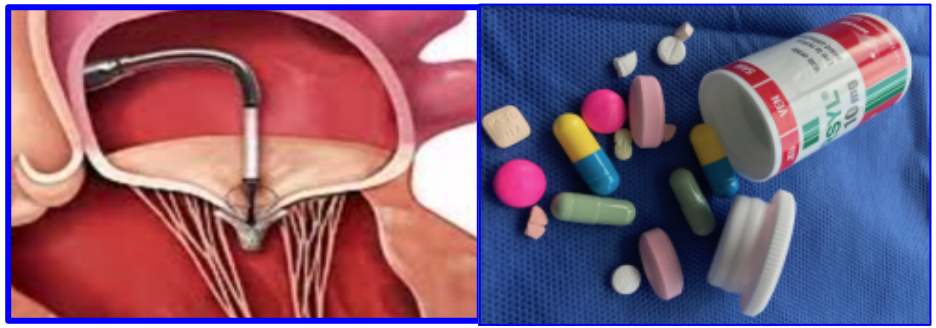
2 Years results of the Mitra.fr trial

Percutaneous Treatment for Secondary MR



Jean François OBADIA - LYON

on behalf of the MITRA-FR Investigators

Declaration of interest

- Consulting/Royalties/Owner/ Stockholder of a healthcare company (abbott, medtronic, Edwards, Landanger, delacroix chevalier, sanofi)

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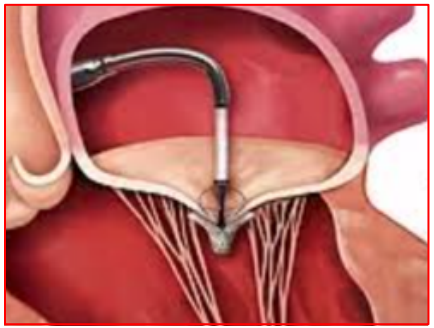
Primary objective : efficacy and safety of percutaneous Mitral Valve Repair in patients with heart failure and severe secondary mitral regurgitation. 12 months ➔ 24 months



EuroIntervention 2015;10:1354-1360

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ORIGINAL ARTICLE

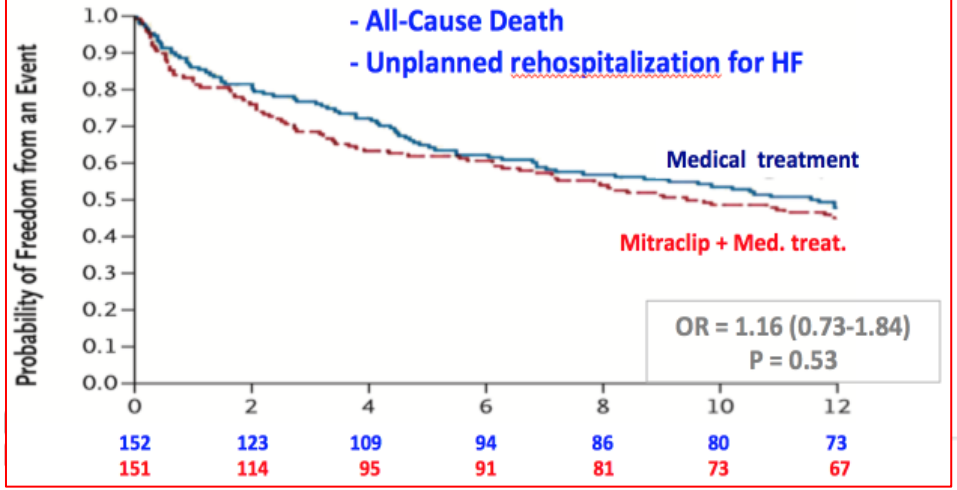
Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation

J.-F. Obadia, D. Messika-Zeitoun, G. Leurent, B. Iung, G. Bonnet, A. Piriou, T. Lefèvre, C. Piot, F. Rouleau, D. Carrié, M. Nejjari, P. Ohlmann, E. Leclercq, C. Saint Etienne, E. Teiger, L. Leroux, N. Karam, N. Michel, M. Gilard, F. Donal, J.-N. Trochu, B. Cormier, X. Armoiry, F. Boutitie, D. Maucort-Boulch, E. Barnel, G. Samson, P. Guerin, A. Vahanian, and N. Mewton, for the MITRA-FR Investigators.

