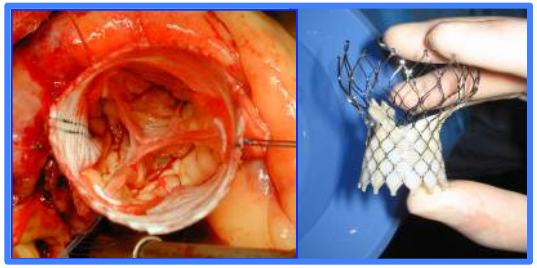
Professor Jean-François OBADIA
Hôpital Louis Pradel
- LYON - France

- **1 400 open heart Surgery / y**
- 300 beating heart coronary Revasc
- 600 pediatric
- 500 General Thoracic
- 300 Vascular Surgery

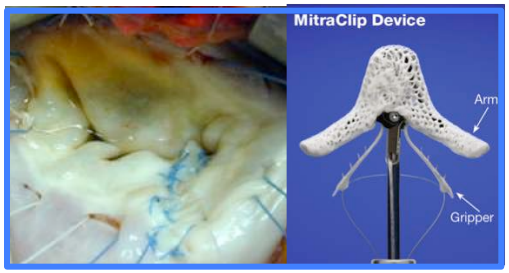
- **Transplantation**
  - 40 Heart / y
  - 30 Lung / y
  - x Heart/lung
  - 25 Cardiac Assistance
  - 100 ECMO

- **Conservative Valvular Sugery**

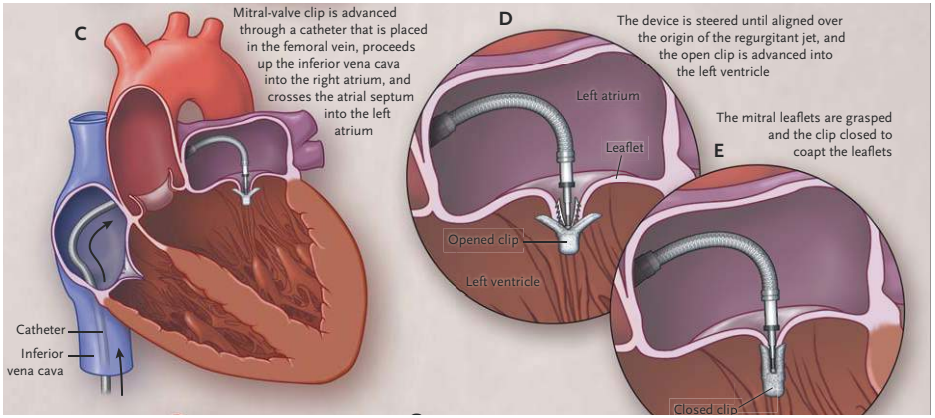
Aortic

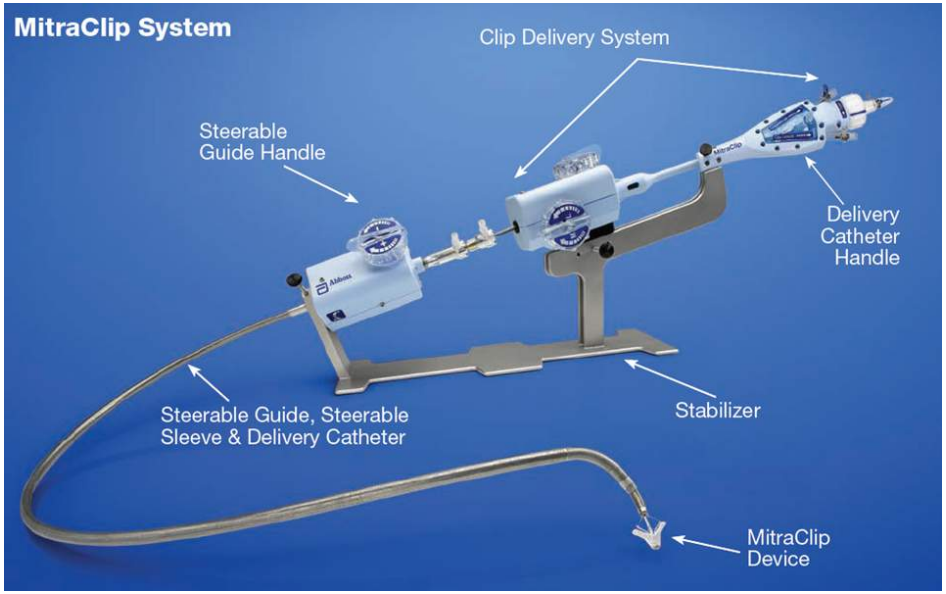


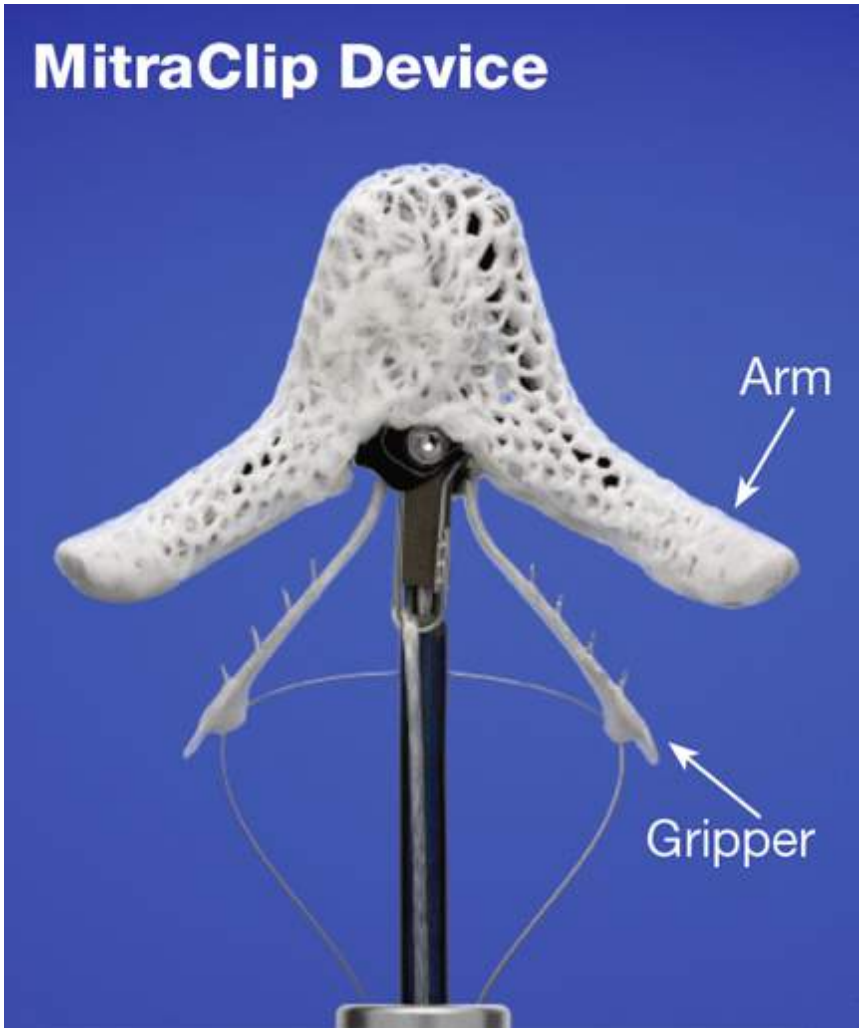
Mitral



Mitraclip : Indications passées, présentes et futures

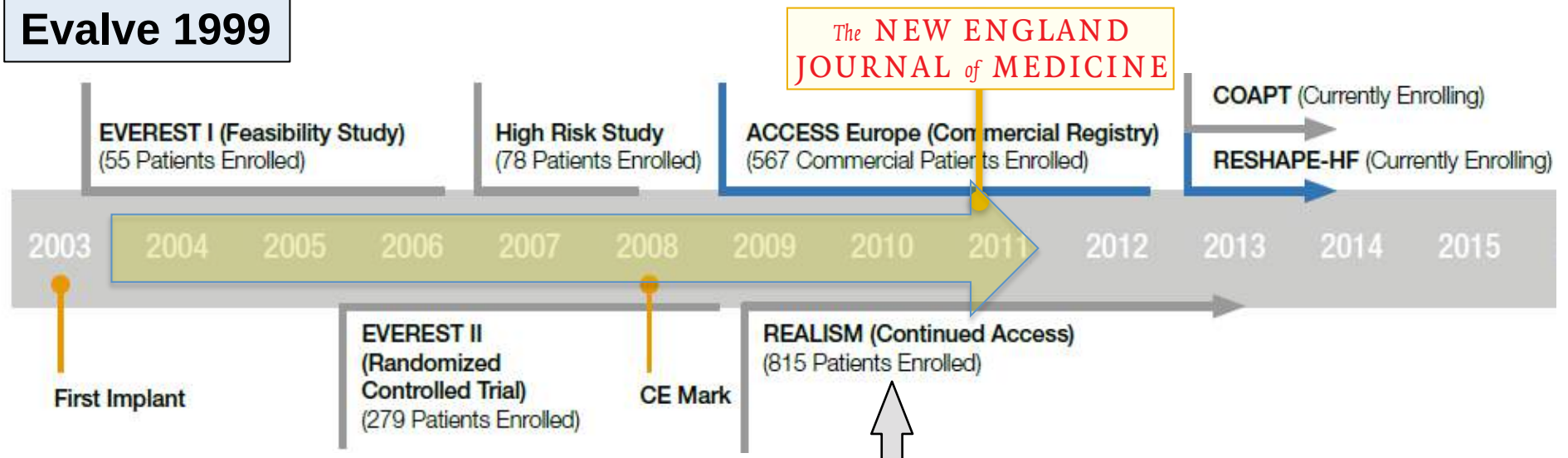




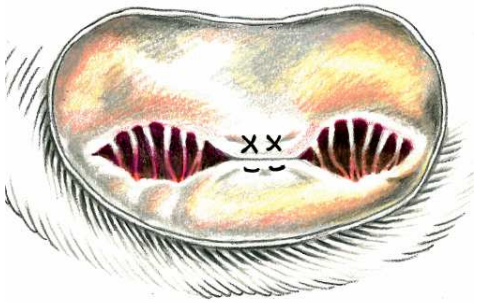


Mitraclip : 1) Indications passées ?

Evalve 1999



Premiers patients français

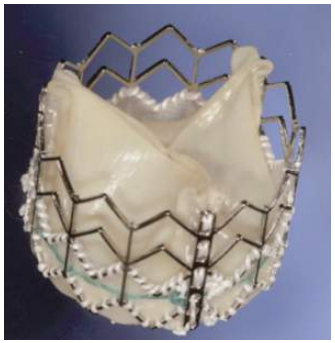


Mitraclip : 1) Indications passées ?

