomised, parallel assignment, open-label	• Age ≥18 years • Patient is determined to be at prohibitive risk for mitral valve surgery by the heart team (CLASP IID cohort only). • Patient is on stable HF medications/Guideline Directed Medical Therapy (CLASP IIF cohort only) • Patient is determined to be a candidate for TMVR by the heart team for both PASCAL and MitraClip • Mitral regurgitation (3+ to 4+) by echo • Suitable valve and regurgitant jet morphology • Elevated corrected BNP > 400 pg/ml OR Corrected NT-pro BNP of > 900 pg/ml OR HF hospitalisation within 12mo (CLASP IIF cohort only) • LVEF ≥ 20% (and ≤ 50%; CLASP IIF cohort only)	• TEE is contraindicated or high risk • Mitral valve anatomy which may preclude proper PASCAL or MitraClip access. • Refractory HF requiring advanced intervention (i.e. left ventricular assist device, Status ≤5 heart transplantation) (ACC/AHA Stage D heart failure) • Clinically significant, untreated coronary artery disease • Recent stroke • Other severe valve disorders requiring intervention • Need for emergent or urgent surgery for any reason or any planned cardiac surgery within the next 12 months • Any prior mitral valve surgery or transcatheter mitral valve procedure (excluding chordal replacement or surgical annuloplasty repair) • Severe tricuspid regurgitation or tricuspid valve disease requiring surgery • Rheumatic heart disease • Severe aortic stenosis or regurgitation • Known history of untreated, severe carotid stenosis • Recent DVT or (PE), severe COPD • Pregnant or planning pregnancy within next 12 months. • Concurrent medical condition with a life expectancy of less than 12 months in the judgment of the Investigator • Participation to another trial.	Active	CLASP IID trial showed that transcatheter mitral edge-to-edge repair with the PASCAL system is non-inferior to MitraClip for major adverse events among patients with degenerative MR and prohibitive surgical risk.
Annuloplasty						
CARILLON	REDUCE FMR (NCT02325830)	Randomised, parallel assignment, sham controlled	• Age ≥18 years • Diagnosis of dilated ischemic or non-ischemic cardiomyopathy • FMR: 2+ (Moderate), 3+ (Moderate/Severe), or 4+ (Severe)	• Hospitalisation in past three months due to MI, CABG, and/or unstable angina • Hospitalisation in the past 30 days for coronary angioplasty or stent placement or need for percutaneous	163	The Carillon device significantly reduced mitral regurgitant volume and left ventricular volumes in symptomatic patients

			• NYHA II, III, or IV • Six Minute Walk distance of at least 150 meters and no farther than 450 meters • EF ≤ 50 % • LVEDD >55mm or LVEDD/Body Surface Area (BSA) > 3.0cm/m2 • Stable heart failure medication regimen for at least three (3) months prior to index procedure	• Subjects expected to require any cardiac surgery within one year • Subjects expected to require any percutaneous coronary intervention within 30 days of enrolment • Pre-existing device (e.g., pacing lead) in coronary sinus / great cardiac vein or anticipated need for CRT within twelve months • Presence of a coronary artery stent under the CS / GCV in the implant target zone • Presence of left atrial appendage clot. • Presence of primary renal dysfunction or significantly compromised renal function as reflected by a serum creatinine > 2.2 mg/dL OR eGFR < 30 ml/min • Inability to undertake a six-minute walk test due to physical restrictions/limitations • Chronic severe pathology limiting survival to less than 12-months		with functional mitral regurgitation receiving optimal medical therapy.
	EMPOWER (NCT03142152)	Randomised, parallel assignment, double masking	• Diagnosis of ischemic or non-ischemic cardiomyopathy • Symptomatic functional (secondary) mitral regurgitation of at least 1+ (Mild) severity Note: 4+ can only be included if multidisciplinary site assessment (including a surgeon) determines that surgery is not necessary within the 1-year follow-up period for this study. • NYHA Class II, III, or IV • Six Minute Walk distance ≥ 150 meters and ≤ 450 meters • Left Ventricular Ejection Fraction ≤ 50% • LVEDD ≥ 60 mm and LVESD ≤ 70 mm • Corrected BNP of ≥ 300 pg/ml, or corrected NT-proBNP ≥ 1200 pg/ml, or one or more heart failure hospitalisations within six months prior to consent • Guideline directed heart failure medication regimen.	• Pre-existing device (e.g., pacing lead) in coronary sinus (CS) / great cardiac vein (GCV) • Class I indication for cardiac resynchronisation therapy (CRT), or anticipated need for CRT within twelve (12) months • Presence of a mechanical or bio-prosthetic mitral valve or, mitral valve annuloplasty, or leaflet repair device • Significant organic mitral valve pathology (e.g., moderate or severe myxomatous degeneration, with or without mitral leaflet prolapse, rheumatic disease, full or partial chordal rupture), as assessed by the Imaging Core Laboratory • Severe tricuspid regurgitation associated with right ventricular dysfunction and enlargement, as assessed by the Imaging Core Laboratory • Severe mitral annular calcification • Severe aortic stenosis • Expected to require any cardiac surgery, including surgery for coronary artery disease (CAD) or valve disease within one (1) year • Presence of left atrial appendage (LAA) clot or presence of LAA occluder • Chronic, severe, medical conditions or pathology, other than heart failure, that will prevent likely survival beyond twelve (12) months ○ An entire list of eligibility is available in the clinical investigational plan	Active	Active