Mitra.fr 27-08-2018

Primary composite endpoint *(99% follow-up)*

- All-Cause Death
- Unplanned rehospitalization for HF



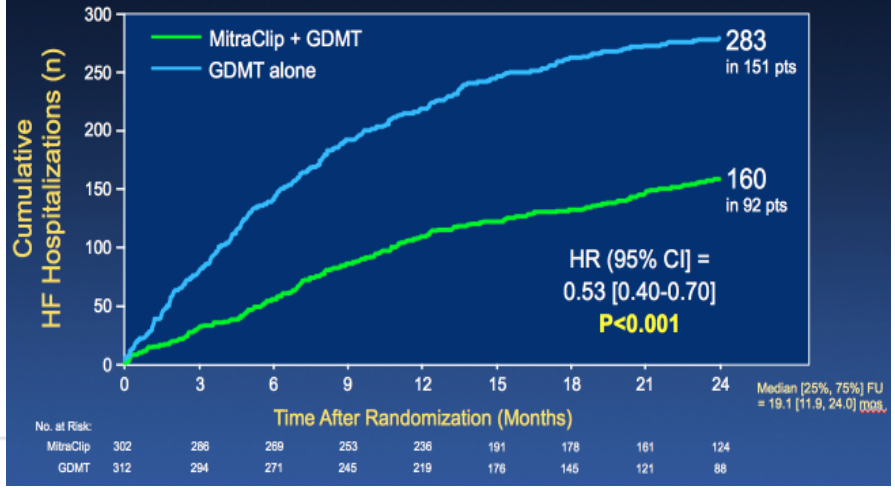
ORIGINAL ARTICLE

Transcatheter Mitral-Valve Repair in Patients with Heart Failure

G.W. Stone, J.A. Lindenfeld, W.T. Abraham, S. Kar, D.S. Lim, J.M. Mishell, B. Whisenant, P.A. Grayburn, M. Rinaldi, S.R. Kapadia, V.R. Rajagopal, I.J. Sarembock, A. Brieke, S.O. Marx, D.J. Cohen, N.J. Weissman, and M.J. Mack, for the COAPT Investigators*

Coapt 23-09-2018

All Hospitalizations for HF within 24 months



Study funding

* **Study Sponsor:** Hospices Civils de Lyon

Academic Study supported by a French Research Program grant from ministry of Health "**PHRC**"

* **Abbott Vascular involvement :**
  - Proctoring of the teams
  - Financing 84% of the clips

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- **Primary Endpoint "Composite" :** All-Cause Deaths or first Unplanned rehospitalization for Heart failure

- **Inclusion Criteria**
  - **Symptomatic despite GDMT (NYHA ≥II).**
  - **At least one hospitalization for HF within 12 months preceding randomization**
  - **Severe Secondary MR ➔ ERO > 20 mm² or R.vol>30 mL/beat**
  - **15% < EF < 40%**
  - **Not eligible for surgery by a local Heart Team, (No central eligibility)**
  - **Centralized echocardiographic Corelab**

**Obadia et al. Eurointervention 2015;10:1354-1360*

Baseline characteristics 1/2

Characteristics	Percutaneous Repair Group (n=152)	Optimal Medical Treatment Group (n=152)	P value
Age year mean (±SD)	70.1 ± 10.1	70.6 ± 9.9	0.69
>75 year n (%)	51 (33.6)	59 (38.8%)	0.40
Males n - (%)	120 (78.9)	107 (70.4%)	0.11
Ischemic Cardiomyopathy n - (%)	95 (62.5)	85 (56.3%)	0.29
NYHA Class II n - (%)	56 (36.8)	44 (28.9%)	
NYHA Class III n - (%)	82 (53.9)	96 (63.2%)	0.27
NYHA Class IV n - (%)	14 (9.2)	12 (7.9%)	
LVEF mean (±SD)	33.3 ± 6.5	32.9 ± 6.7	0.79
Effect regurg. Orif. area - mm² mean (±SD)	31 ± 10	31 ± 11	0.42