The NEW ENGLAND JOURNAL of MEDICINE

TAVI ➔ Sept. 2010 Partner

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery



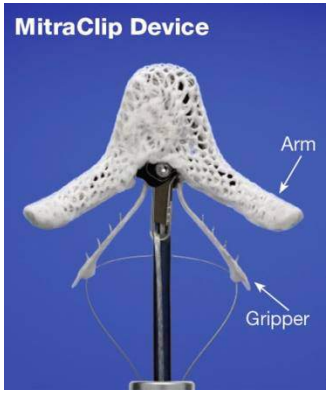
1) STS score > 10 %

2) Not suitable candidate
- for 2 Surgeons

The NEW ENGLAND JOURNAL of MEDICINE

MitraClip ➔ Avril 2011 Everest

Percutaneous Repair or Surgery for Mitral Regurgitation



1) **Symptomatique**
   - **EF > 25 %**
   - **ESD < 55mm**
2) **Asymptomatique**
   - **EF < 60 %**
   - **ESD > 45 mm**

Mitraclip : 1) Indications passées ?

EVEREST II ➔ 279 patients underwent Randomization

184 patients were assigned to percutaneous-repair group

95 patients were assigned to surgery group

3 who did not receive the device and were assumed to have MR 3+ or 4+ were included

6 were withdrawn or lost to follow-up

6 were excluded
4 were withdrawn or lost to follow-up
2 had missing MR grade

181 (98%) were included in 12-month efficacy analysis

89 (94%) were included in 12-month efficacy analysis

2 who had missing 12-month MR grade were included

20 were excluded
6 were withdrawn or lost to follow-up
14 had missing MR grade

18 were excluded
9 were withdrawn or lost to follow-up
9 had missing MR grade

161 (88%) were included in 48-month efficacy analysis

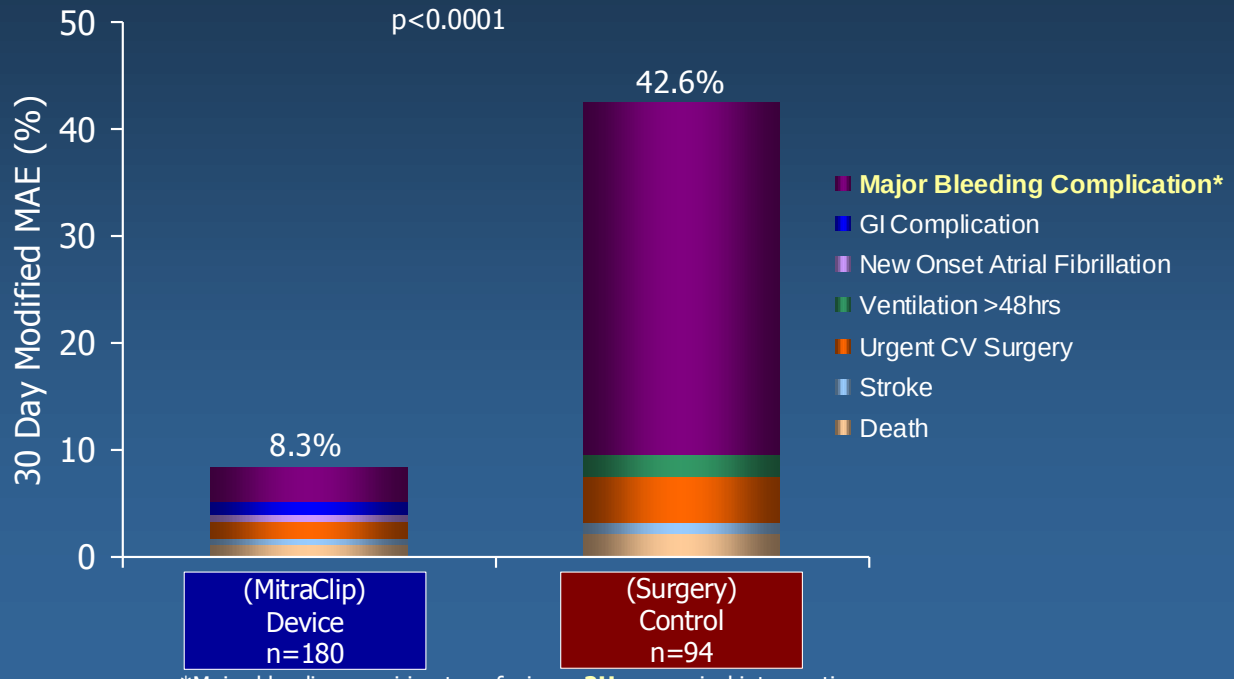
73 (77%) were included in 48-month efficacy analysis

Mitraclip : 1) Indications passées ?

30 Day Modified * MAE

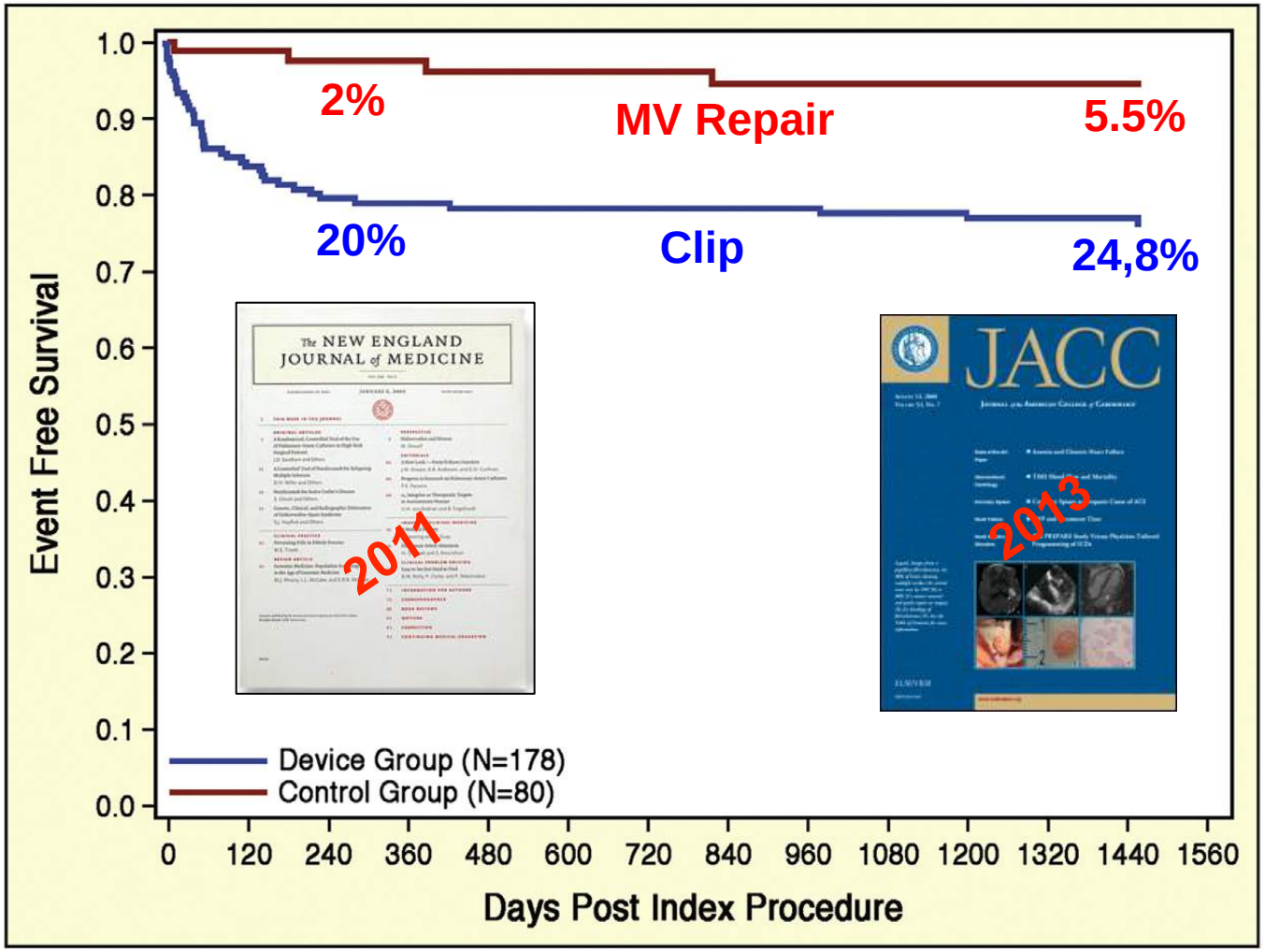
Intent to Treat, Hierarchical Events

Safety endpoint met with a wide margin

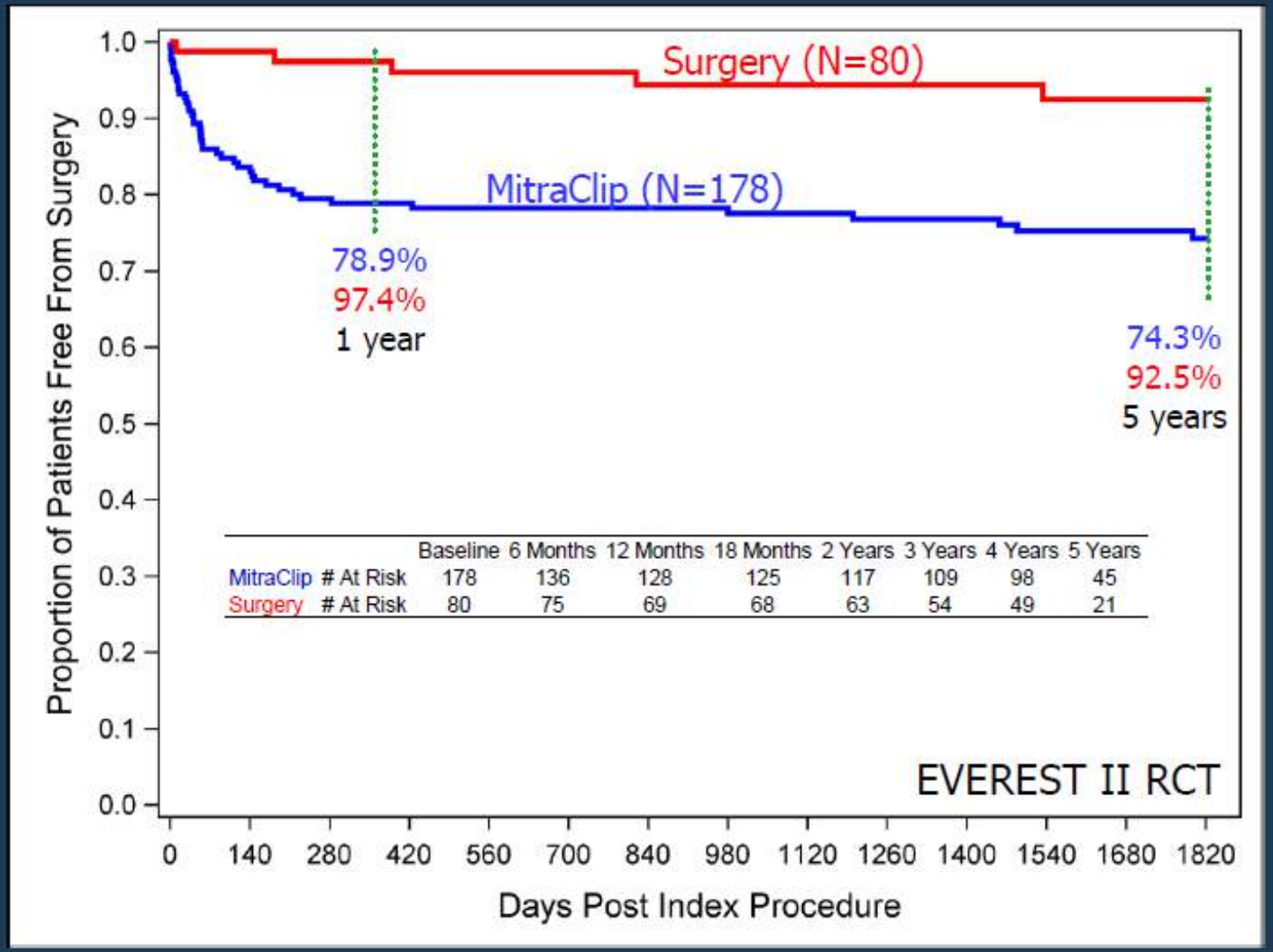


*Major bleeding requiring transfusion = **2U**, or surgical intervention.

