2019 euro PCR

The MitrAl Valve rEpaiR Clinical (MAVERIC) trial

First worldwide presentation of the two year follow-up in 45 patients with functional mitral regurgitation

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2019 euro PCR

Speaker's name: Simon Redwood

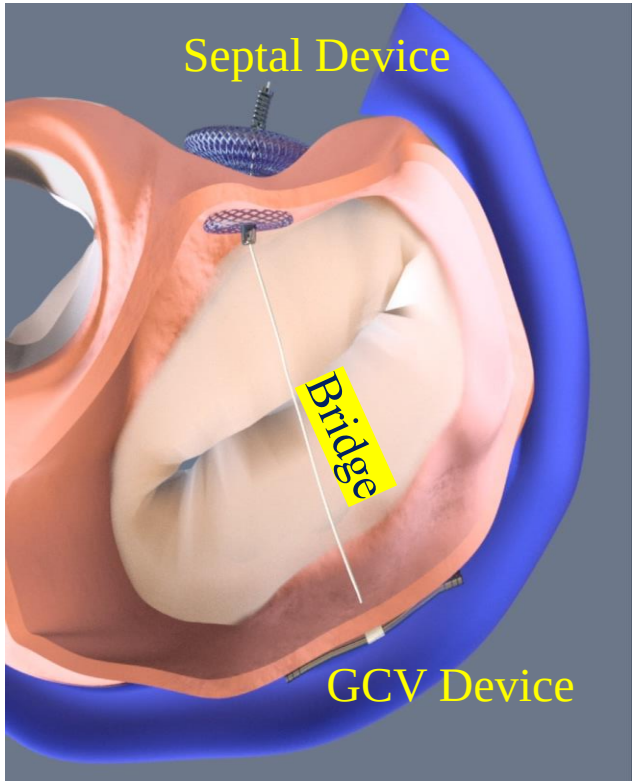
I have the following potential conflicts of interest to report:

- Study Proctor: MVRx, Inc.

Background

- Patients with systolic heart failure and functional mitral regurgitation (FMR) have limited therapeutic options
  - Medical therapy and resynchronization therapy have limited efficacy
  - Surgery rarely offered
    - Patients have comorbidities and often are high surgical risk
    - Lack of evidence leading to Class IIb, Level of Evidence C – in patients who have other indications for surgery (eg requiring CABG)
  - Other transcatheter repair devices have shown mixed results
    - eg COAPT vs MITRA-FR
  - Transcatheter repair of FMR with annular reshaping is desirable if shown to be safe and effective

ARTO™ System description



GCV=great cardiac vein

- ***Immediate and direct* A-P diameter shortening** to treat functional mitral regurgitation
- **No compression of left circumflex artery**
- Venous based delivery under fluoroscopic imaging
- Acutely **reversible or removable**
- **12 Fr** Delivery System
- **No residual ASD**, no trauma to native mitral valve leaflets or chords
- Ample room for future septal access

MAVERIC EU/AU STUDY DESIGN

Multi-Centre, Single Arm 45 Patient Safety and Efficacy Study

30 day, 6 month, 1 year, **2 year** and 3 year clinic/echo visit follow-up

Primary Outcome Measures:

- Safety: MACE at 30 days
- Efficacy: MR Grade at 30 days

Secondary Outcome Measures

- NYHA Class
- HF Hospitalization
- Device success

Major Inclusion Criteria:

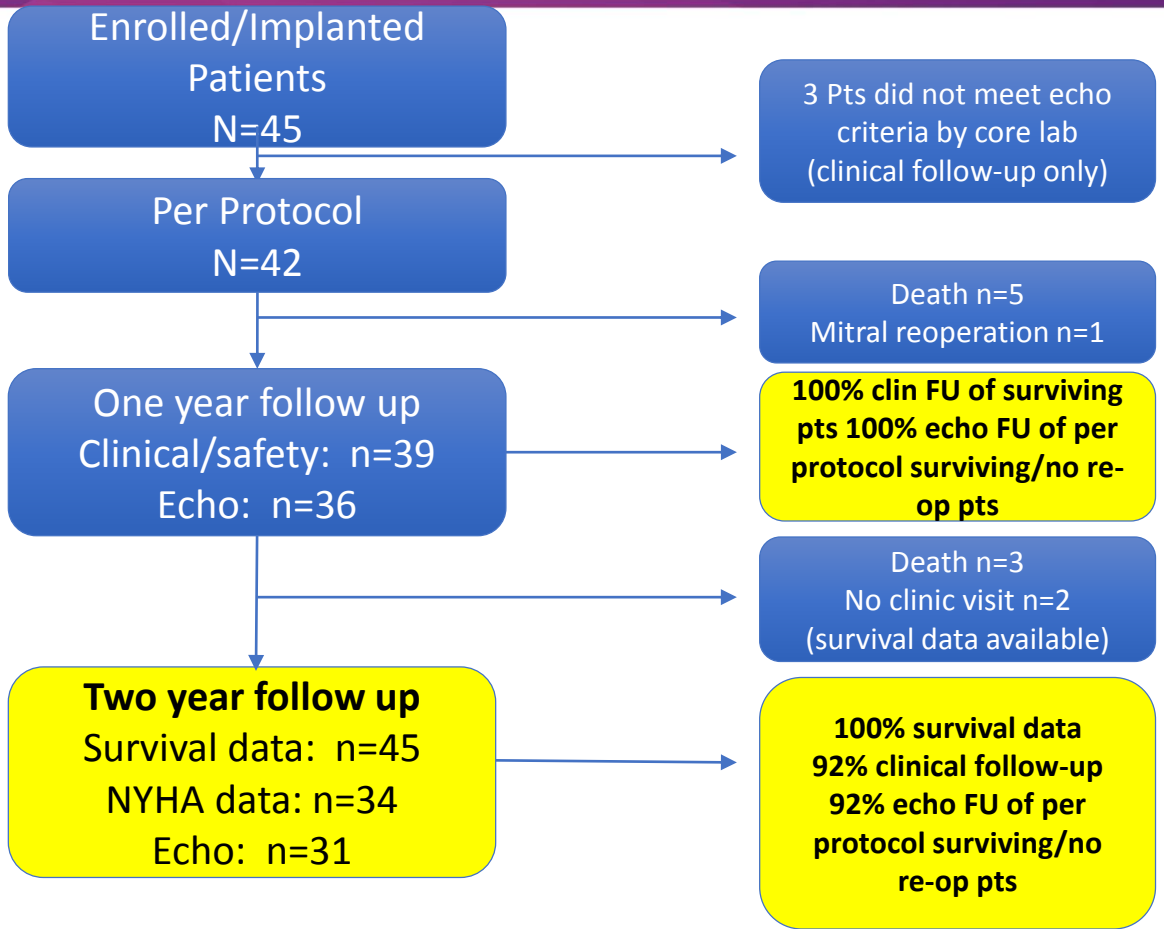
- MR Grade ≥ 2+
- NYHA Class II-IV
- Optimized medical therapy

Major Exclusion Criteria:

- Significant structural abnormality of the mitral valve
- Known need for any cardiac surgery
- Life expectancy <1 year