60%

2/3

EF=33%

S=31mm²

Baseline characteristics 2/2

Characteristics	Percutaneous Repair Group	Optimal Medical Treatment Group	P value
NTproBNP - ng/L median [IQR]	3407 [1948; 6790]	3292 [1937; 6343]	0.97
Implantable cardioverter-defibrillator	90 (59.2%)	82 (53.9%)	0.42
Diuretics	151 (99.3%)	149 (98.0%)	0.62
Beta-blockers	134 (88.2%)	138 (90.8%)	0.57
ACE- inhibitor / ARB	111 (73.0%)	113 (74.3%)	0.55
Mineralocorticoid Receptor Antagonist	86 (56.6%)	80 (53.0%)	0.56
ARB and Neprilysin Inhibitor	14 (10.0%)	17 (12.1%)	0.70
Systolic Blood Pressure mmHg mean (±SD)	109 ± 16	108 ± 18	0.78

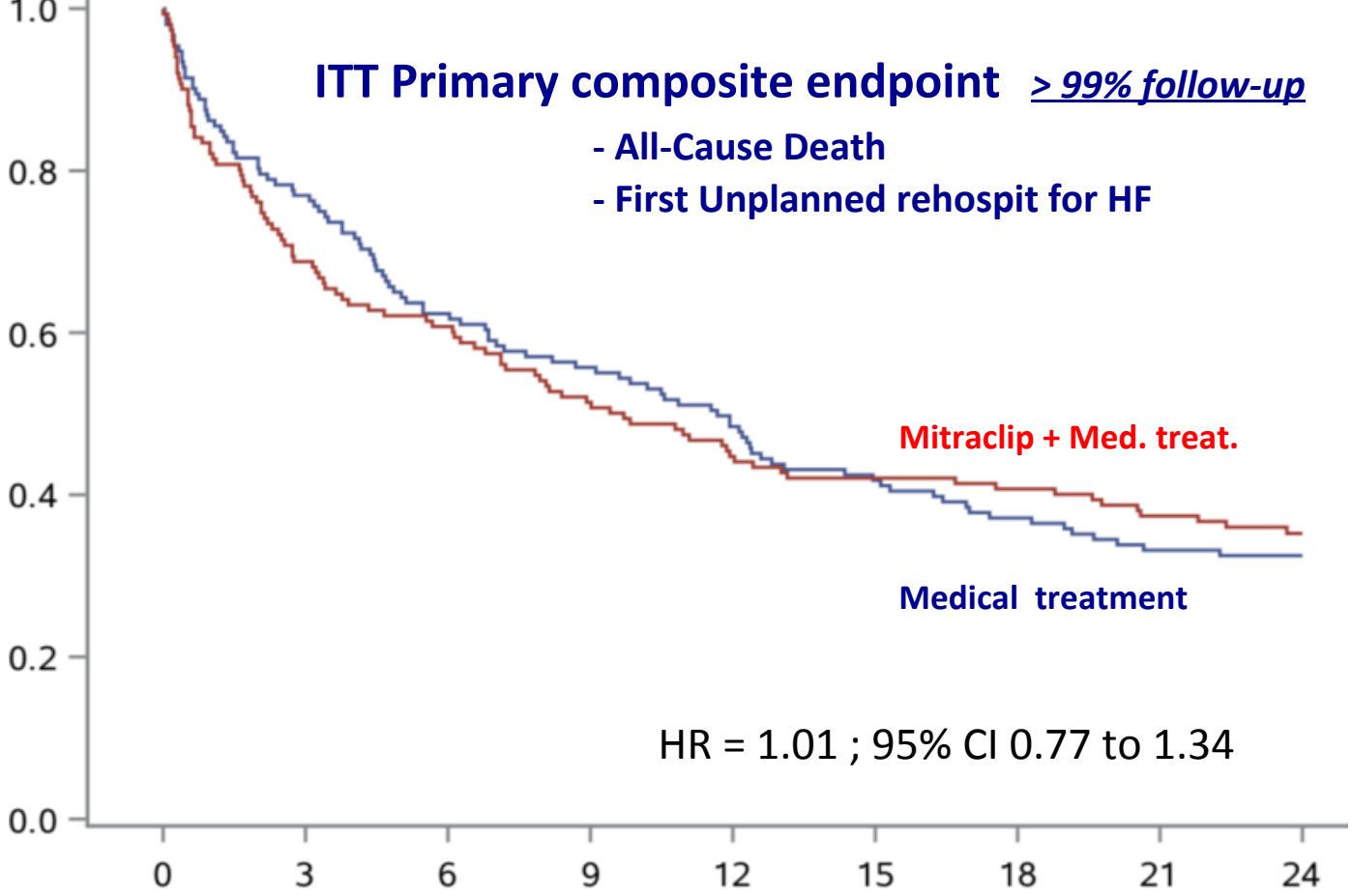
Efficacy and Safety after 24 months