Mitraclip : 1) Indications passées ?



Kaplan-Meier Freedom From MV Surgery in MitraClip Group or Re-operation in Surgery Group



	Baseline	6 Months	12 Months	18 Months	2 Years	3 Years	4 Years	5 Years
MitraClip # At Risk	178	136	128	125	117	109	98	45
Surgery # At Risk	80	75	69	68	63	54	49	21

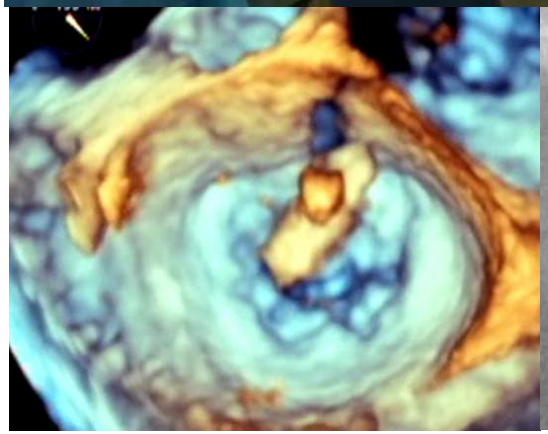
Long-Term Durability of Clinical Success

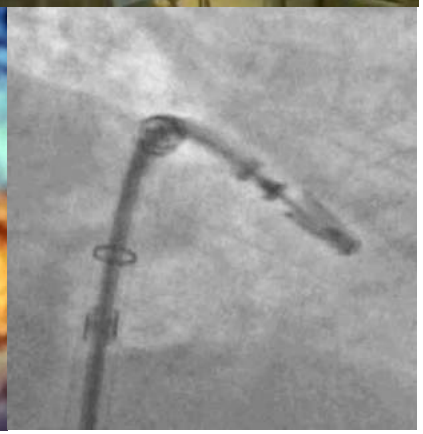
5-Year Outcomes in Patients Who Were Alive and Free From MR 3+/4+ and MV Surgery (or Re-Operation) at 1 Year

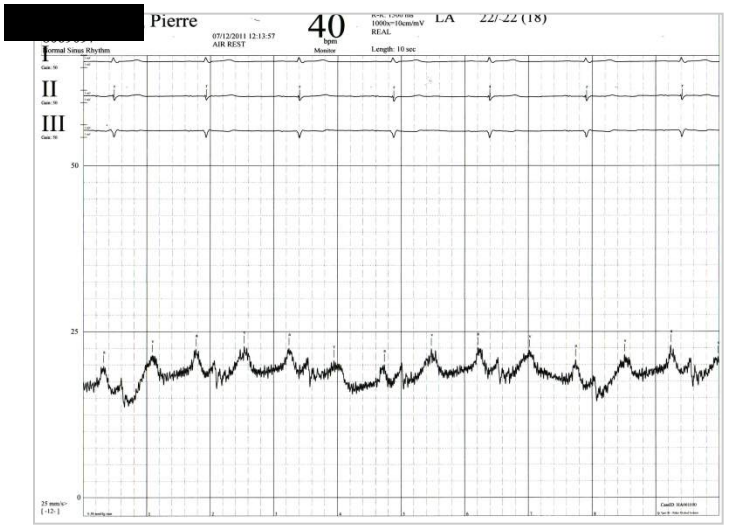
	EVEREST II RCT Clinical Success Groups	
Outcome	MitraClip (N=97)	Surgery (N=64)
Freedom From Death at 5 Years	87%	90%
Freedom From MV Surgery (or Re-operation) at 5 Years	94%	95%
MR ≤ 2+ at 5 Years	86%	97%
MR ≤ 1+ at 5 Years	47%	92%
NYHA Class III/IV (%) Baseline → 5 Years	47% → 6%	40% → 3%
Mean Change in LVEDV From Baseline to 5 Years	-27 ml	-45 ml
Mean Change in Diastolic SLAD From Baseline to 5 Years	0.0 cm	-0.4 cm

MR, NYHA and LV data are from survivors with paired data; freedom from events data are from Kaplan-Meier estimates

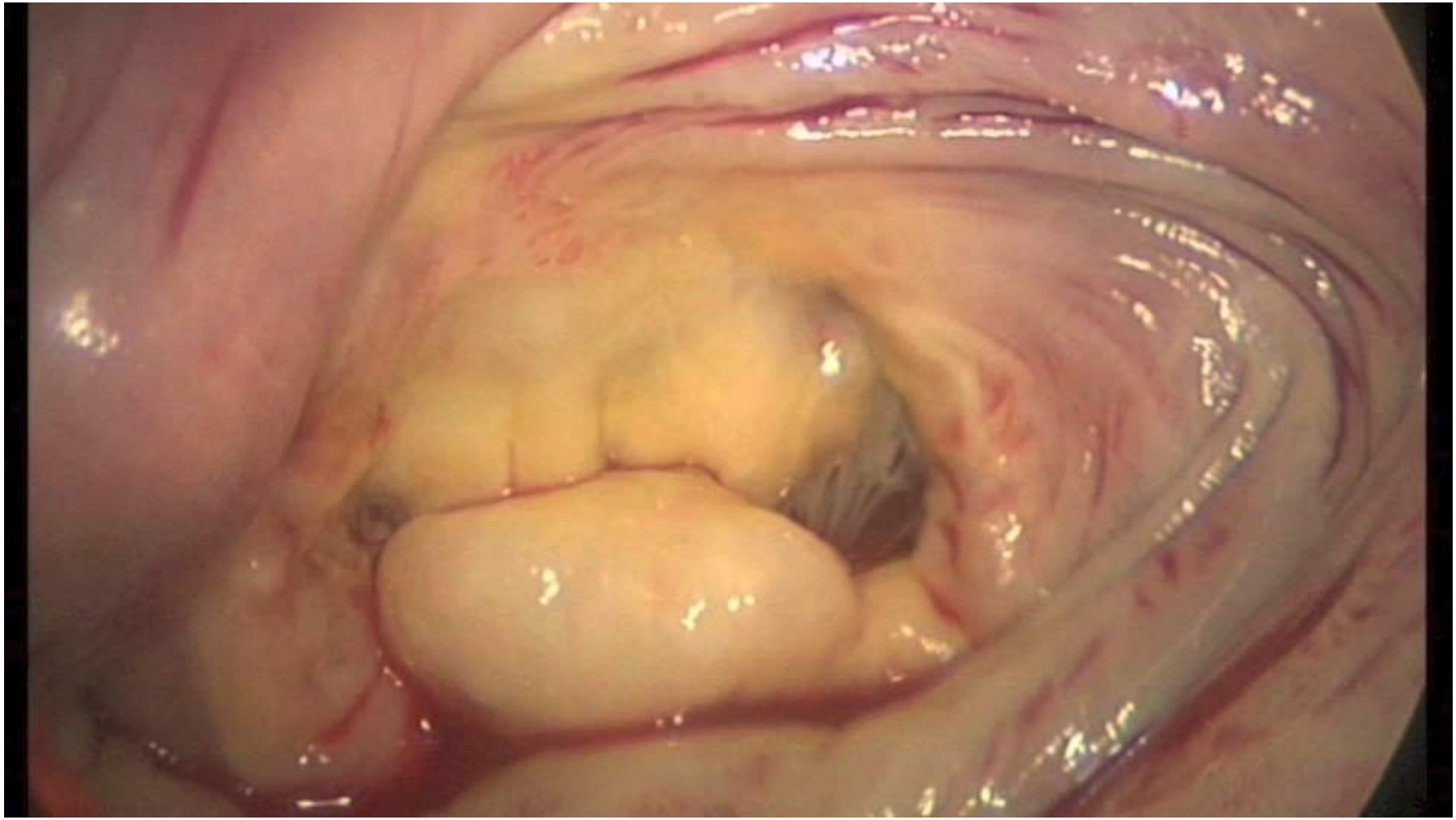
Mitraclip : 1) Indications passées ?







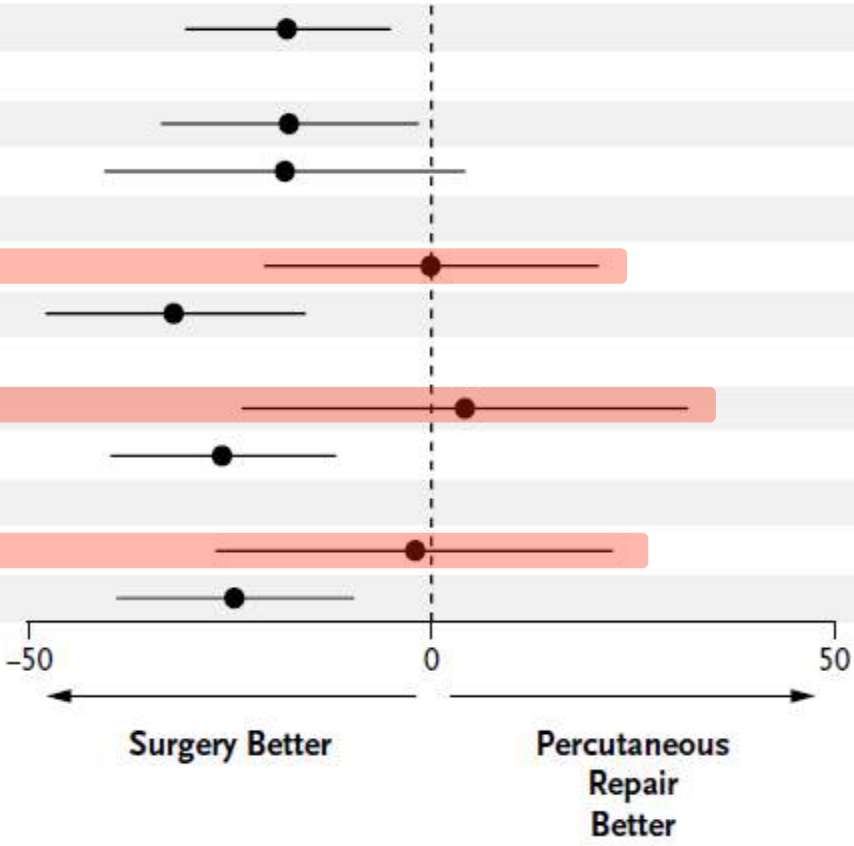
Mitraclip : 1) Indications passées ?