Echo Core Lab: Bertrand Cormier, All Events CEC Adjudicated, Study Mgmt: CERC

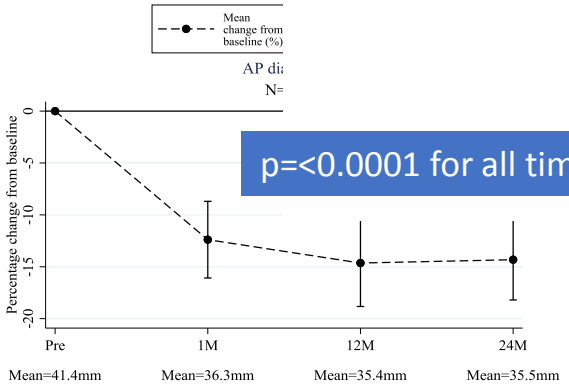
MAVERIC EU/AU Trial Patient Flow



MAVERIC Baseline Characteristics

Characteristic	All Patients (N=45)
Age (mean, std)	69.6 ± 12.4
Male Gender (%)	60.0
STS Score (mortality)	3.8± 3.4
Ischemic Aetiology (%)	41.8
HF Hospitalizations Prior 2 Years (mean ±sd)	0.7 ± 0.8
LVEF %	40.4 ± 9.0
Hypertension (%)	46.7
Prior MI (%)	37.8
Previous PCI (%)	33.3
Previous CABG (%)	13.3
Atrial Fibrillation (%)	44.4
Mod/Severe Renal Insuff(%)	55.8
COPD (%)	21.4
Mod/Severe Pulm HTN (%)	47.7

MAVERIC EU/AU: AP diameter immediately reduced and maintained at 2 years



p=<0.0001 for all timepoints vs baseline

14%

N=30

MAVERIC EU/AU: Immediate/Sustained MR Grade Reduction to 2 years

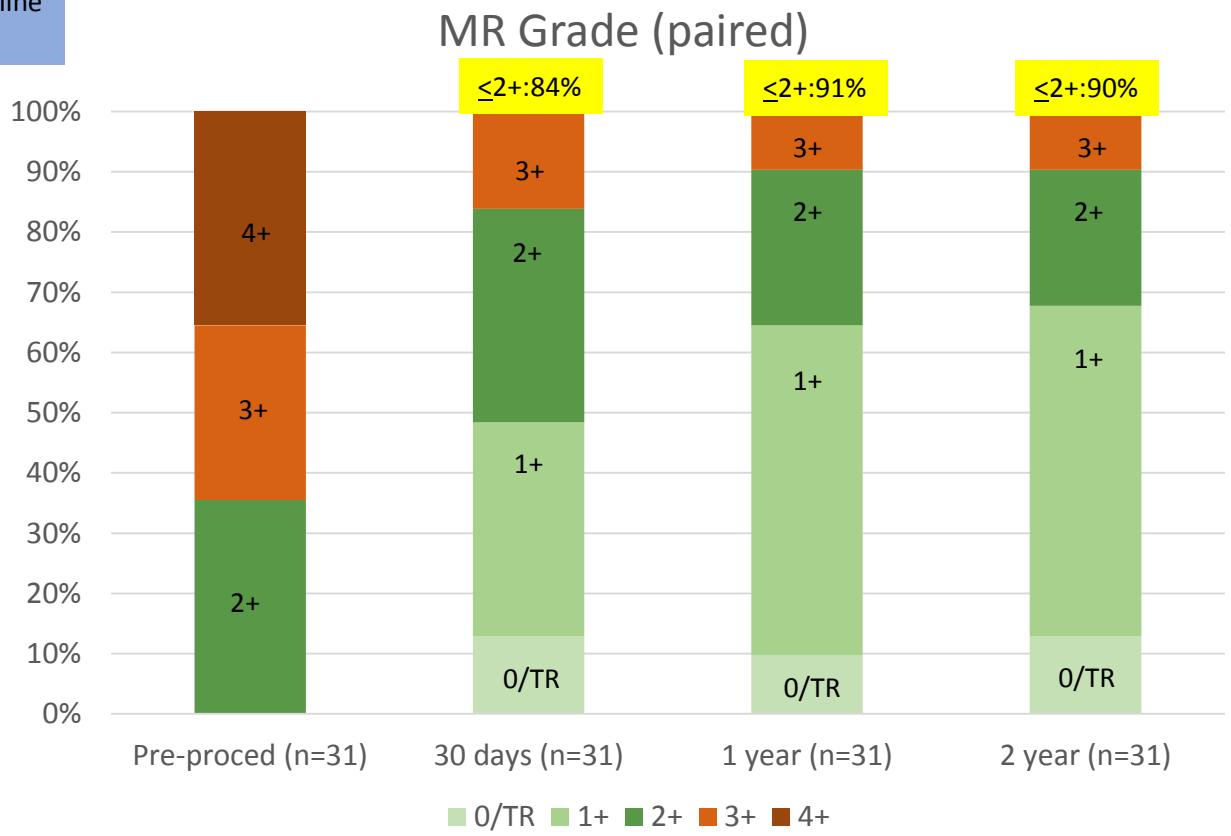
92% echo follow-up and core lab analysis