* Safety	Peri procedural complications
Urgent conversion to heart surgery	0
Peri-procedural Mortality (at 3 days)	0
Vascular complication requiring surgery / Hemorrhage transfusion	5 (3.5%)
Cardiac embolism (Gas embolism / Stroke)	2 (1.4%)
Tamponade	2 (1.4%)
2 years follow-up	0
* Efficacy Technical Implantation Success MVARC	132/138 (> 95 %)

- 1 Clip ➔ 46%
- 2 Clips ➔ 45%
- 3+ Clips ➔ 9%

ITT Primary composite endpoint *> 99% follow-up*

- All-Cause Death
- First Unplanned rehospit for HF



Control group	152	116	94	84	73	63	56	50
Intervention group	151	103	91	77	67	63	61	56

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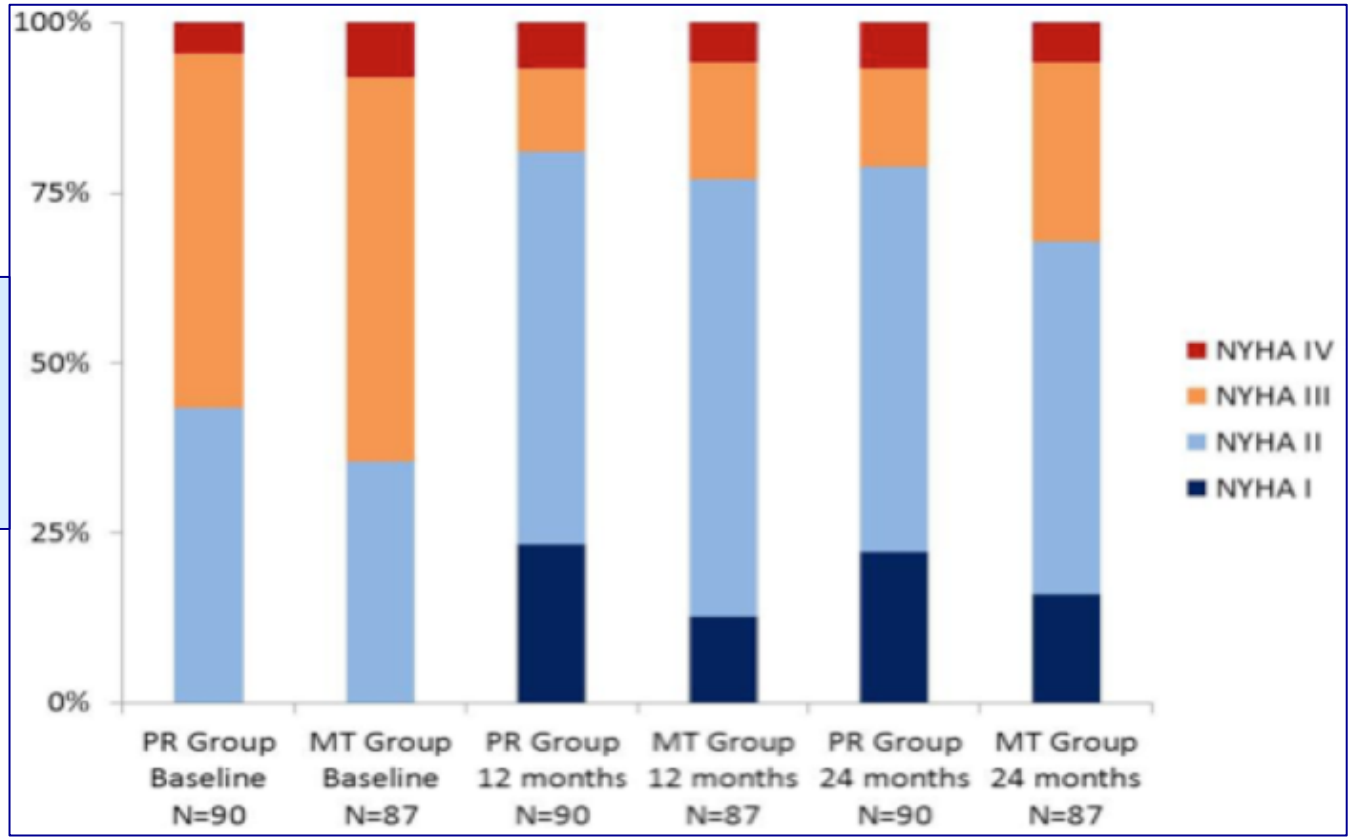
NYHA
at 12 and 24 months