Mitraclip : 1) Indications passées ?

EVEREST II RCT Subgroup Analyses

Subgroup	Percutaneous Repair	Surgery	P Value for Interaction
	no. of events/total no. (%)		
All patients	100/181 (55)	65/89 (73)	
Sex			0.97
Male	63/114 (55)	43/59 (73)	
Female	37/67 (55)	22/30 (73)	
Age			0.009
≥70 yr	52/86 (60)	23/38 (61)	
<70 yr	48/95 (51)	42/51 (82)	
MR			
Functional	26/48 (54)	12/24 (50)	0.02
Degenerative	74/133 (56)	53/65 (82)	
LVEF			0.06
<60%	35/68 (51)	15/28 (54)	
≥60%	64/111 (58)	50/61 (82)	

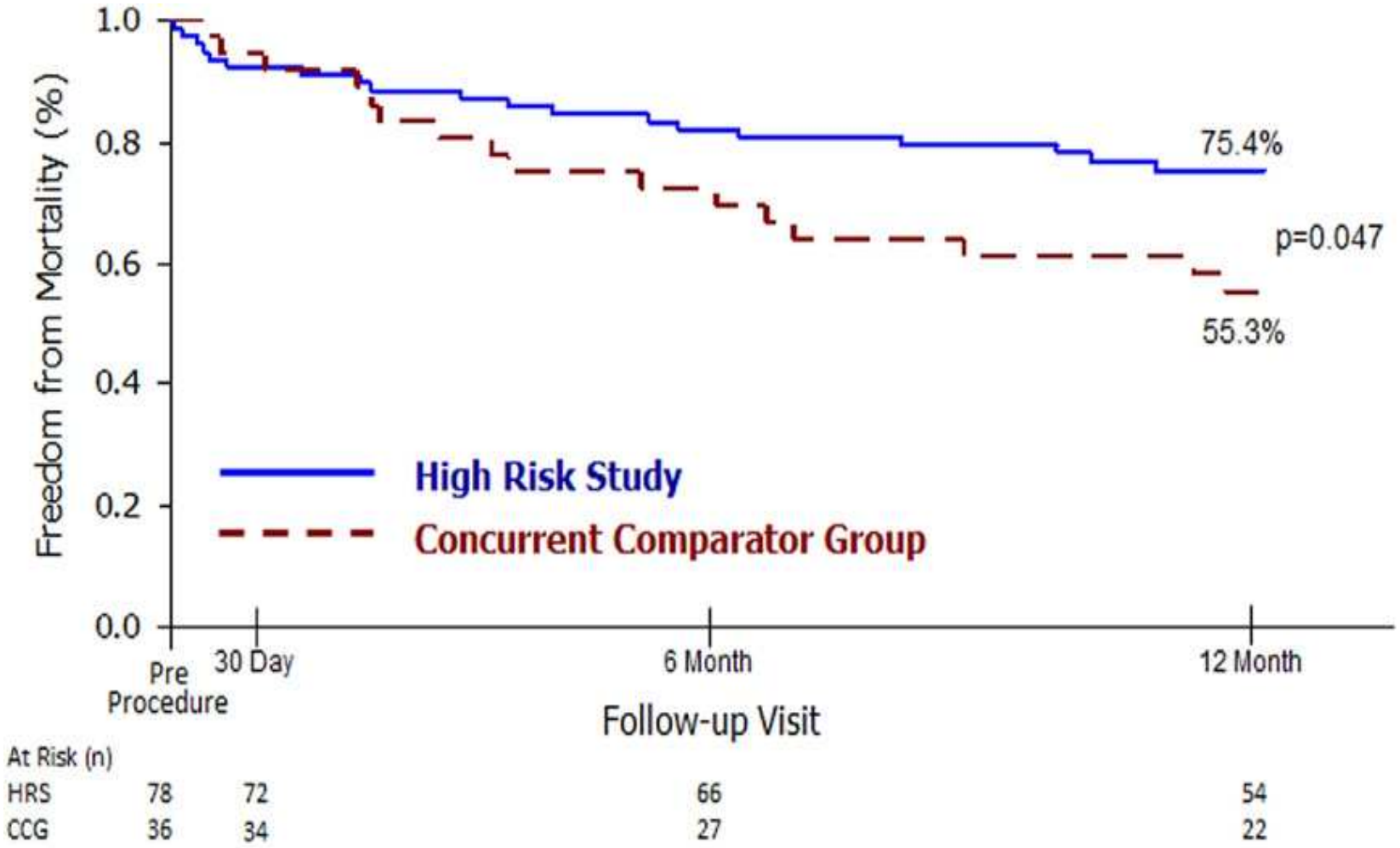


Feldman et al. NEJM, 2011
* Intention to Treat Cohort

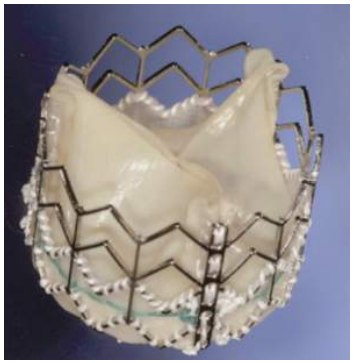
Acute and 12-Month Results With Catheter-Based Mitral Valve Leaflet Repair

The EVEREST II (Endovascular Valve Edge-to-Edge Repair) High Risk Study

JACC 2012



Mitraclip : 1) Indications passées ?



2011

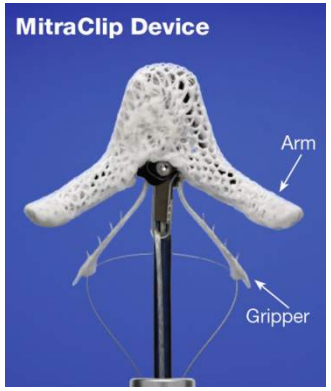
2002

Randomized Classical Indicatios

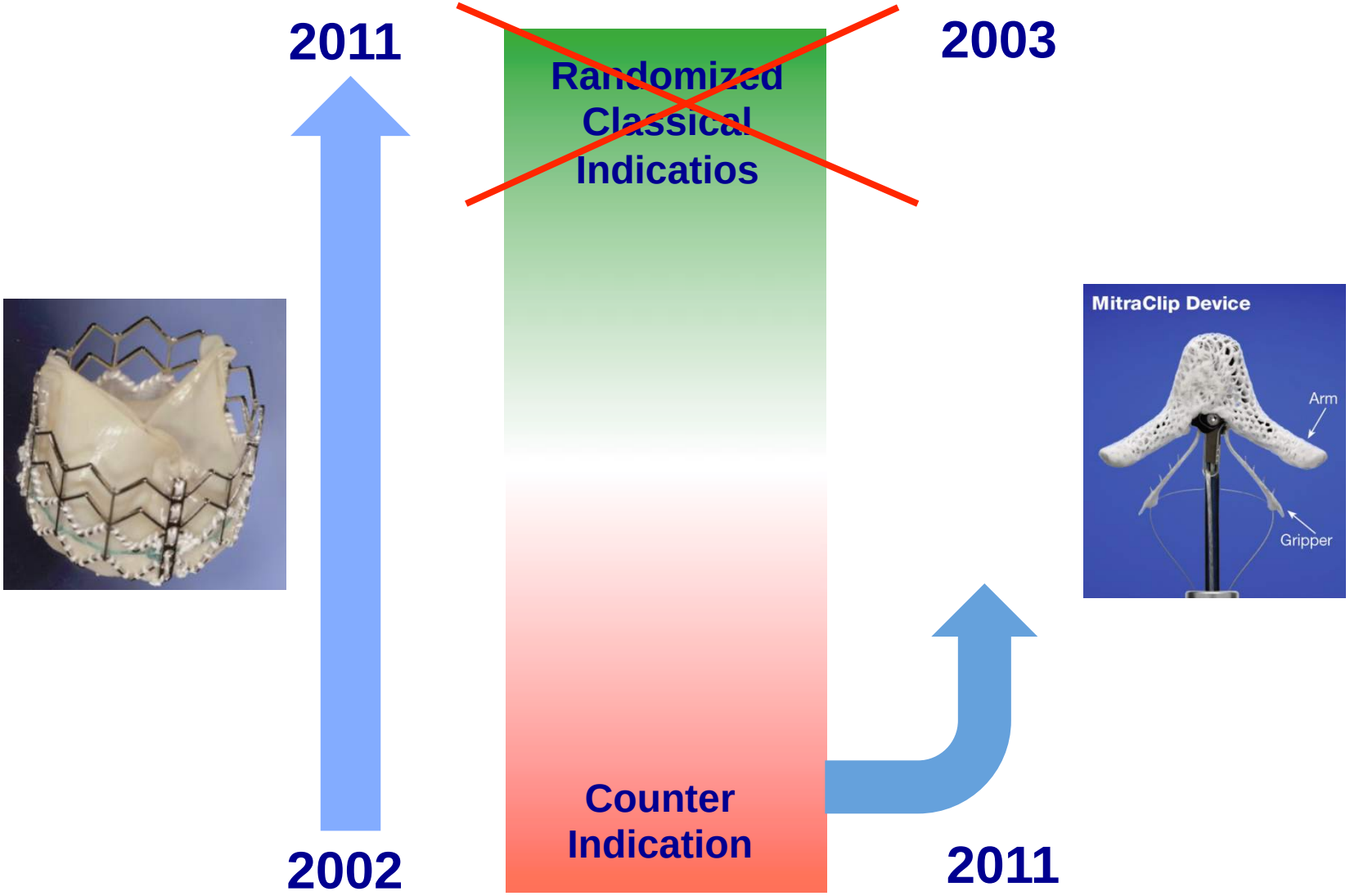
Counter Indication

2003

2011



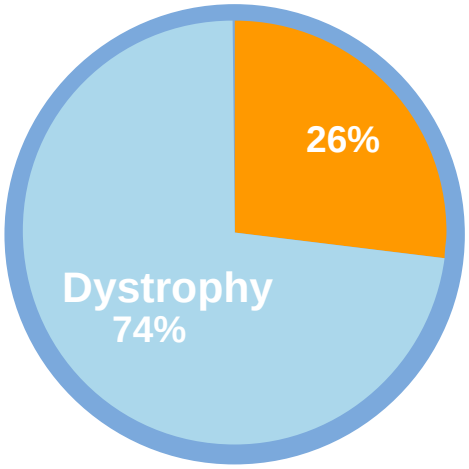
Mitraclip : 1) **Indications passées ?**
2) **Indications présentes ?**



Mitraclip : 1) **Indications passées ?** = DMR

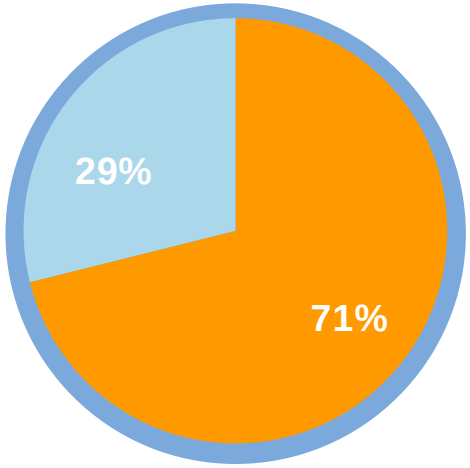
2) **Indications présentes ?** = FMR

EVEREST II
(Randomized Controlled Trial*)