P=<0.0001 all time points vs baseline
P=NS between timepoints

Pre-pr: **65% ≤ 3/4+**

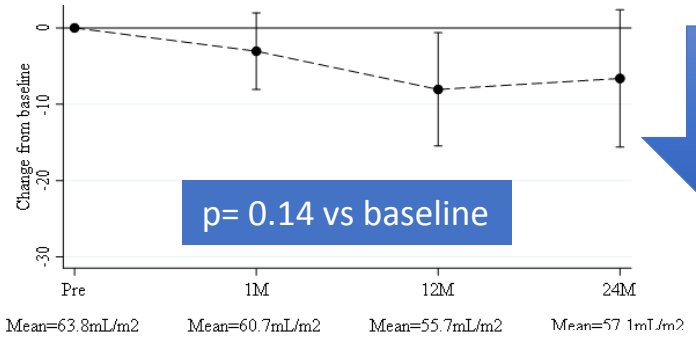
1 year: **65% ≤ 1+**
91% ≤ 2+

2 year: **68% ≤ 1+**
90% ≤ 2+



MAVERIC EU/AU: LV and LA Volumes Reduced at 30 days and Improved at 2 years

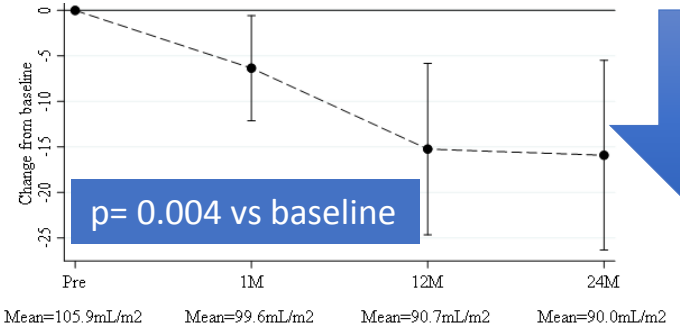
LVESVi



11%

p= 0.14 vs baseline

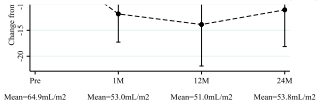
LVEDVi



15%

p= 0.004 vs baseline

LAVi

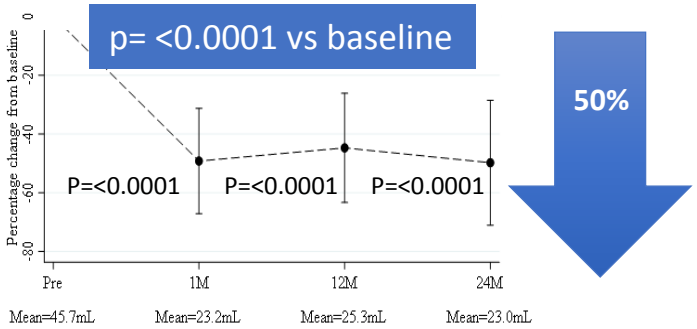


17%

p= 0.004 vs baseline

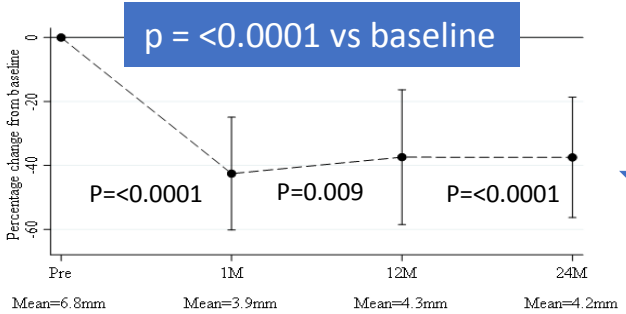
MAVERIC EU/AU: 50% reduction in Regurgitant Volume, 44% reduction in EROA and 39% reduction in Vena Contracta

