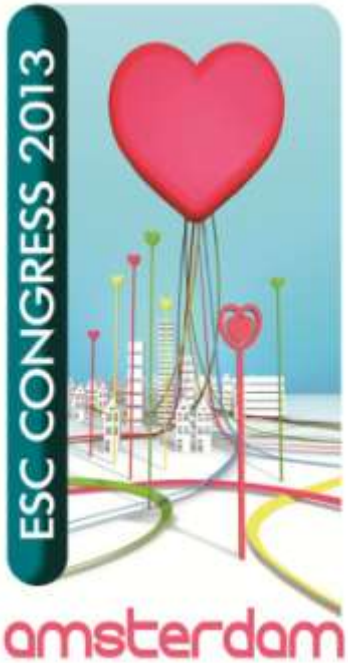


LO MEJOR SOBRE INSUFICIENCIA CARDIACA Y MIOCARDIOPATIAS

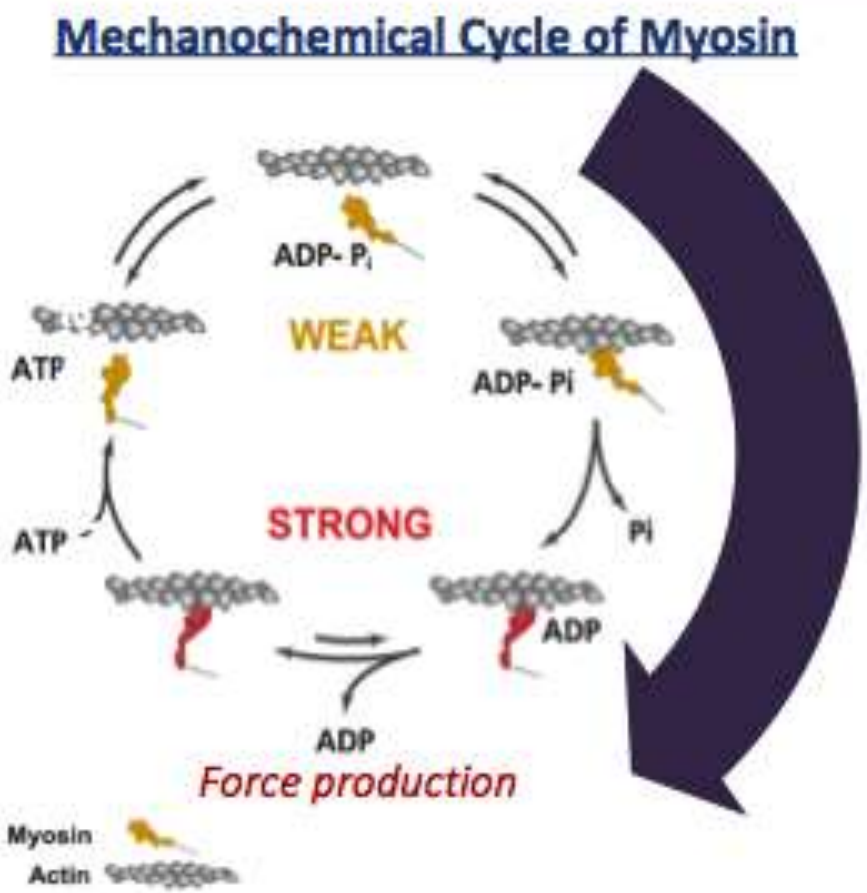
Dr. Nicolás Manito

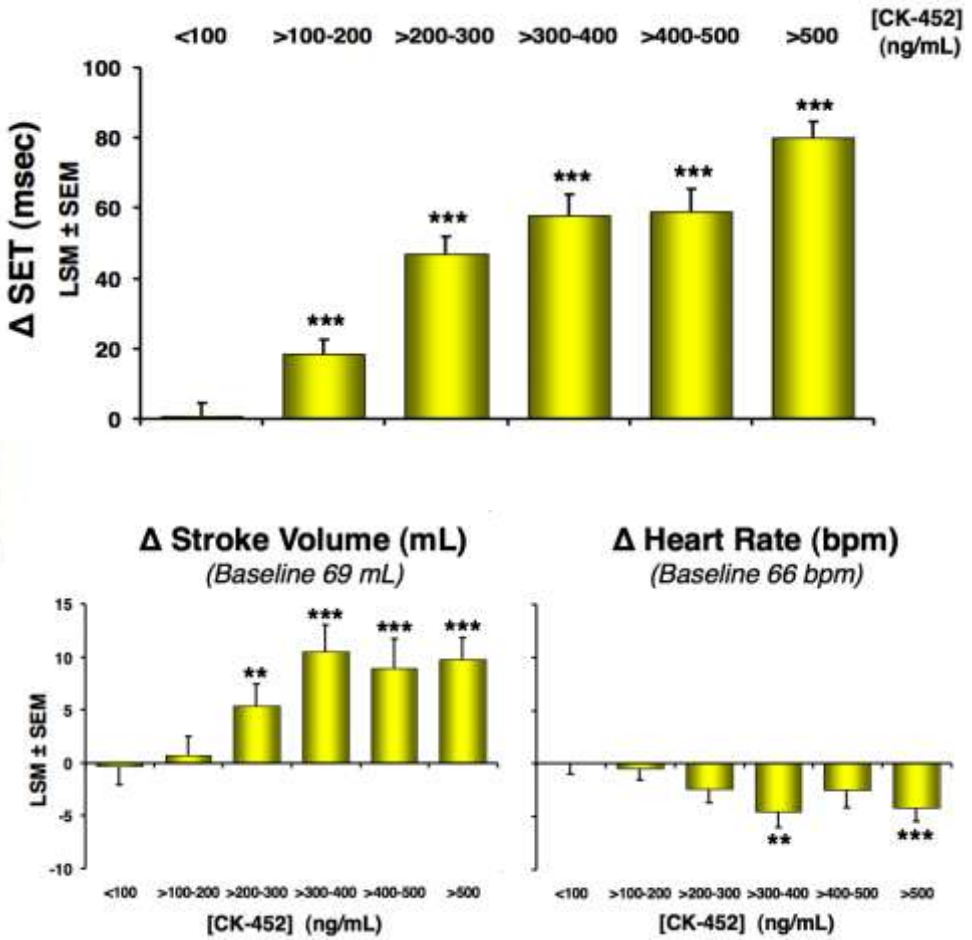
Jefe Clínico de la Unidad de Insuficiencia Cardiaca y Trasplante cardiaco
Hospital Universitario de Bellvitge, Barcelona

INSUFICIENCIA CARDIACA – MIOCARDIOPATIAS . ESC 2013

- **INSUFICIENCIA CARDIACA AGUDA:**
  - **ATOMIC**
  - **RELAX-AHF (subgrupos)**
  - **IABP-SHOCK II**
- **INSUFICIENCIA CARDIACA CRÓNICA:**
  - **SHIFT**
  - **RAFT**
  - **ASTRONAUT**
  - **DIAGNOSTICO NO INVASIVO CONGESTIÓN PULMONAR**
- **DISPOSITIVOS:**
  - **IN-TIME**
- **REGISTROS DE IC:**
  - **HEART FAILURE LT ESC REGISTRY**
- **INVESTIGACIÓN BÁSICA:**
  - **MELUSIN GENE THERAPY IN CARDIOMYOPATHIES**
- **GRUPOS ESPAÑOLES :**
  - **REGISTRO GECAME DE CARDIOTOXICIDAD**
- **SESIONES:**
  - **BIOMARCADORES**
  - **IC CON FUNCIÓN SISTÓLICA PRESERVADA (HFPEF)**