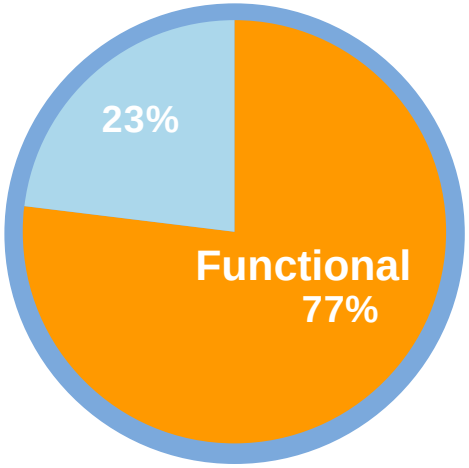
- 258 patients
- Device time – 146 minutes
- Implant rate – 89%

EVEREST II/REALISM
(High Risk Cohort^)



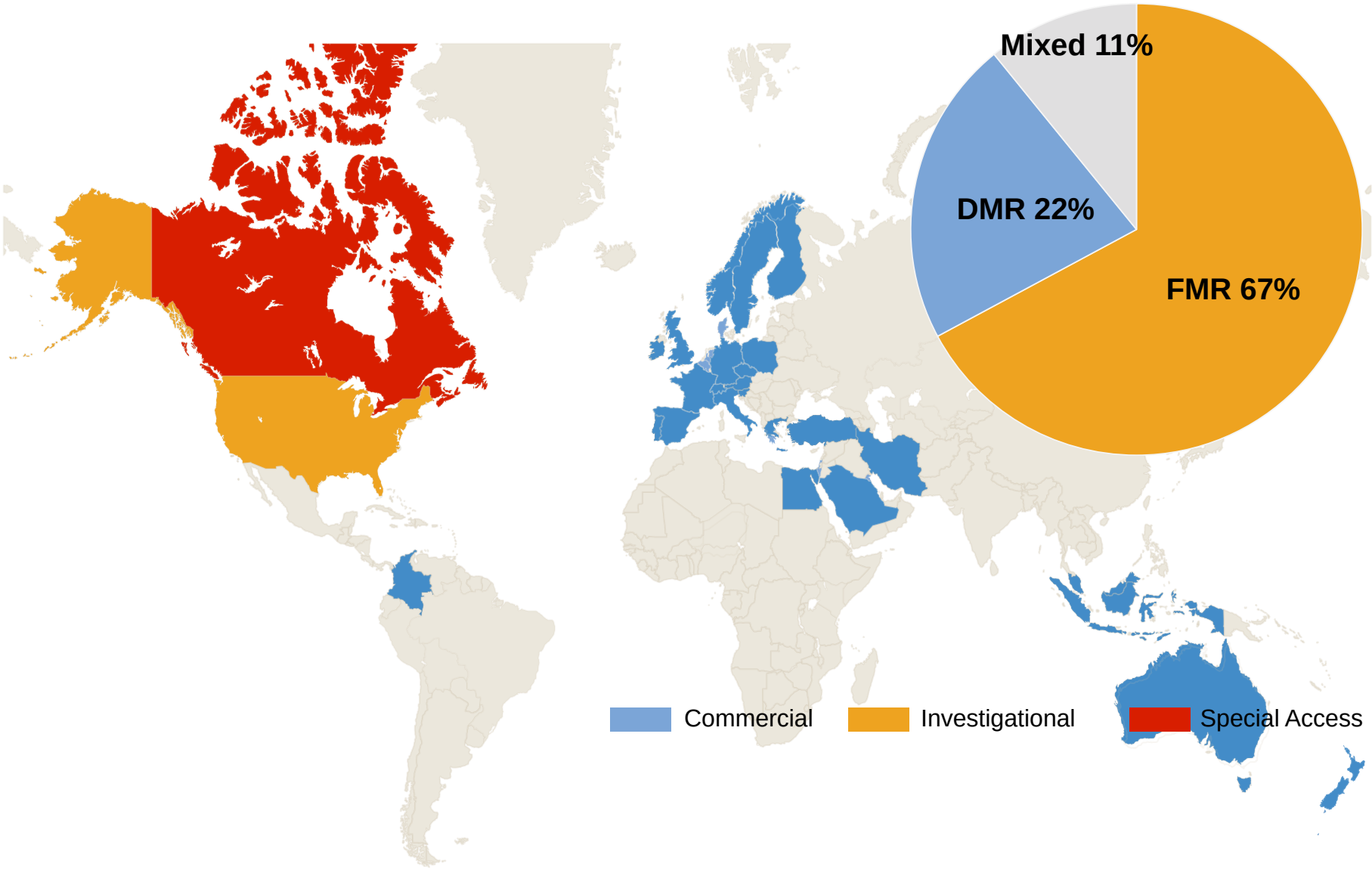
- 211 patients
- Device time – 128 minutes
- Implant rate – 95%

ACCESS EU
(Europe**)



- 567 patients
- Device time – 117 minutes!
- Implant rate – 99.6%

Mitraclip : 2) Indications présentes ?



Mitraclip : 2) Indications présentes en Juillet 2014

Study	Population	N*
EVEREST I (Feasibility)	Feasibility patients	55
EVEREST II (Pivotal)	Pre-randomized patients	60
EVEREST II (Pivotal)	Non-randomized patients (High Risk Study)	78
EVEREST II (Pivotal)	Randomized patients (2:1 Clip to Surgery)	279 184 Clip 95 Surgery
REALISM (Continued Access)	Non-randomized patients	899
Compassionate/Emergency Use	Non-randomized patients	66
ACCESS Europe Phase I	Non-randomized patients	567
ACCESS Europe Phase II	Non-randomized patients	286
Commercial Use	Commercial patients	13,738
Total		**15,933** **+95 surgery**

*Data as of 31/7/2014. Source: Abbott Vascular

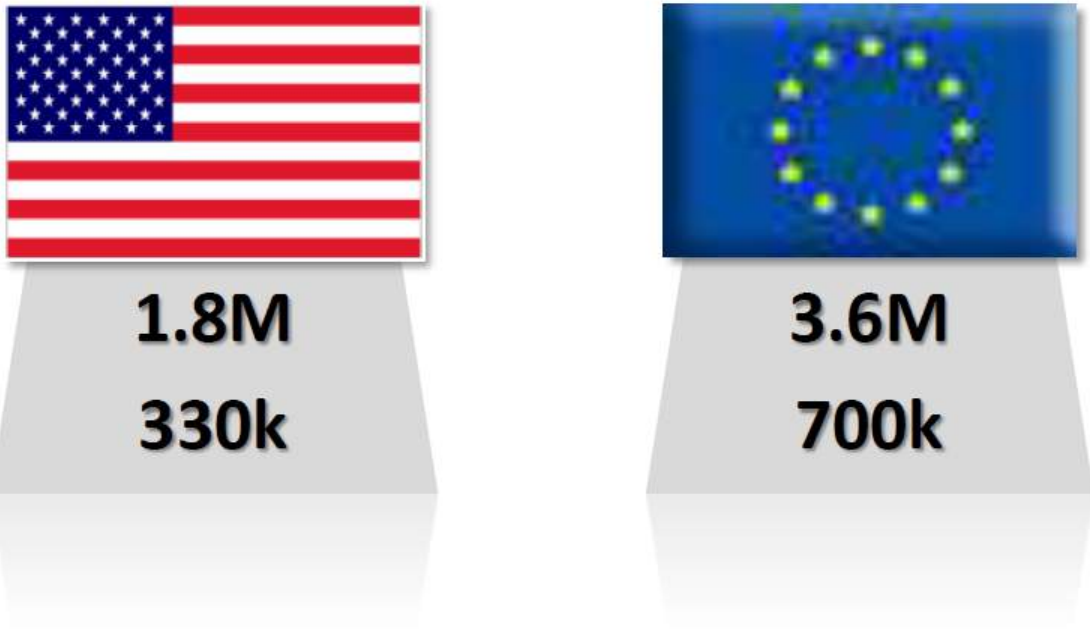
Montreal

Mitral Market Overview

Prevalence Estimates

Munich

Literature suggests that there are 5x more patients with severe mitral regurgitation than severe Aortic Stenosis



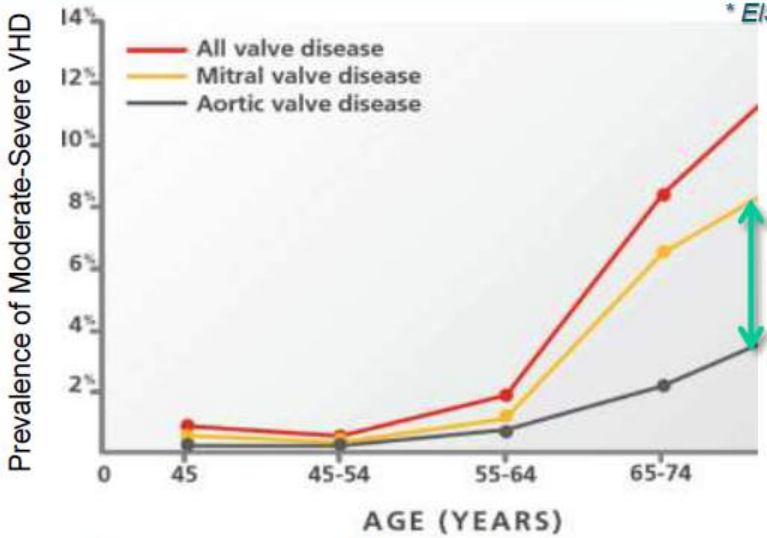
euro PCR 2013

1 – Nkomo, Lancet 2006, Burden of valvular heart diseases: a population-based study
2 – Iung, Curr Prob Cardiol 2007, Valvular Heart Disease in the Community: A European Experience
3 - Cosmi (2002), Faggiano (2003), Aronow (1991), Iivanainen (1996), Internal Analysis

TAVI vs TMVR

Technology Started	Apr-2002	Jun-2003
Number of Implants (approx) to date	> 100,000	<10,000
Market Size Estimates (2014)*	$2 Bi (in High Risk Patients ONLY)	$1.2 Bi (???)