Regurgitant Volume



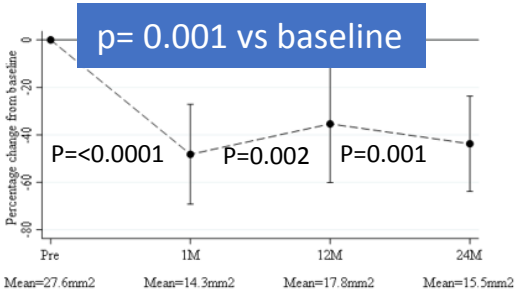
50%

EROA



44%

Vena Contracta



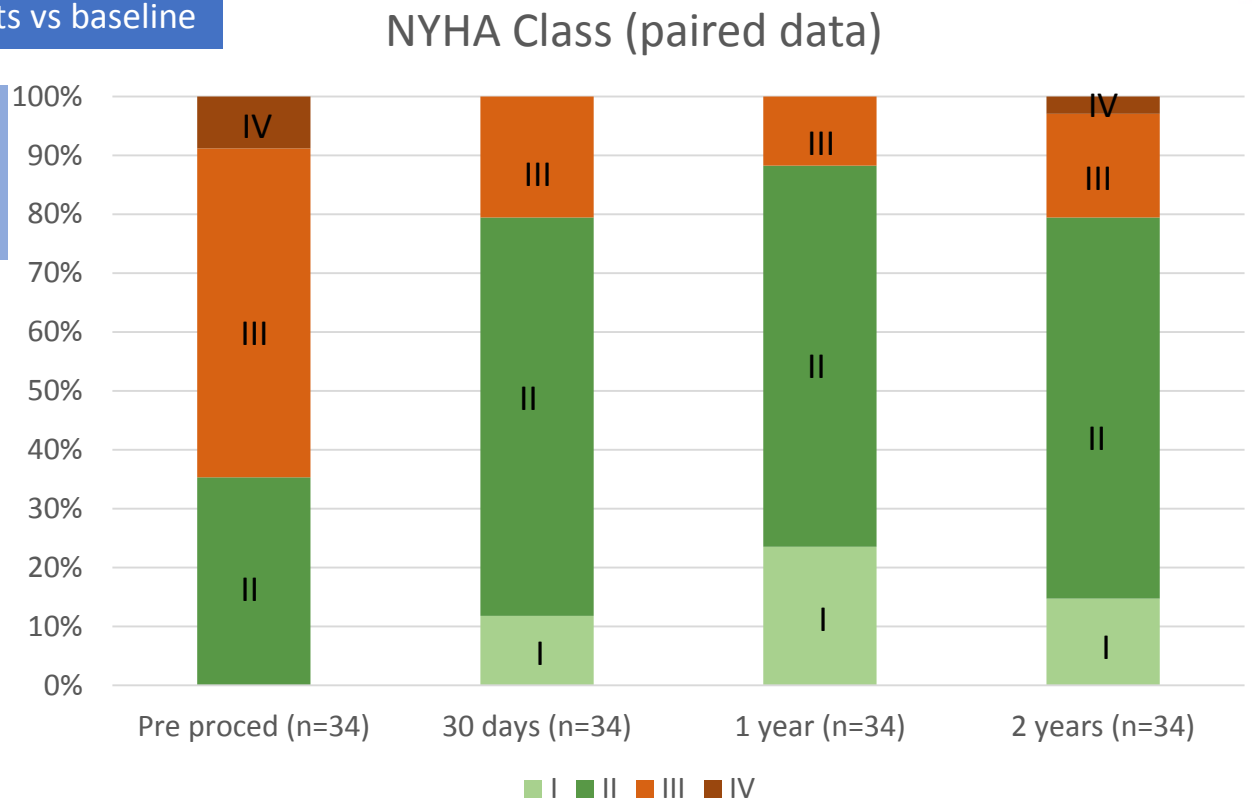
39%

MAVERIC EU/AU: Sustained NYHA Improvement to 2 years