Omecamtiv Mecarbil (OM) is a Novel Selective Cardiac Myosin Activator

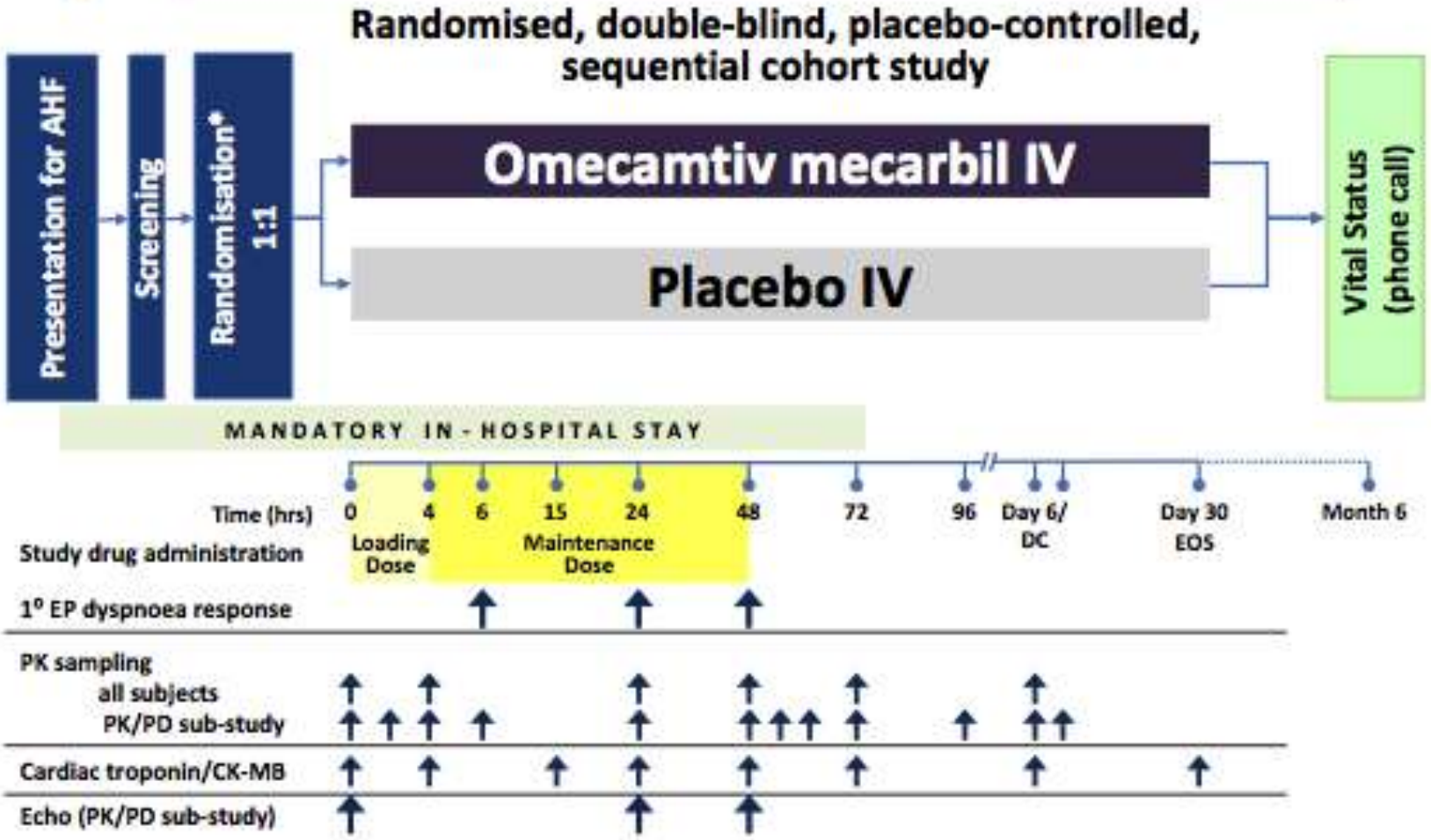




No aumenta VO2, ni Ca++ intracelular

Cleland JGF et al. Lancet 2011; 378: 676–83

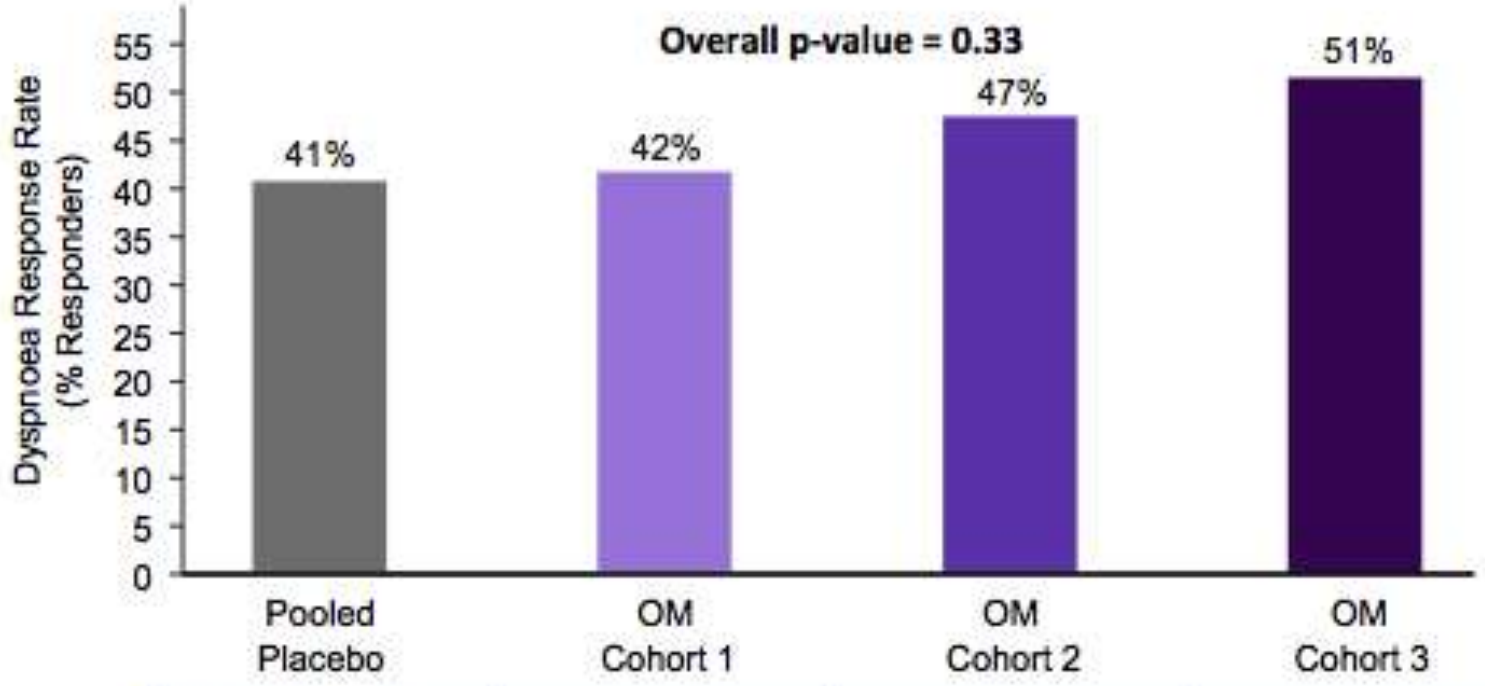
Study Design



* Randomisation within 24 hours of initial IV diuretic (Amendment 2)

Primary Efficacy Endpoint: Dyspnoea Response (Likert Scale)

Pooled Placebo



Response Rate Ratio*	**1.03**	**1.15**	**1.23**
95% CI	**(0.79, 1.35)**	**(0.90, 1.47)**	**(0.97, 1.55)**