Worst-case Scenario



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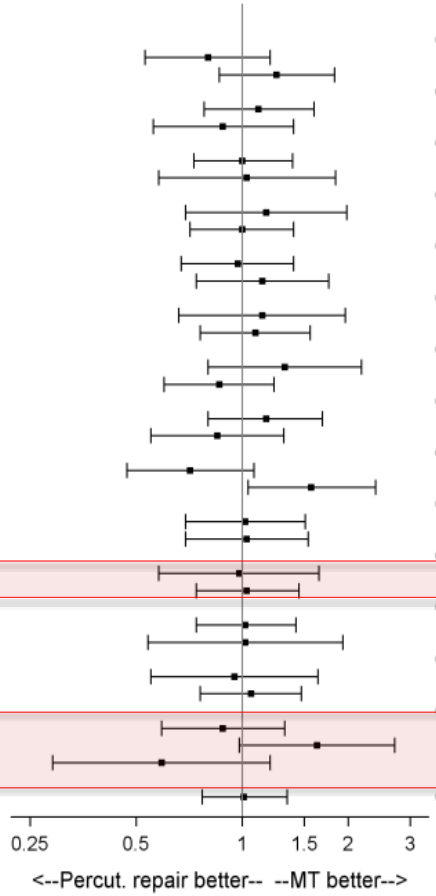
Sub-group Analysis at 24 months

Subgroup	Percut. repair Events/N (%)		Medical treatment Events/N (%)		HR (95% CI)	P Value*
CENTRE SIZE						0.11
N <= 15 Randomized patients	42/75	(56.0)	49/74	(66.2)	0.80 (0.53, 1.20)	
N > 15 Randomized patients	55/77	(71.4)	53/78	(67.9)	1.25 (0.86, 1.83)	
AGE						0.44
<= 75 Yr	63/101	(62.4)	60/93	(64.5)	1.11 (0.78, 1.60)	
> 75 Yr	34/51	(66.7)	42/59	(71.2)	0.88 (0.56, 1.40)	
GENDER						0.94
Male	77/120	(64.2)	74/107	(69.2)	1.00 (0.73, 1.39)	
Female	20/32	(62.5)	28/45	(62.2)	1.03 (0.58, 1.84)	
NYHA						0.62
Class II	34/56	(60.7)	25/44	(56.8)	1.17 (0.69, 1.98)	
Class III/IV	63/96	(65.6)	77/108	(71.3)	1.00 (0.71, 1.40)	
ISCHEMIC CARDIOMYOPATHY						0.58
Yes	58/95	(61.1)	57/85	(67.1)	0.97 (0.67, 1.40)	
No	39/57	(68.4)	44/66	(66.7)	1.14 (0.74, 1.76)	
PULMONARY ARTERY PRESSURE						0.88
< 50 mmHg	30/53	(56.6)	24/45	(53.3)	1.14 (0.66, 1.96)	
≥ 50 mmHg	55/74	(74.3)	66/88	(75.0)	1.09 (0.76, 1.56)	
ATRIAL FIBRILLATION						0.17
Yes	34/49	(69.4)	30/48	(62.5)	1.32 (0.80, 2.18)	
No	55/93	(59.1)	68/99	(68.7)	0.86 (0.60, 1.23)	
PREVIOUS HOSPIT FOR CHF						0.28
< 2	59/97	(60.8)	54/88	(61.4)	1.17 (0.80, 1.69)	
≥ 2	38/55	(69.1)	47/63	(74.6)	0.85 (0.55, 1.31)	
CREATININE						0.01
< 1 5 mg/dl	40/76	(52.6)	58/85	(68.2)	0.71 (0.47, 1.08)	
≥ 1 5 mg/dl	56/72	(77.8)	43/66	(65.2)	1.57 (1.04, 2.39)	
HEMOGLOBINE						0.90
< Median	49/76	(64.5)	44/66	(66.7)	1.02 (0.69, 1.51)	
≥ Median	46/73	(63.0)	52/80	(65.0)	1.03 (0.69, 1.54)	
LVEF						0.87
< 30%	24/37	(64.9)	36/48	(75.0)	0.98 (0.58, 1.65)	
≥ 30%	73/115	(63.5)	66/103	(64.1)	1.03 (0.74, 1.45)	
TRICUSPID REGURGITATION						0.99
Mild	69/111	(62.2)	79/119	(66.4)	1.02 (0.74, 1.42)	
Moderate/Severe	22/29	(75.9)	17/23	(73.9)	1.02 (0.54, 1.93)	
LV TELEDIASTOLIC DIAMETER						0.75
< 65 mm	26/44	(59.1)	27/46	(58.7)	0.95 (0.55, 1.64)	
≥ 65 mm	71/108	(65.7)	74/105	(70.5)	1.06 (0.76, 1.47)	
MITRAL REGURGITANT ORIFICE						0.81
< 30 mm2	45/77	(58.4)	53/80	(66.3)	0.88 (0.59, 1.32)	
30-40 mm2	33/46	(71.7)	32/52	(61.5)	1.63 (0.98, 2.71)	
> 40 mm2	19/29	(65.5)	17/20	(85.0)	0.59 (0.29, 1.20)	
OVERALL	97/152	(63.8)	102/152	(67.1)	1.01 (0.77, 1.34)	0.92