Millipede IRIS	A Feasibility Study of the Millipede Transcatheter Annuloplasty Ring System in Patients with Functional Mitral Regurgitation (NCT04147884)	Single-arm, open-label	• age ≥18 years
			• Moderate-severe (3+) or severe (4+) FMR
			• Subject is symptomatic (NYHA Class II-IV) despite guideline directed medical therapy, including CRT if indicated
			• The local site heart team concurs that mitral valve surgery will not be offered as a first-line treatment option
			• Subject is a candidate for annuloplasty based on the criteria below as assessed by the investigative site (and confirmed by the Case Review Committee [CRC]):
			  ○ EF ≥ 25%
			  ○ LVEDD≤ 65 mm
			  ○ Coaptation distance < 10 mm
			  ○ Absence of posterior wall aneurysm
				• Severe calcification of mitral annulus or leaflets
				• Anatomic features that make the subject unsuitable for annuloplasty with the Millipede System
				• Transfemoral venous and transseptal access not feasible
				• Subject on the waiting list for transplant or prior heart transplant.
				• CVA or TIA, percutaneous coronary, carotid, or other endovascular intervention, carotid surgery within 30 days prior to study enrollment
				• Any open coronary or vascular surgery (other than carotid surgery), or cardiac resynchronisation therapy within 3 months prior to study enrolment
				• Untreated clinically significant CAD requiring revascularisation
				• Any planned cardiac surgery within the next 12 months
				• Need for emergent or urgent surgery for any reason
				• Severe aortic valve stenosis and/or aortic valve regurgitation, right-sided CHF, prosthetic heart valve in any position, renal insufficiency (eGFR <20mL/min) and is not on dialysis
				• Life expectancy less than 12 months
				• Subjects in whom TEE is contraindicated
				• History of (ASD) closure or patient foramen ovale (PFO) closure
				• Subject has fixed pulmonary artery systolic pressure > 70 mmHg
				• Female subject who is breast feeding or is pregnant
				• Subject is participating in another study that has not reached its primary endpoint or subject intends to participate in another investigational device clinical trial within 12 months after index procedure
				• Subject has a history of endocarditis within 6 months of index procedure or evidence of an active systemic infection or sepsis
				• Subject has documented hypersensitivity to contrast or nickel or titanium that cannot be adequately premedicated, severe liver disease, intracardiac thrombus, has oxygen-dependent COPD, Hgb <8 g/dL, platelet count <50,000 cells/mm3 or >700,000 cells/mm3, or white blood cell count <1,000 cells/mm3
					4	Active

AMEND	AMENDTM Mitral Valve Repair System,	Single-arm, Open-label	• age ≥18 years	• Cardiac or non-cardiac major or progressive disease, which in the investigator's discretion produces an unacceptable increased risk to the patient.	4	Active