92% clinical follow-up of all surviving(n=37)/no-reop (n=36) patients

p= <0.0001 at all timepoints vs baseline

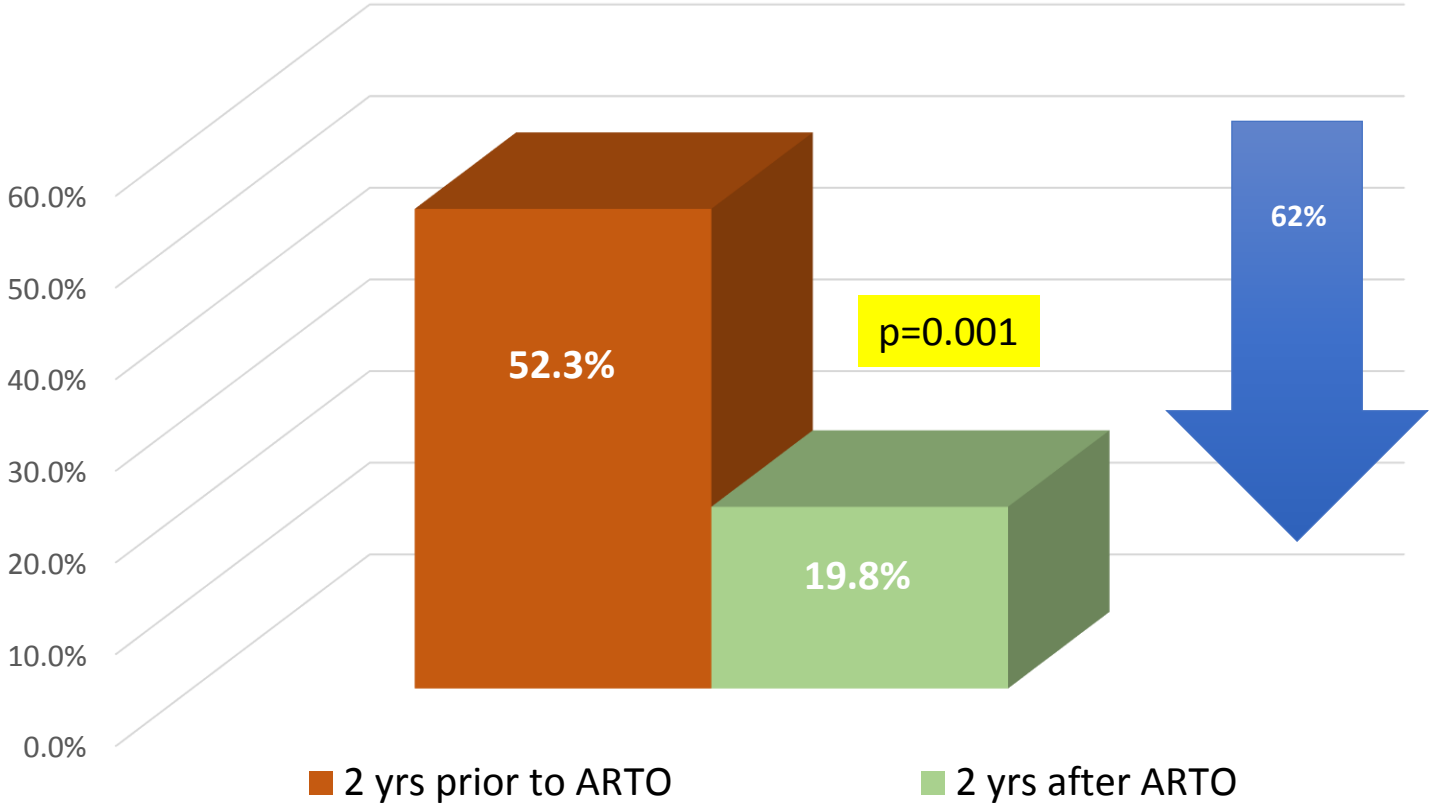
Baseline: 36% Class II
30 days: 80% Class I/II
2 years: 80% Class I/II