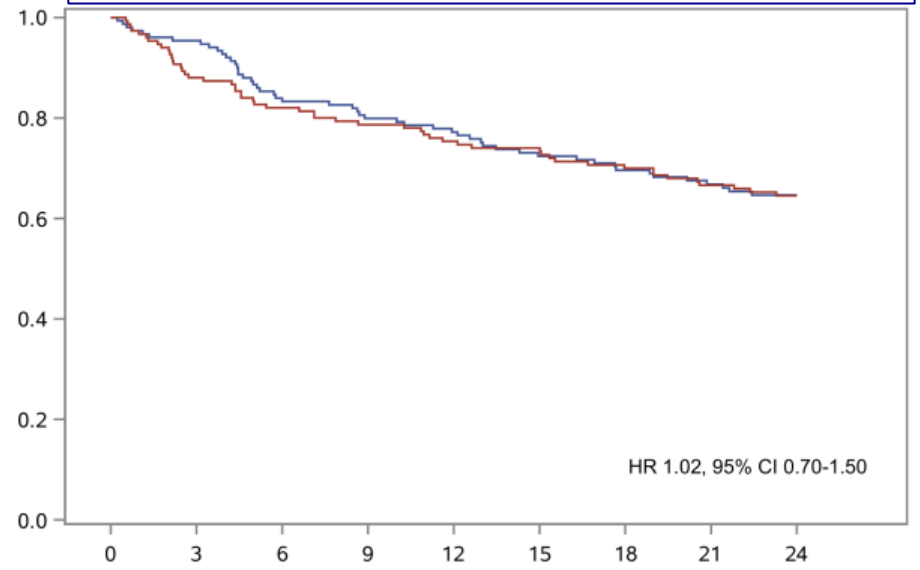
* P-Value is the test of interaction between treatment and eachsubgroup unadjusted for multiplicity

24 months Per-protocol Analysis	Percutaneous Repair Group (N=109)	Medical Treatment Group (N=137)	Hazard Ratio [b] (95%CI)
Composite primary outcome: death from any cause or unplanned hospitalization for heart failure – no. (%)	70 (64.2)	94 (68.6)	1.04 (0.76-1.42)
Secondary outcomes			
Death from any cause	37 (33.9)	48 (35.0)	0.99 (0.64-1.52)
Cardiovascular death	34 (31.2)	44 (32.1)	0.99 (0.63-1.55)
Unplanned hospitalization for heart failure	64 (58.7)	87 (63.5)	1.03 (0.74-1.43)
Major adverse cardiovascular	72 (66.1)	94 (68.6)	1.09 (0.80-1.48)