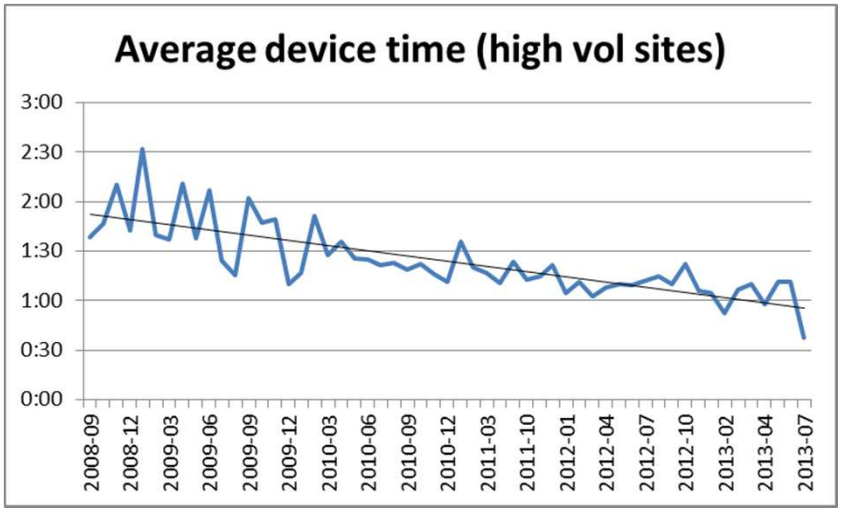
* Elsevier Business Intelligence – Start-Up 2012, Vol17, No.2

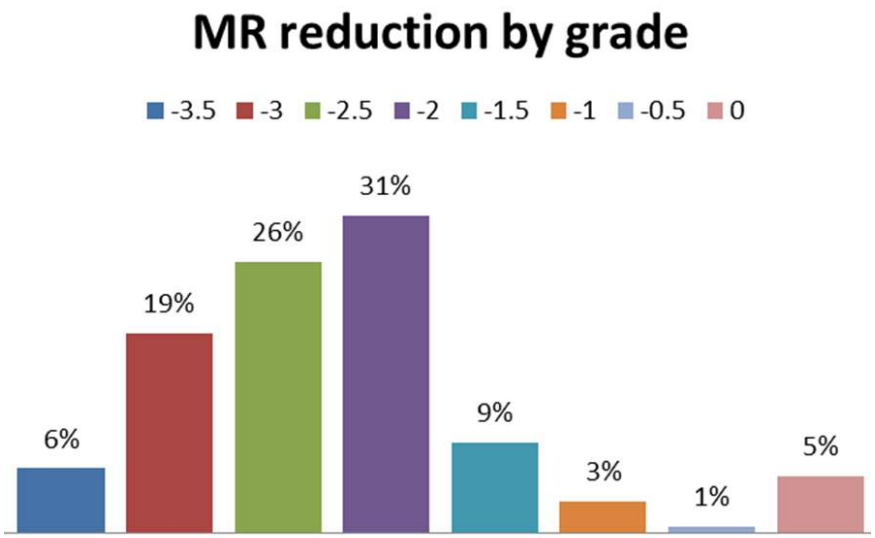


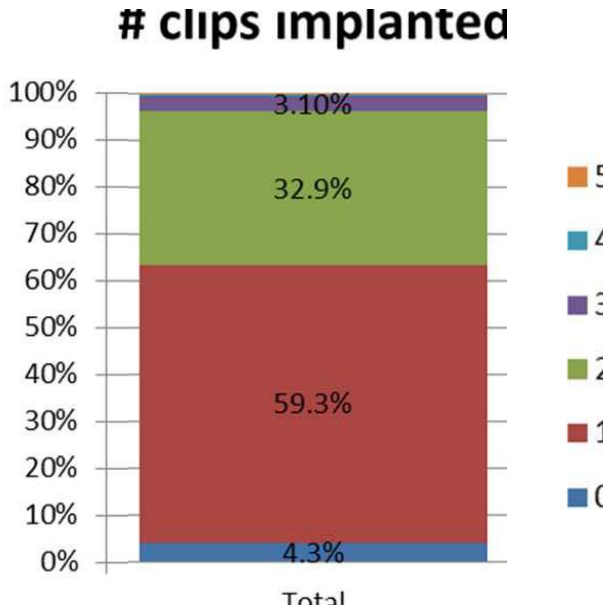
(Nkomo VT,et al. Lancet 2006; 368:1005-11)

Mitral Valve Market ≃ Aortic Valve Market x 4

Mitraclip : 2) Indications présentes ?

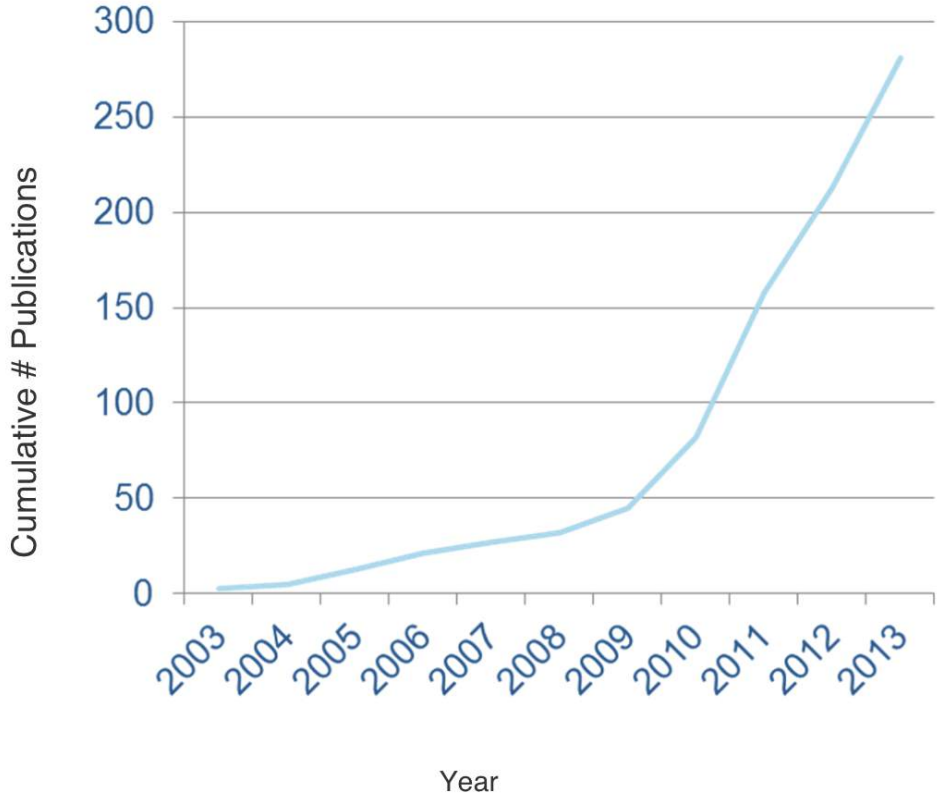






Mitraclip : 2) Indications Présentes?

281 total publications on MitraClip therapy (2003-2013)



The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 APRIL 14, 2011 VOL. 364 NO. 15

Percutaneous Repair or Surgery for Mitral Regurgitation

Ted Feldman, M.D., Elyse Foster, M.D., Donald G. Glower, M.D., Saibal Kar, M.D., Michael J. Rinaldi, M.D., Peter S. Fail, M.D., Richard W. Smalling, M.D., Ph.D., Robert Siegel, M.D., Geoffrey A. Rose, M.D., Eric Engeron, M.D., Catalin Loghin, M.D., Alfredo Trento, M.D., Eric R. Skipper, M.D., Tommy Fudge, M.D., George V. Letsou, M.D., Joseph M. Massaro, Ph.D., and Laura Mauri, M.D., for the EVEREST II Investigators*

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Acute and 12-Month Results With Catheter-Based Mitral Valve Leaflet Repair

The EVEREST II (Endovascular Valve Edge-to-Edge Repair) High Risk Study

European Heart Journal
doi:10.1093/eurheartj/ehs109

ESC/EACTS GUIDELINES

Guidelines on the management of valvular heart disease (version 2012)

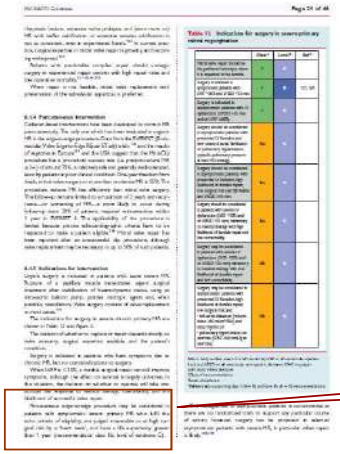
The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

European Journal of Heart Failure
doi:10.1093/eurjhf/hfs079

MitraClip therapy in daily clinical practice: initial results from the German transcatheter mitral valve interventions (TRAMI) registry

Mitraclip : 2) Indications présentes ?

ESC/EACTS 2012 Guidelines on the Management of Valvular Heart Disease



Indication for primary MR

“Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary MR who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a ‘heart team’, and have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).” *page 21*

Indication for secondary MR

“The percutaneous mitral clip procedure may be considered in patients with symptomatic severe secondary MR despite optimal medical therapy (including CRT if indicated), who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a team of cardiologists and cardiac surgeons, and who have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).” *page 25*

Mitraclip : 2) Indications présentes ?

ESC-EACTS EUROPEAN SOCIETY OF CARDIOLOGY **2012**

Table 13 Indications for mitral valve surgery in chronic secondary mitral regurgitation

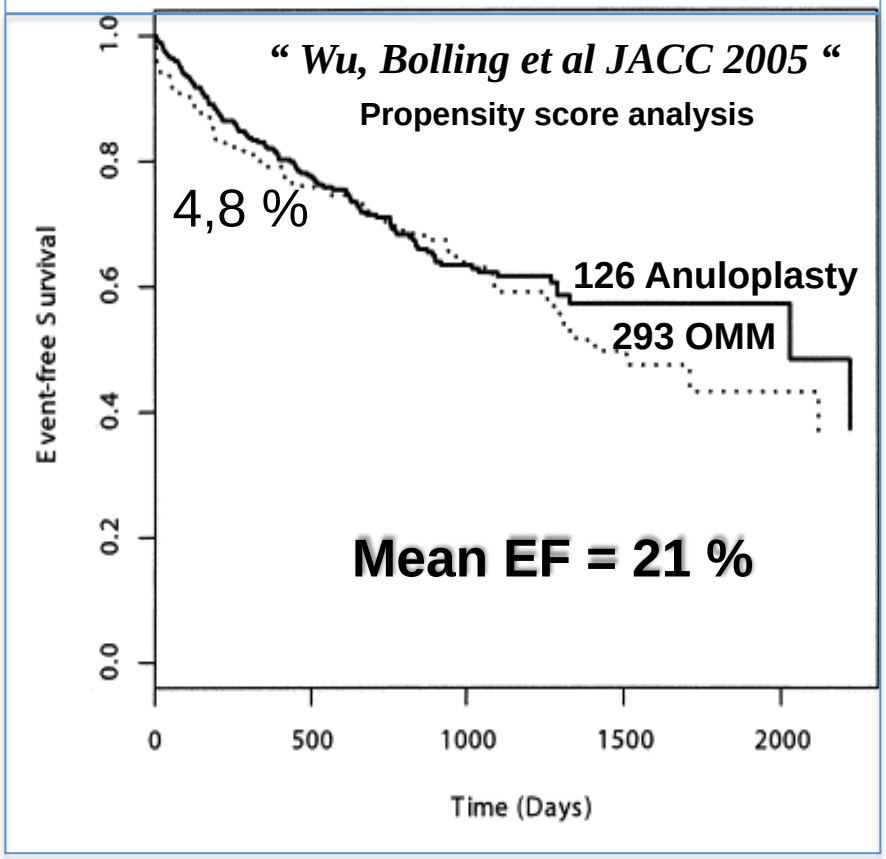
	Class [a]	Level [b]
Surgery is indicated in patients with severe MR[c] undergoing CABG, and LVEF >30%.	I	C
Surgery should be considered in patients with moderate MR undergoing CABG.[d]	IIa	C
Surgery should be considered in symptomatic patients with severe MR, LVEF <30%, option for revascularization, and evidence of viability.	IIa	C
Surgery may be considered in patients with severe MR, LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have low comorbidity, when revascularization is not indicated.	IIb	C

6.2.4 Percutaneous intervention

Experience from a limited number of patients in the EVEREST trials and from observational studies suggests that percutaneousedge-to-edge mitral valve repair is feasible—at low procedural risk—in patients with secondary MR in the absence of severe tethering and may provide short-term improvement in functional condition and LV function.136,137 These findings have to be confirmed in larger series with longer follow-up and with a randomized design. Data on coronary sinus annuloplasty are limited and most initial devices have been withdrawn

Mitraclip : 2) Indications présentes ?