MAVERIC EU/AU: Low Rate of Heart Failure Hospitalisation To 2 Years

CEC Adjudicated Event	30 days N=45 N (KM%)	1 year N=44 cumulative N (KM %)	2 year N=44 Cumulative N (KM%)
HF Hospitalisation	0 (0)	4 (9.3%)	8 (19.8%)
Death	0 (0)	5 (11.3%)	8 (18.1%)
HF Hospitalisation or Death	0 (0)	8 (18.0%)	14(31.9%)

MAVERIC EU/AU: Heart Failure Hospitalisation 2 years prior to/after ARTO



MAVERIC EU/AU: Major Adverse Events to Two Year Follow-Up

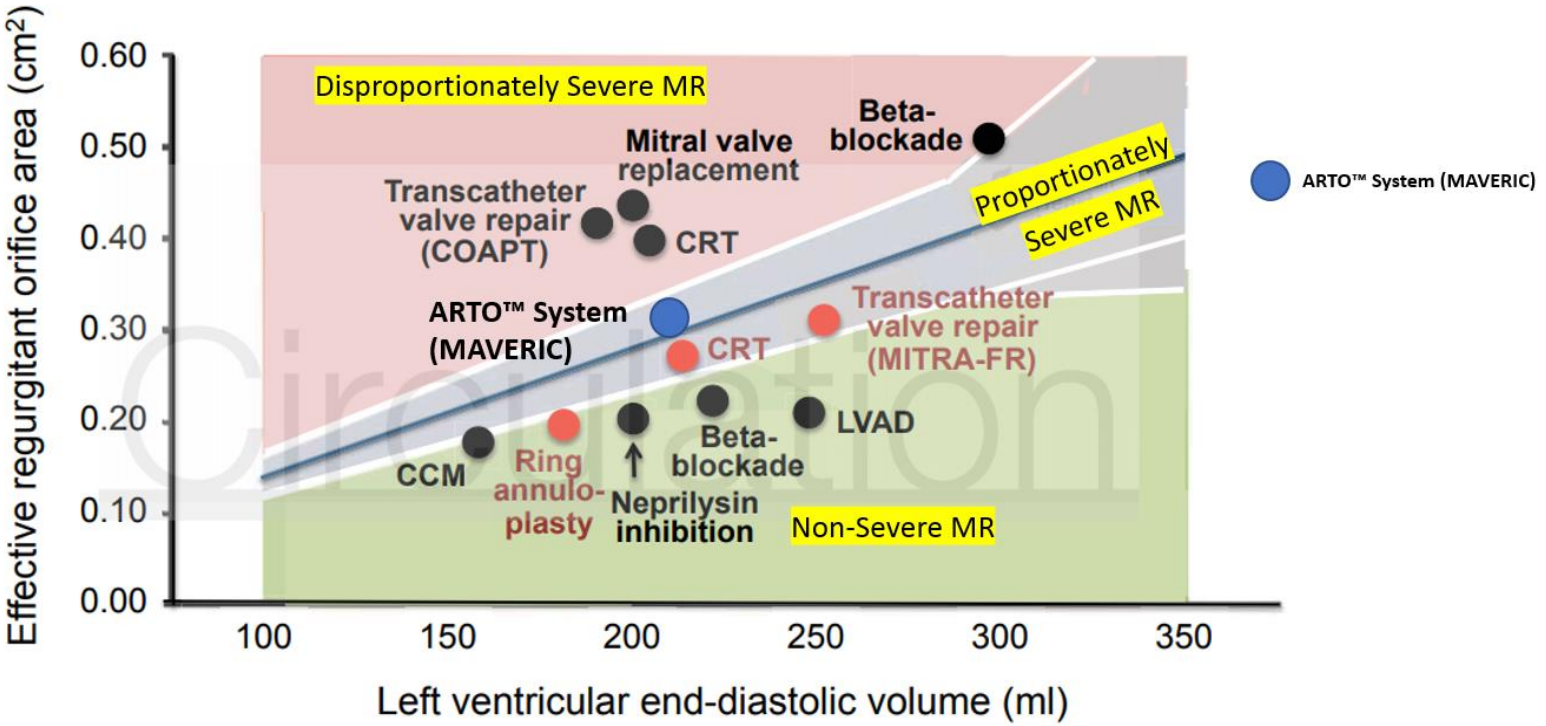
CEC Adjudicated Event	30 days N=45 N(KM %)	1 year N=44 N (KM%)	2 Year N=44 N(KM%)
Safety Composite Endpoint at 1 year*	2(4.4%)	8 (17.8%)	11(24.4%)
Death	0	5 (11.3%)	8(18.1%)
Cardiovascular	0	5 (11.3%)	8(18.1%)
Non-cardiovascular	0	0	0
Stroke	0	1 (2.3%)	1(2.3%)
Myocardial Infarction	0	1 (2.3%)	1(2.3%)
Device Related Cardiac Surgery	0	1 (2.3%)	1(2.3%)
Cardiac Tamponade	1 (2.2%)	1 (2.2%)	1(2.2%)
Renal Failure	1 (2.2%)	3 (7.0%)	3(7.0%)