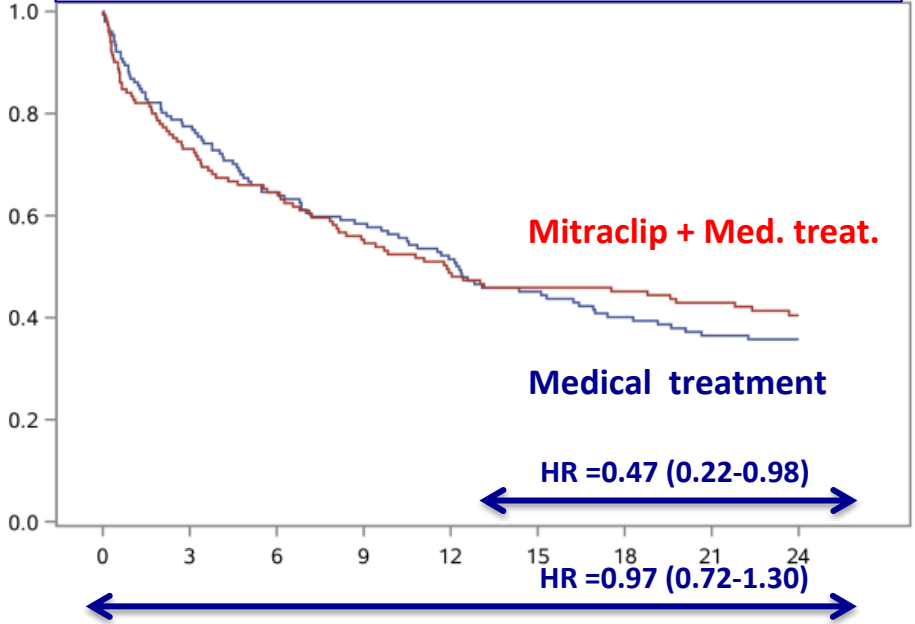
ITT Primary composite endpoint *(95% follow-up)*

- All-Cause Death
- First Unplanned rehospit for HF

Mortality



Incidence of first hospitalization for HF



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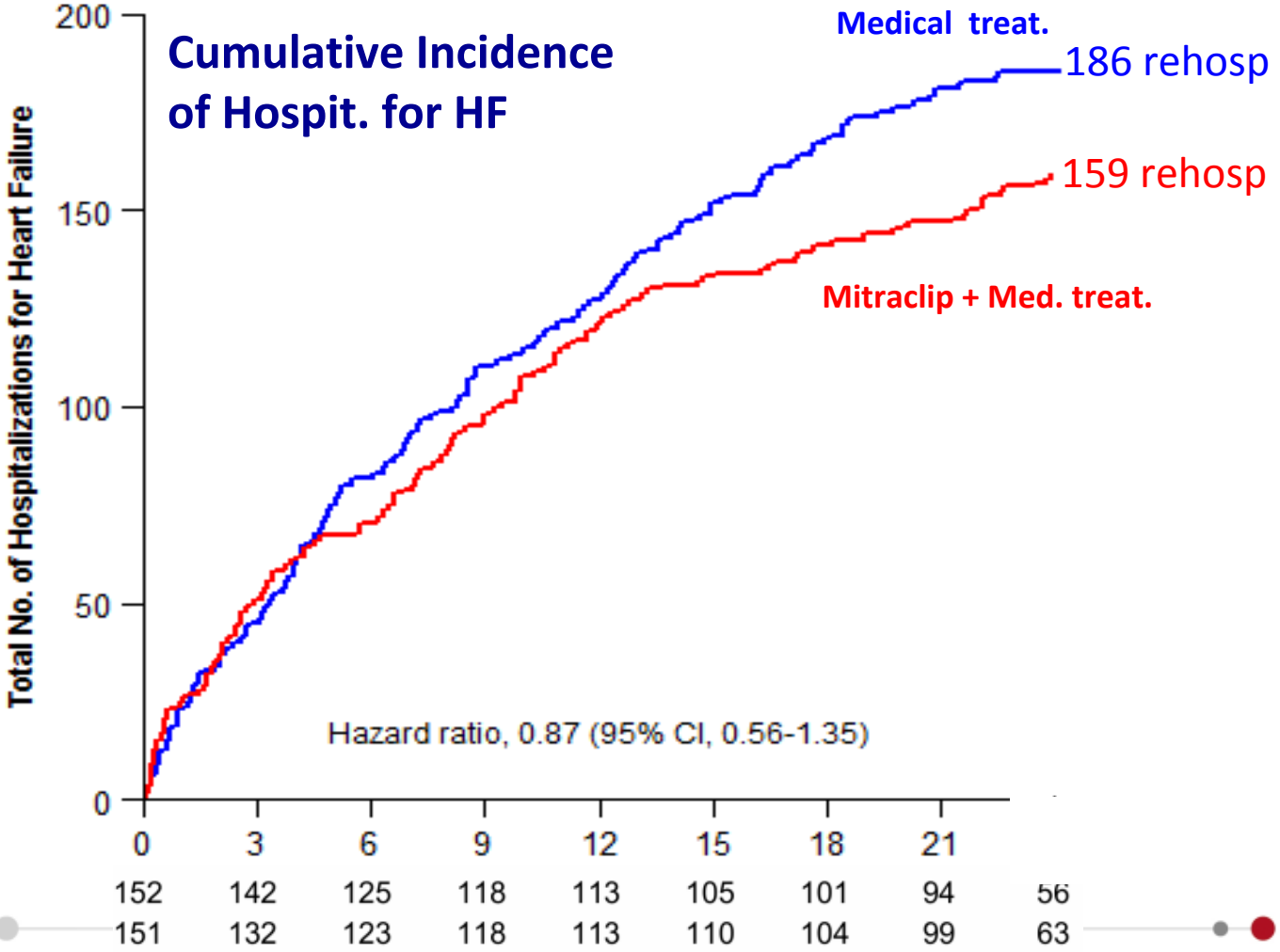
Cumulative Incidence of Hospit. for HF