Survival Rate



Recurrent MR > 20 %

JASE 2011 Jeffrey J. Silbiger, New York

Predictor	Source
Leaflet deformation indices	
Tenting height ≥ 1.0 cm	Magne et al[57]
Tenting height ≥ 1.1 cm	Calafiore et al[94]
Tenting area ≥ 2.5 cm^2	Magne et al[57]
Tenting area ≥ 1.6 $cm^{2,*}$	Kongsaerepong et al[93]
Posterior leaflet angle ≥ 45	Magne et al[57]
Distal anterior leaflet angle > 25	Lee et al[55]
Annular size	
Mitral annular dimension ≥ 3.7 cm*	Kongsaerepong et al[93]
MR jet characteristics	
Grade > 3.5*	Kongsaerepong et al[93]
Central or complex	McGee et al[63]
LV factors	
Systolic sphericity index ≥ 0.7	Gelsomino et al[95]
LV end systolic volume ≥ 145 mL	Gelsomino et al[95]
Restrictive LV diastolic filling pattern	Eremiene et al[96]

Sophism !!! The surgical difficulties to correct efficiently the FMR does not implies that it will be a success for per-cutaneous procedure, it only means that this pathology is more complex to treat.

Mitraclip : 2) Indications présentes ?

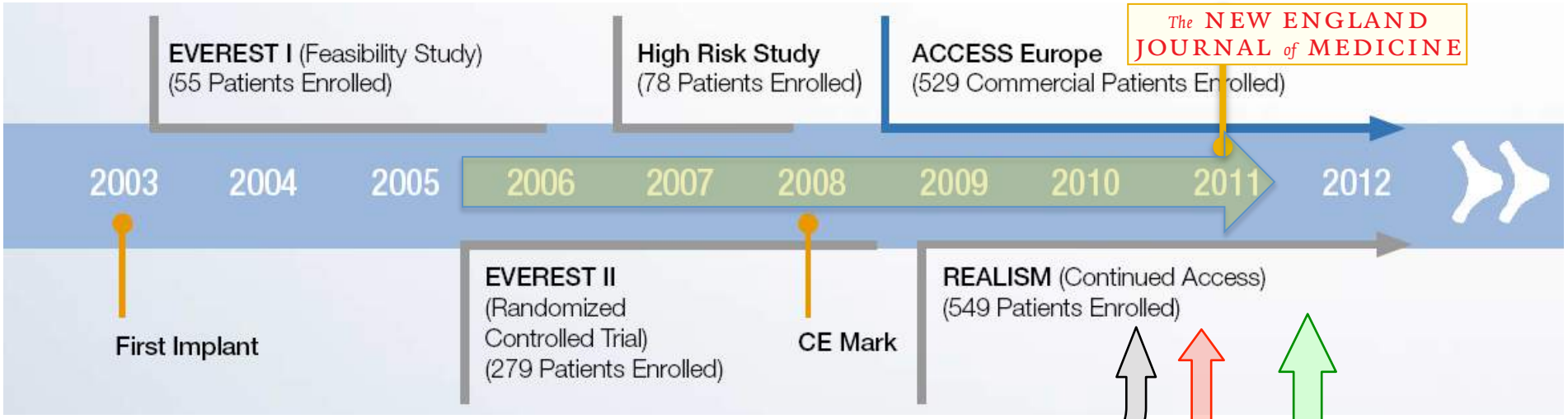
ACC/AHA Reco. for chronic primary MR

Recommendations	COR	LOE
Transcatheter mitral valve repair may be considered for severely symptomatic patients with chronic severe primary MR who have a reasonable life expectancy but a prohibitive surgical risk because of severe comorbidities	IIb	B

Nishimura et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease. Circulation 2014;129:e521-643

	COAPT	RESHAPE-HF	MITRA.fr
Sponsor	Abbott Vascular	Abbott Vascular	PHRC / Abbott
Méthodology	Prospective, randomized	Prospective, randomized	Prospective, randomized
Comparison	Optimal Medical Medicatio	Optimal Medical Medication	Optimal Medical Medication
MR etiology	Secondary MR	Secondary MR	Secondary MR
Ejection Fraction	> 30%	15 to 40%	15 to 40%
Hospitalisation HF < 12 months ?		100%	100%
High Risk Patients	Surgical CI (heart team)		Surgical CI (heart team)
NHYA	II, III, IV	III, IV	II, III, IV
Principal Criteria	Safety et efficacy (hospit pour CHF)	% all deaths or rehospitalisation rate HF	% all deaths + % rehospitalisation HF
Hypothesis		18 vs 14 % death and 0,6 vs 0,45 hospit	20 vs 35%
Lost pats		15%	10%
Number of inclusions	250 x 2	400 x 2	144 x 2
Number of centres	9	75	18

Mitraclip : 2) Indications Futures?



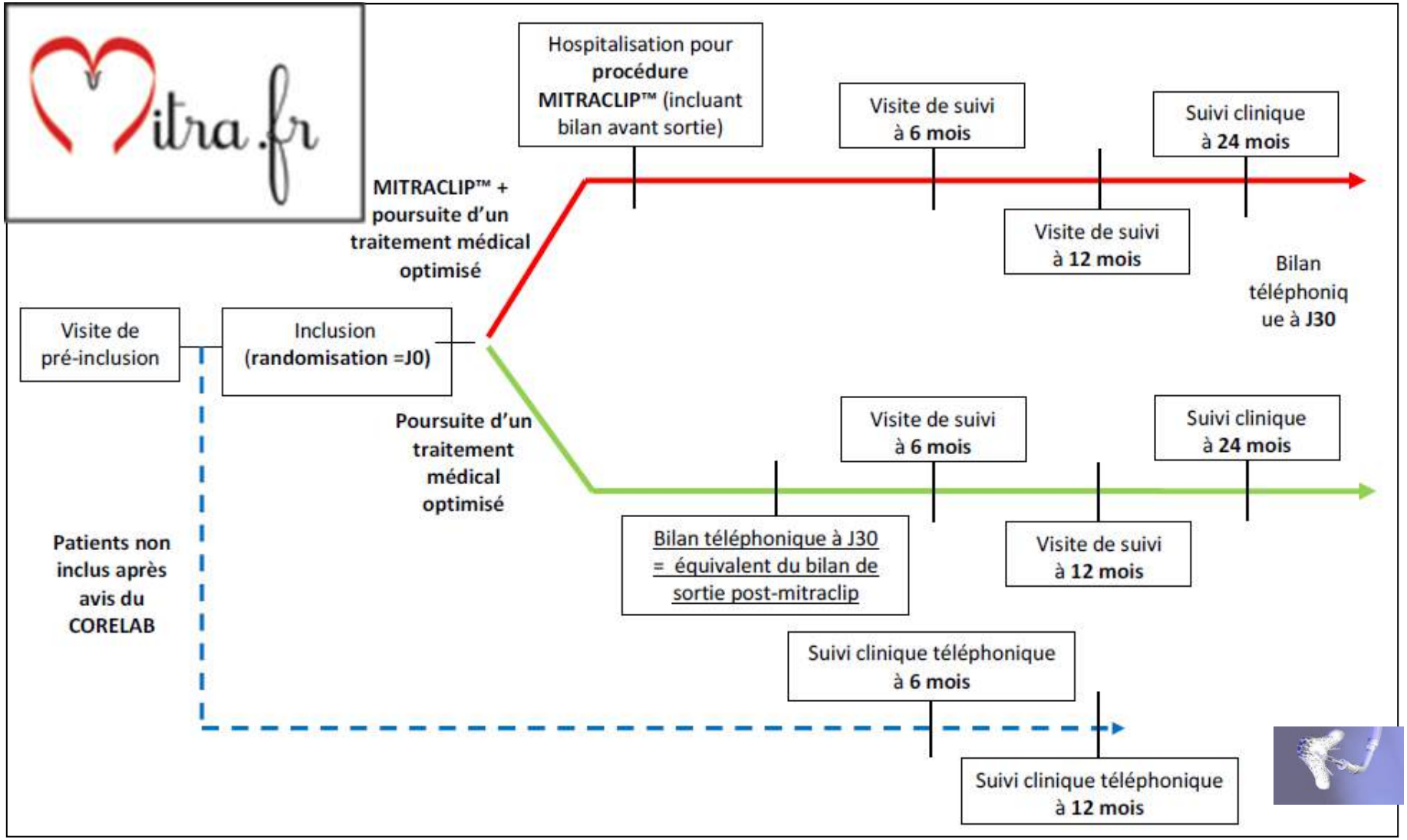
Premiers patients français

STIC 2010 : TECH. INNOV. COUTEUSES
MITRACLIP® pour IM fonctionnelles symptomatiques.
Soumission Oct 2010 → refus Sept 2011