*Death, Stroke, MI, cardiac tamponade, device related cardiac surgery, renal failure

Why is this important?

- At 2 year follow-up, significant reduction in MR grade by all measures.
- The ARTO System is the only transcatheter mitral repair technology to report a significant long term (2 year) reduction in LVEDV in patients with FMR.
- NYHA class after the ARTO procedure demonstrates improved and stable outcomes from the procedure to two years. Importantly, a **62% reduction** in heart failure hospitalisation at 2 years.
- The primary safety composite endpoint is low at 24.4%, as is mortality at 18.1% with no deaths attributed to the device or procedure
- This study demonstrates the 2 year efficacy and safety of the ARTO System for the treatment of functional mitral regurgitation.

MAVERIC patients vs COAPT And MITRA-FR patients



Adapted from: Packer and Grayburn et al., Circulation May 1, 2019

Mortality Cause and Timing

Patient Number	Days post procedure	CV vs non-CV (CEC adjudicated)	Related to Device/Procedure? (CEC adjudicated)	Cause of death (CEC adjudicated)	MR Grade at baseline/latest visit
826-03-1005	32	Cardiovasc	No/No	Ischemic heart disease	2+/2+
826-04-1003	73	Cardiovasc	No/No	Ischemic heart disease	4+++/4+
61-03-1004	176	Cardiovasc	No/No	Heart failure	4+/2+
61-01-1006	258	Cardiovasc	No/No	Heart Failure	3+/2+
61-03-1003	279	Cardiovasc	No/No	Heart failure	4+/1+
371-01-1010	567	Cardiovasc	No/No	Heart failure	3+/1+
371-01-1005	568	Cardiovasc	No/No	Heart failure	3+/1+
826-03-1003	592	Cardiovasc	No/No	Heart failure	4+/2+