	Annuloplasty Ring Applied in a Transcatheter Method (NCT02602613)		• Patient requires mitral valve annuloplasty for MR without the need for concomitant cardiovascular surgical procedures. • NYHA ≥2 • High risk to undergo mitral valve surgery as assessed by heart team.	• Life expectancy of less than 12 months. • Heavily calcified annulus or leaflets. • Previous or active endocarditis. • Active infection. • A previously implanted prosthetic mitral valve or annuloplasty ring/band. • Contraindicated to have general anaesthesia. • Pregnant or lactating patient. • Drug or alcohol abuse. • Participation in concomitant research studies of investigational products that will interfere with the study.		
Chordal Repair						
Neochord	TACT trial (NCT01784055)	Prospective, observation cohort	• Grade 3+ or 4+ mitral valve regurgitation	• Heavily calcified valves • Valvular retraction with severely reduced mobility • Active bacterial endocarditis • Complex mechanism of MR (leaflet perforation, etc.) • Significant tethering of leaflets • Inflammatory valve disease	100	Off-pump transapical implantation of artificial chordae to correct MR is technically safe and feasible.
TVMR						
Tendyne	Feasibility Study of the Tendyne Mitral Valve System for Use in Subjects with Mitral Annular Calcification (NCT03539458)	Single-arm, open-label	• age ≥18 years • Heart Team determines subject is not a suitable candidate for conventional surgical treatment due to degree of MAC present and the subject will likely benefit from transcatheter valve implantation • Symptomatic SMR • NYHA ≥ II (if Class IV, patient must be ambulatory)	• Presence of Left Ventricle or Left Atrium thrombus • Chest condition that prevents transapical access • EF <25% • LVEDD > 7.0 cm • Severe mitral stenosis not amenable to balloon valvuloplasty or transcatheter therapy • Prior intervention with permanently implanted mitral device (e.g. MitraClip) • Mitral pathoanatomy and Left Ventricular Outflow tract anatomy deemed not suitable for Tendyne mitral valve implantation • Any planned cardiac surgery or intervention that is 30 days prior and 30 days post that is not concomitant with the Tendyne procedure • Cardiac resynchronisation therapy (CRT) device or implantable pulse generator (IPG) implanted within three months of planned implant procedure • Myocardial Infarction (MI) within 30 days of the planned implant procedure • Symptomatic, or ischemia-associated coronary artery disease (e.g., active ischemia) amenable to revascularisation and thus requiring stenting or CABG	11	Device success and freedom from device and procedure related serious adverse events at 30 days

				• Cerebrovascular accident (CVA) within six months of planned implant procedure • Unresolved severe symptomatic carotid stenosis (> 70% by ultrasound) • Cardiogenic shock or hemodynamic instability requiring inotropes or mechanical support devices within 1 month prior to planned implant procedure • Severe tricuspid regurgitation or severe right ventricular dysfunction • Hypertrophic or restrictive cardiomyopathy, constrictive pericarditis or any other structural heart disease causing heart failure other than dilated cardiomyopathy of either ischemic or non-ischemic aetiology • Any of the following: leukopenia, acute anaemia, thrombocytopenia, history of bleeding diathesis, or coagulopathy if cannot be adequately treated • History of endocarditis within 6 months of planned implant procedure • Active systemic infection requiring antibiotic therapy • Subject unable or unwilling to take anticoagulation with warfarin for a minimum of 6 months following Tendyne valve implantation • FEV1 < 50% of predicted or < 1L • Subject has known hypersensitivity to procedural or post-procedural medications, nickel, or titanium, refuses blood transfusions, COPD requiring continuous home oxygen therapy or chronic outpatient oral steroid use, pulmonary arterial hypertension (fixed PAS >70mmHg), haemodialysis due to chronic renal failure (≥ Stage 4 CKD). • Pregnant, lactating, or planning pregnancy within next 12 months. • Currently participating in an investigational drug or another device trial that has not reached its primary endpoint • Subjects with non-cardiac co-morbidities that are likely to result in a life expectancy of less than 12 months		
	SUMMIT (NCT03433274)	Randomised, parallel assignment, open-label	• Symptomatic, moderate-to-severe or severe mitral regurgitation, or severe mitral annular calcification (MAC) • NYHA ≥ II (if Class IV, patient must be ambulatory)	• Mitral valvular vegetation or mass • EF < 25% • LVEDD > 7.0 cm • Prior surgical or interventional treatment of mitral valve involving implantation of prosthetic material • Aortic valve disease requiring surgery or transcatheter intervention	Active	Mortality and HF hospitalisation at 12 months (randomised and MAC cohort); composite of mortality, HF hospitalisation, stroke, reintervention