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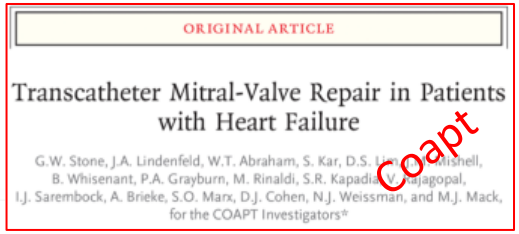

	Mitra-fr (n=304)	COAPT (n=614)
Roll in period	5 patient / Center	3 patient / center
Enrolment / Inclusion / center	3.2 years : 8.2 / Center ➔ 2,6/y	4.8 years : 7.8 / center ➔ 1.6/y
Technical Implantation success	96%	98%
EROA (mean ± SD)	31 ± 10 mm^2	41 ± 15 mm^2
LVEDV (mean ± SD)	135 ± 35 mL/m^2	101 ± 34 mL/m^2
GDMT at baseline and FU	variable adjustment in each group per "real-world" practice	GDMT at baseline few major changes during FU
Mortality at 1y and 2y	≈ 23% and 34%	≈ 20% and 46%/29%
MR ≥ 3+ at BL ➔ 12m ➔ 24m	8% ➔ 17% ➔ ?	7.4% ➔ 5% ➔ 0.9%


ORIGINAL ARTICLE

Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation

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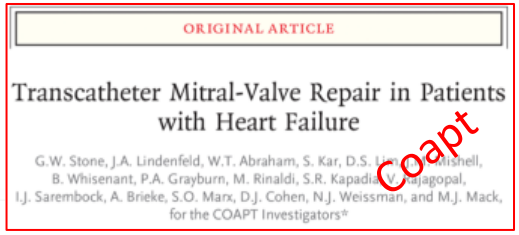
ORIGINAL ARTICLE

Transcatheter Mitral-Valve Repair in Patients with Heart Failure

Coapt

But

- Only ERO can be compared (MR grades not standardized)
- No major differences in NYHA class and LVEF
- Shorter 6-min walk test distance in Coapt (≈50 m)
- Mortality in control group : 46 % in Coapt / 34% in Mitra.fr

Confirmation :

- High mortality rate during FU
- Mitraclip well tolerated after 2 years

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Conclusion

Manuscript Online ➔

- The 24 months results of the MITRA-FR trial confirms that the addition of percutaneous clip to medical treatment did not decrease the rate of death or unplanned hospitalization for heart failure.
- After 24 months we have seen trends in subgroup or post hoc analysis but the lack of power limits the relevance of such analysis.
- Next steps ➔ Mitra.fr patients up to 5 years
  ➔ Meta-analysis on individual data