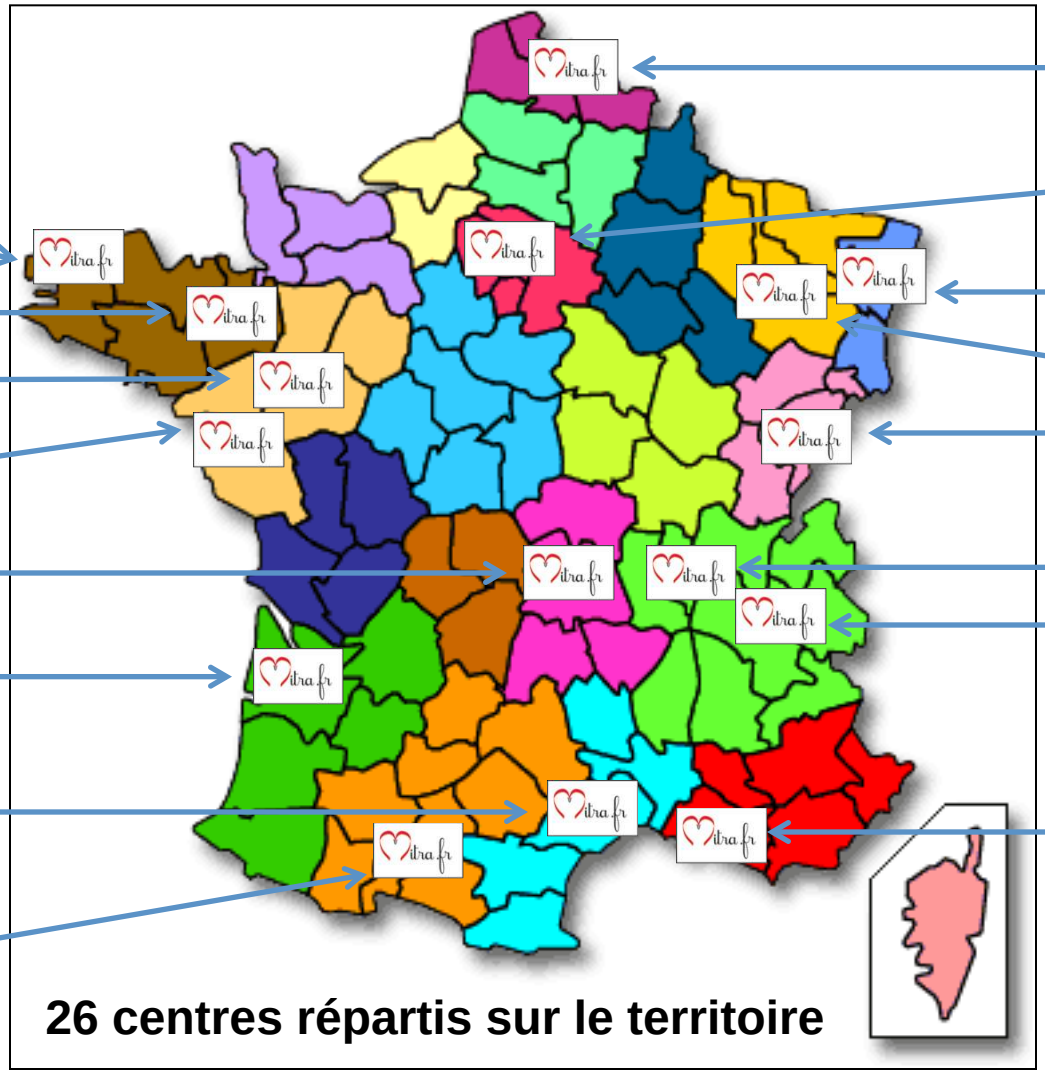
PHRC 2012 : Appel à projet DGOS
MITRACLIP® pour IM fonctionnelles symptomatiques.
Soumission Janvier 2012 → Acceptation Décembre 2012

Inclusion 01 / 2014

Mitraclip : 2) Indications Futures?



Mitraclip : 2) Indications Futures?



Brest

Rennes

Angers

Nantes

Clermont-Ferrand

Bordeaux

Montpellier (CHU et Clinique Millénaire)

Toulouse (CHU, Clinique Pasteur)

Lille

Créteil, Le Plessis-Robinson, Massy, Bichat, Le Chesnay

Strasbourg

Nancy

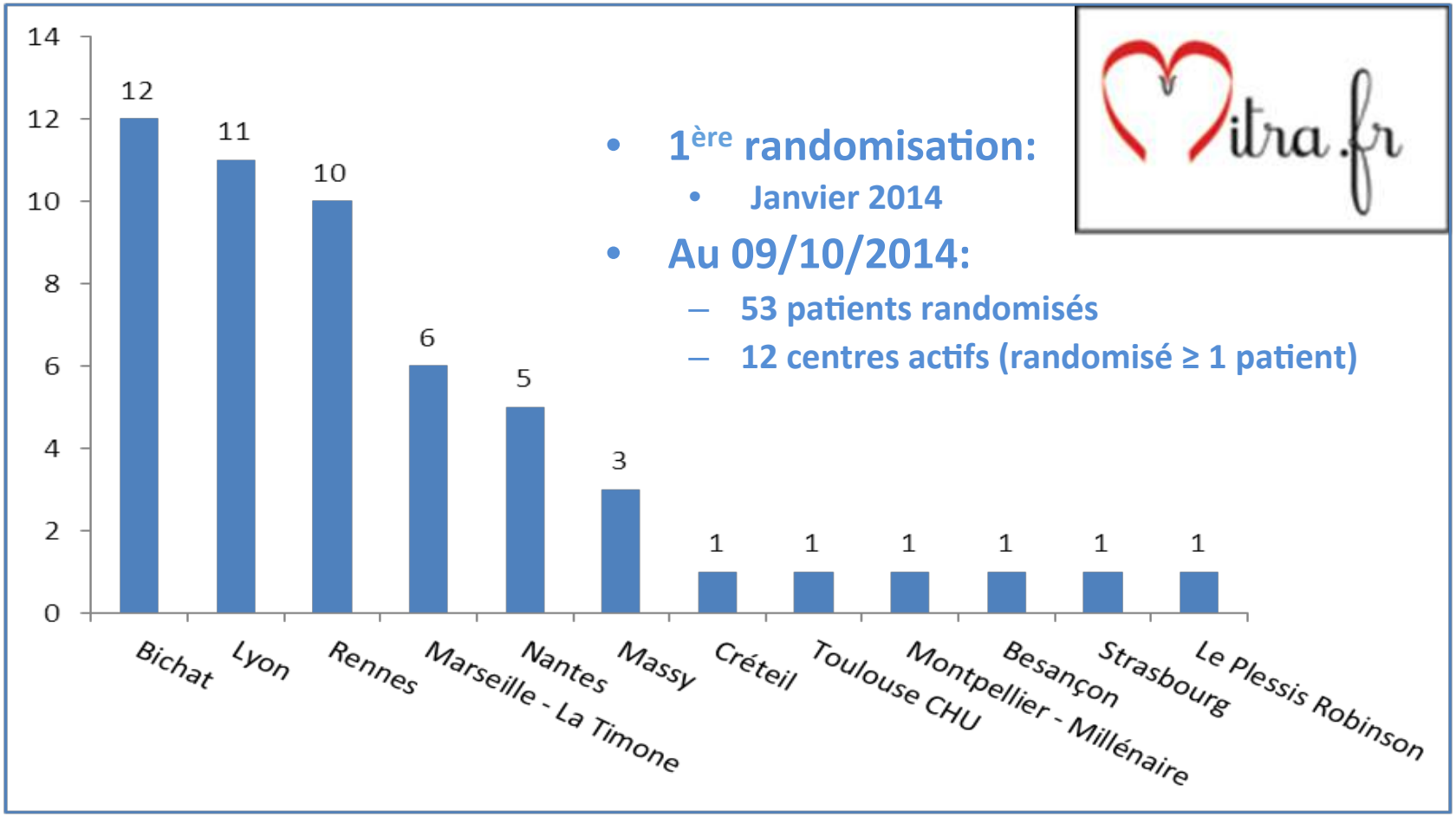
Besançon

Lyon

Grenoble

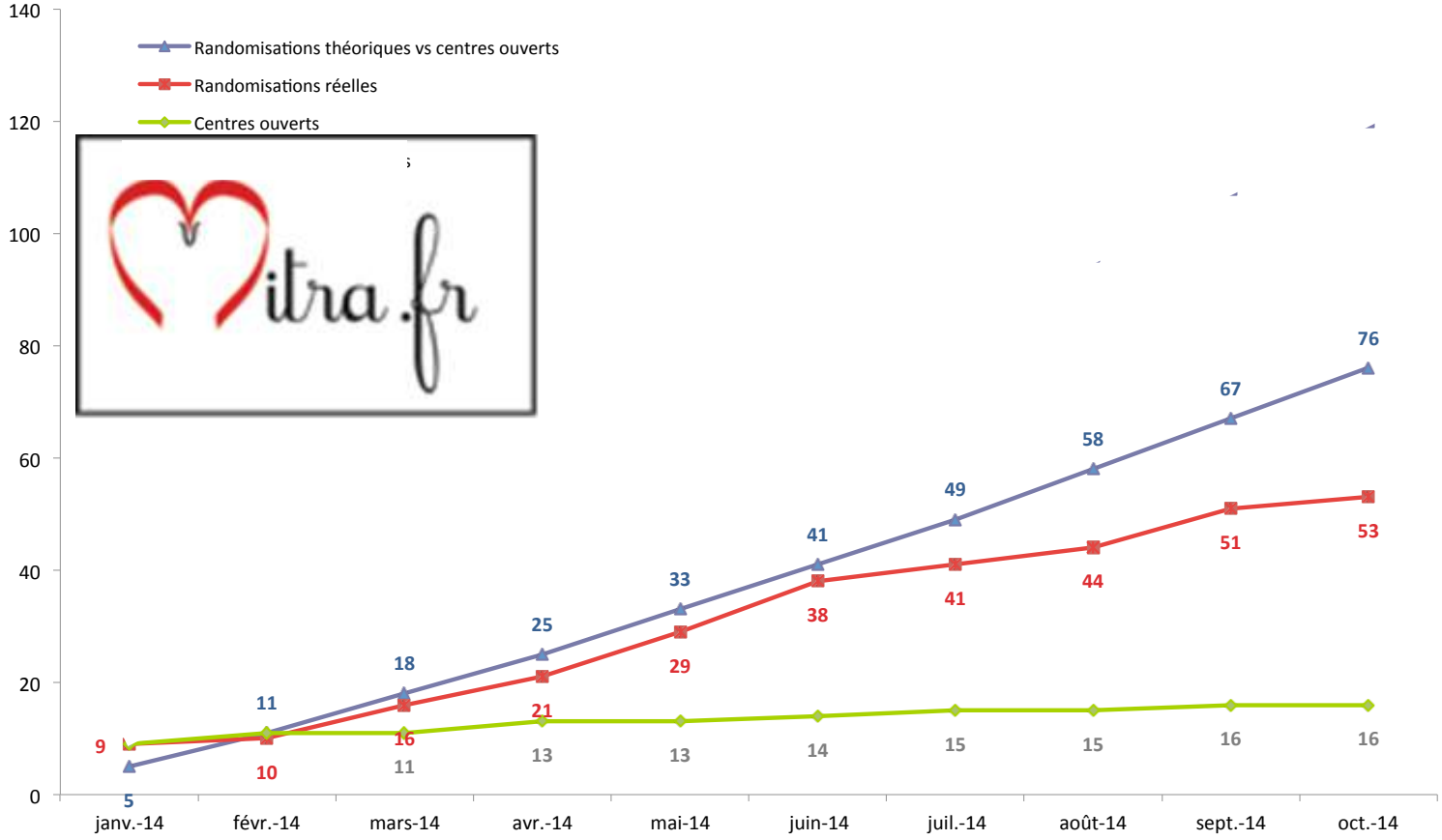
Marseille (La Timone, Saint Joseph)

Mitraclip : 2) Indications Futures ?



Mitraclip : 2) Indications Futures ?

Courbes de randomisation (09/10/2014)



CONCLUSION: Indications passées, présentes et futures

In Mitraclip We trust !!!

BUT

Evaluation ! Evaluation ! Evaluation !

IM Fonctionelle
- volume de régurgitation > 30 mL/batt
- SOR > 20 mm²

Classe fonctionnelle NYHA ≥ II
FEVG entre 15 et 40%
hospitalisation pour ICC dans les 12 mois
Traitement médical optimisé de l'ICC
Non opérable« heart team ».
Core-Lab (hôpital Bichat)