				• Severe tricuspid regurgitation or any tricuspid valve disease requiring surgery or transcatheter intervention • Any planned surgical / interventional procedure within 60 day prior to or following subject randomisation • Subject undergoing haemodialysis due to chronic renal failure • Mitral pathoanatomy and left ventricular outflow tract anatomy deemed not suitable for Trial device implantation • Subjects with non-cardiac comorbidities that are likely to result in a life expectancy of less than 12 months		(non-randomised cohort)
Expanded Clinical Study of Tendyne Mitral Valve System (NCT02321514)	Single-arm, open-label	• age ≥18 years • Severe PMR or SMR aetiology according to MVARC (Mitral Valve Academic Research Consortium) 2015 defined as: ○ PMR: EROA ≥ 40 mm^2 or regurgitant volume ≥ 60ml ○ SMR: EROA ≥ 20 mm^2 or regurgitant volume ≥ 30ml • NYHA ≥ II while on guideline directed medical therapy (GMDT), including device therapy (CRT) if indicated. • Heart team determines patient is not a suitable candidate for traditional surgical treatment according to valid guidelines.	• Severe mitral annular calcification, severe mitral stenosis, valvular vegetation or mass. • Left Ventricle or Left Atrium thrombus. • Patient has a chest condition that prevents transapical access. • EF <30% • LVEDD > 7.0 cm • Prior surgical or interventional treatment of mitral or aortic valves. • Any planned surgery or interventional procedure within the period of 30 days prior to 30 days following the implant procedure. • Cardiac resynchronisation therapy device or implantable pulse generator implanted within three months of planned implant procedure. • Myocardial Infarction (MI) within 30 days of the planned implant procedure. • Symptomatic, unresolved multi-vessel coronary artery disease (CAD) or unprotected left main coronary artery disease requiring stenting or Coronary Artery Bypass Grafting (CABG). • Cerebrovascular accident (CVA) within six months of planned implant procedure. • Unresolved severe symptomatic carotid stenosis (> 70% by ultrasound). • Cardiogenic shock or hemodynamic instability requiring inotropes or mechanical support devices at the time of planned implant procedure. • Severe tricuspid regurgitation, tricuspid valve disease requiring surgery or severe right ventricular dysfunction. • Hypertrophic or restrictive cardiomyopathy, constrictive pericarditis or any other structural heart disease causing	191	Safety assessed by freedom from device or procedure related adverse events at 30 days Performance assessed by freedom from device malfunction at 30 days

				heart failure other than dilated cardiomyopathy of either ischemic or non-ischemic aetiology. • Any of the following: leukopenia, acute anaemia, thrombocytopenia, history of bleeding diathesis, or coagulopathy if cannot be adequately treated. • History of endocarditis within six months of planned implant procedure. • Active systemic infection requiring antibiotic therapy. • Known hypersensitivity or contraindication to procedural or post-procedural medications (e.g., contrast solution, anti-coagulation therapy) which cannot be adequately managed medically or hypersensitivity to nickel or titanium. • Patient has COPD and on home oxygen, on haemodialysis patient refuses blood transfusions, pulmonary arterial hypertension (fixed PAS >70mmHg). • Pregnant, lactating, or planning pregnancy within next 12 months. • Participating or planning participation in an investigational drug or another device study. • Patients with non-cardiac co-morbidities that are likely to result in a life expectancy of less than one year.		
Intrepid	APOLLO (NCT03242642)	Randomised, parallel assignment, open-label	• Moderate to severe or severe symptomatic MR • Local site multidisciplinary heart team experienced in mitral valve therapies agrees that the subject is unsuitable for treatment with approved transcatheter repair or conventional mitral valve intervention	• prior transcatheter mitral valve procedure with device currently implanted • anatomic contraindications • prohibitive mitral annular calcification • EF <30% • need for emergent or urgent surgery • hemodynamic instability	Active	All-cause mortality, stroke, reoperation (or reintervention) and cardiovascular hospitalisation at 1 year (randomised and single-arm cohort), all-cause mortality and HF hospitalisation (MAC cohort)
TIARA	TIARA I (NCT02276547)	Single-arm, open-label	• Severe symptomatic mitral regurgitation (Stage D) • High surgical risk for open mitral valve surgery • Subject meets the anatomical eligibility criteria for available size(s) • NYHA Class III or IV heart failure	• DMR deemed by the heart team to be operable. • Prohibitive risk, deemed too frail or listed for cardiac transplant. • Unsuitable cardiac structure	27	Freedom from all-cause mortality and major adverse events, stroke, MI, renal failure requiring dialysis, life-threatening bleeding, and cardiac surgical or transcatheter reintervention at 30 days
	TIARA II (NCT03039855)	Single-arm, open-label	• Severe MR • High surgical risk for open mitral valve surgery • Subject meets anatomical eligibility criteria	• Deemed too frail by objective frailty assessments • Previous cardiac procedures: any mitral valve replacement surgery and cardiac transplant • Unsuitable cardiac structure	115	Freedom from all-cause mortality, MAE and reduction of MR to optimal or acceptable at 30 days