*Ratio of response rate to Pooled Placebo

p-value of a CMH test among all 3 Placebo arms = 0.32

RELAX – AHF : SERELAXINA EN INSUFICIENCIA CARDIACA AGUDA

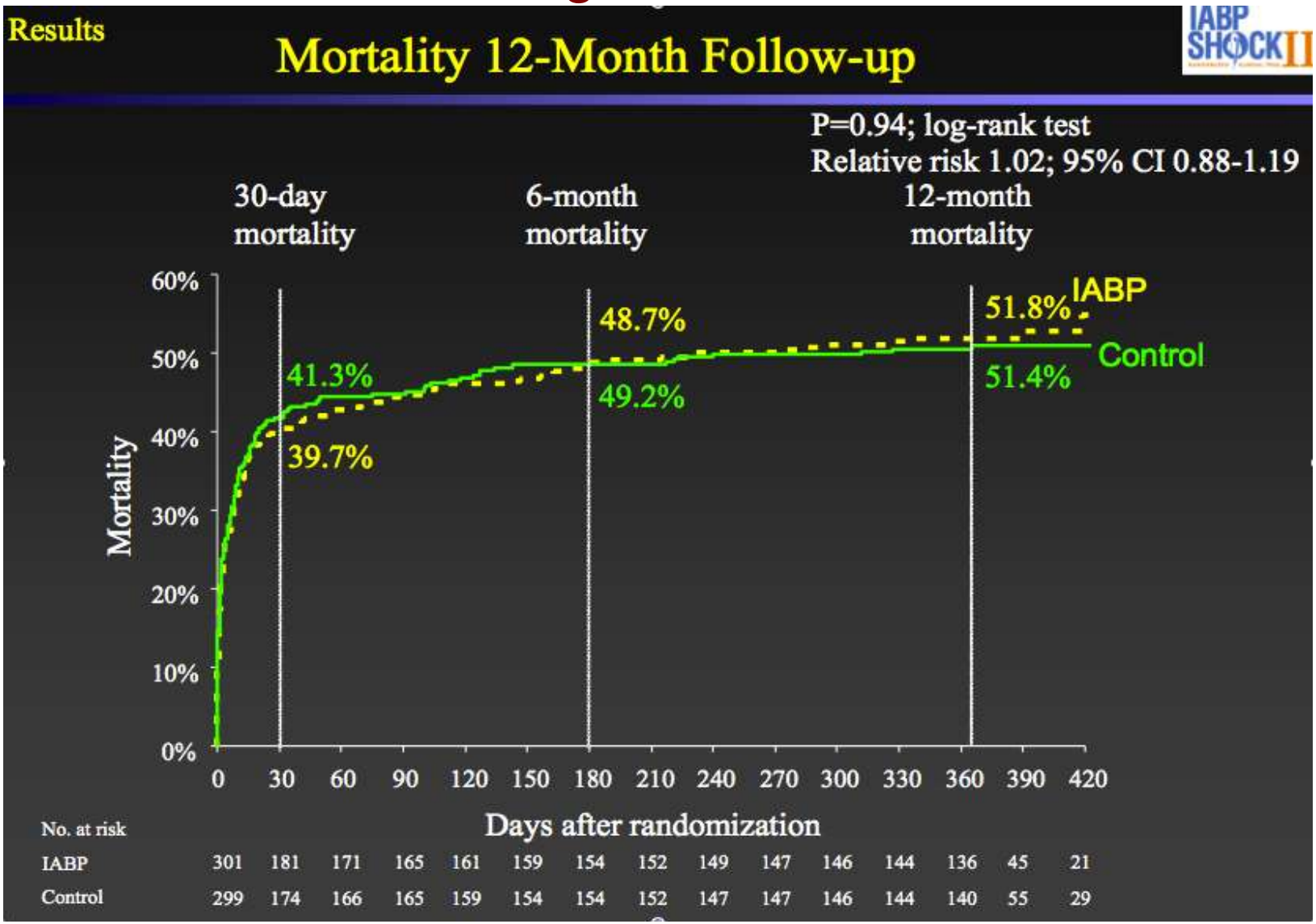
- Serelaxin, compared with placebo:
  - improved the primary efficacy endpoint of dyspnoea relief through Day 5 assessed by the Visual Analogue Scale AUC (p=0.007)
  - provided a numerical increase of the proportion of patients reporting moderately or markedly improved dyspnoea (Likert scale) at 6, 12 and 24 hours (p=0.70)
  - had no effect on secondary efficacy endpoints (CV death or rehospitalization for HF or renal failure through Day 60, or days alive and out of hospital to Day 60)
  - reduced CV (efficacy endpoint) and all-cause 180 Day mortality (safety endpoint) by 37% (HRs [95%CIs], 0.63 [0.41, 0.96], p=0.028 and 0.63 [0.43, 0.93], p=0.02, respectively)

AHF=acute heart failure; AUC=area under the curve; CI=confidence interval; CV=cardiovascular; HF=heart failure; HR=hazard ratio; SBP=systolic blood pressure
Teerlink et al. Lancet 2013;381:29–39

RELAX – AHF : ANÁLISIS DE SUBGRUPOS PREDEFINIDOS

- The effects of serelaxin versus placebo were homogenous across multiple subgroups with respect to the endpoints of the study, including 180-day CV mortality
- Potentially larger mortality benefits were seen in the patients with:
  - older age
  - no previous HF hospitalization
  - not treated with beta-blockers at the time of randomization
  - signs of inflammation (lymphopenia)
  - more severe renal impairment
- The present study is underpowered for the subgroup analyses, particularly for mortality data. These results must be considered as hypothesis-generating.