				• Clinically significant untreated CAD • Subjects on chronic dialysis • Pregnant or planning pregnancy within next 12 months • Documented bleeding or coagulation disorders • Active infections requiring antibiotic therapy • Subjects with a life expectancy less than 12 months		
Evoque Eos	Edwards EVOQUE Eos MISCEND Study (NCT02718001)	Single-arm, open- label	• Clinically significant, symptomatic MR • High risk for open-heart surgery • Meets anatomical criteria	• Unsuitable anatomy • Patient is inoperable	123	Active
SAPIEN M3	ENCIRCLE Trial (NCT04153292)	Single group assignment, open-label	• age ≥18 years • MR ≥ 3+ • NYHA ≥ II • Per the Heart Team, commercially available surgical or transcatheter treatment options are deemed unsuitable due to clinical, anatomic or technical considerations. • Subject's heart failure management has been optimised based on subject characteristics and applicable guidelines, and stable for at least 30 days prior to enrolment.		Active	Composite of death and heart failure rehospitalisation at 1 year, improvement in NYHA, KCCQ scores and MR compared with baseline at 1 year
HighLife	HighLife Transcatheter Mitral Valve Replacement System Study (NCT02974881)	Single group assignment, open-label	• age ≥ 18 years • Severe mitral regurgitation • NYHA II, III or ambulatory IV. • Patient is under maximally tolerated GDMT (incl. CRT) for at least 3 months • Multidisciplinary Heart Team consensus that the patient is inoperable or at high-risk for surgical repair/replacement due to significant co-morbid conditions • Multidisciplinary Heart Team consensus that the patient is not a suitable candidate for other approved percutaneous repair therapy due to anatomical or medical conditions • Patient meets the anatomical criteria for HighLife valve sizing as determined by CT and TEE	• Mitral stenosis • Rheumatic valve disease • Severe calcifications of the mitral annulus and/or mitral leaflets • Prior surgical or interventional treatment of the mitral valve • Unsuitable anatomy for the transapical access • Unsuitable anatomy of the aorta and ilio-femoral vessels for the transfemoral access • Untreated clinically significant coronary artery disease requiring revascularisation • LVEF < 30% • LVEDD > 70mm • Echocardiographic evidence of intracardiac mass, thrombus or vegetation • Hypertrophic Obstructive Cardiomyopathy (HOCM) • Any surgical or interventional procedure (including PCI) done in the past 30 days prior to procedure	5	Freedom from MAEs at 30 days Continued intended performance of bioprosthesis at 30 days Technical success immediately after the procedure

AltaValve	AltaValve Early Feasibility Study (NCT03997305)	Single-arm, Open-label	• age ≥ 18 years • NYHA II-IV. • Severe MR as documented by echo. • Subjects who are at high risk for open-heart surgery as documented by the health care professional (e.g., Heart Team consisting of cardiac surgeon and interventional cardiologist in United States).	• Currently enrolled in any other pre-approval investigational study (does not apply to long-term post-market studies unless these studies might clinically interfere with the current study endpoints (e.g., limit use of study-required medication, etc.)). • Female subjects who are pregnant or planning to become pregnant within the study period. • Known hypersensitivity or contraindication to aspirin, heparin, or Warfarin without adequate alternative medications. • Known hypersensitivity to nitinol (i.e., nickel allergy) or contrast media that cannot be adequately medicated. • EF ≤30% (where current is defined as the latest LVEF measurement completed within 90 days prior to the index procedure). • Concurrent medical condition with a life expectancy of less than 12 months. • Prior mitral valve repair/replacement (excluding prior surgical mitral valve repair, annuloplasty, or MitraClip not interfering with AltaValve placement).	Active	Active

TEER=transcatheter edge-to-edge repair, MR=mitral regurgitation, LV=left ventricular, EF=ejection fraction, RCT=randomised control trial, AF=Atrial fibrillation, HTN=hypertension, AMI=acute myocardial infarction, SMR=secondary mitral regurgitation, RVol=regurgitant volume, EROA=effective regurgitant orifice area, NYHA=New York Heart Association, HF=heart failure, TAVI=transcatheter aortic valve implantation, HCM=hypertrophic cardiomyopathy, CHF=congestive heart failure, OMT=optimal medical therapy, MVA=Mitral valve area, RVD=right ventricular dysfunction, LVEDD=Left ventricular end diastolic dimension, ASD= atrial septal defect