Intraaortic balloon support for myocardial infarction with cardiogenic shock.



Intraaortic balloon support for myocardial infarction with cardiogenic shock.

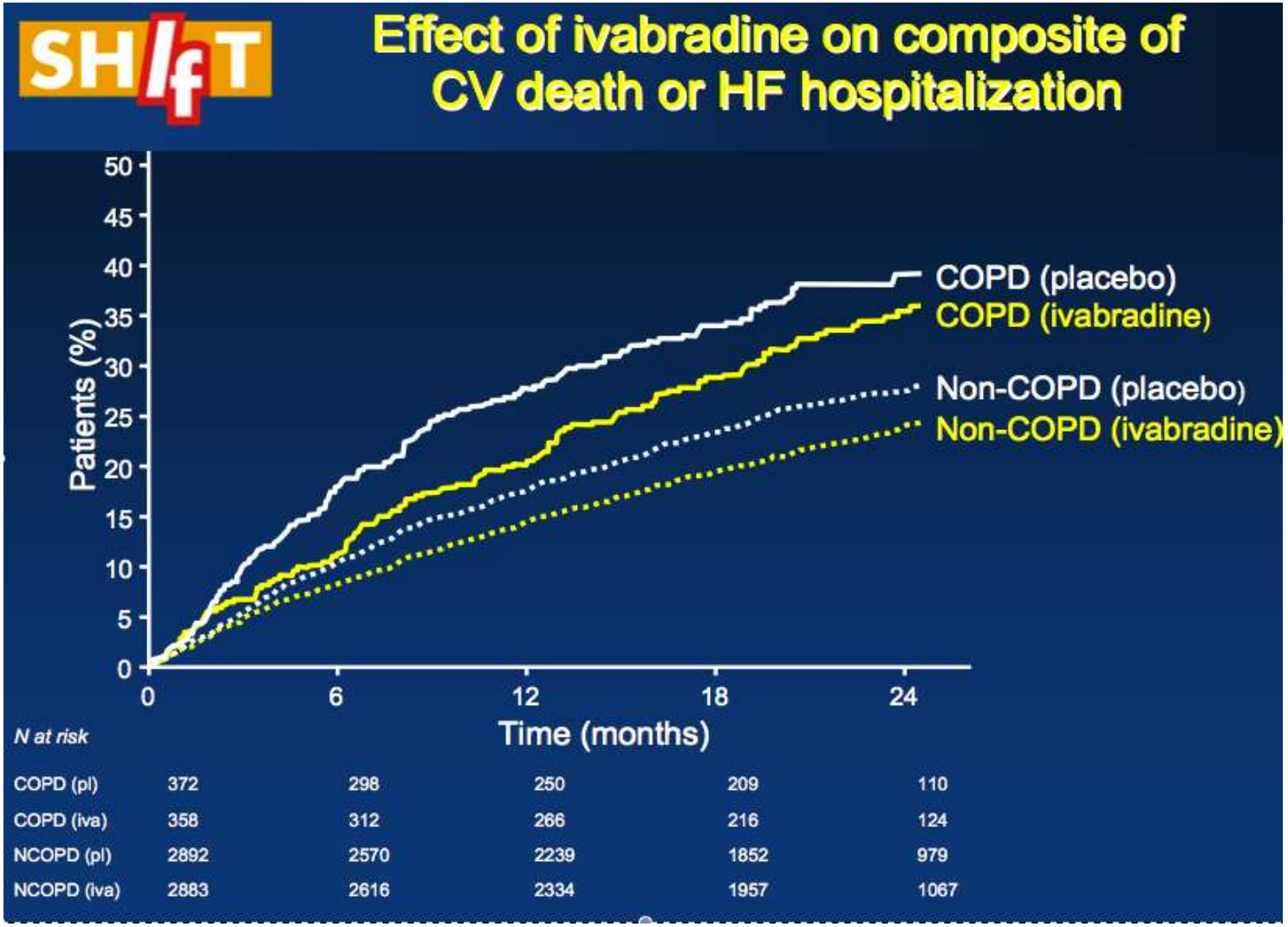
Results

Multivariable Predictors of 12-Month Mortality

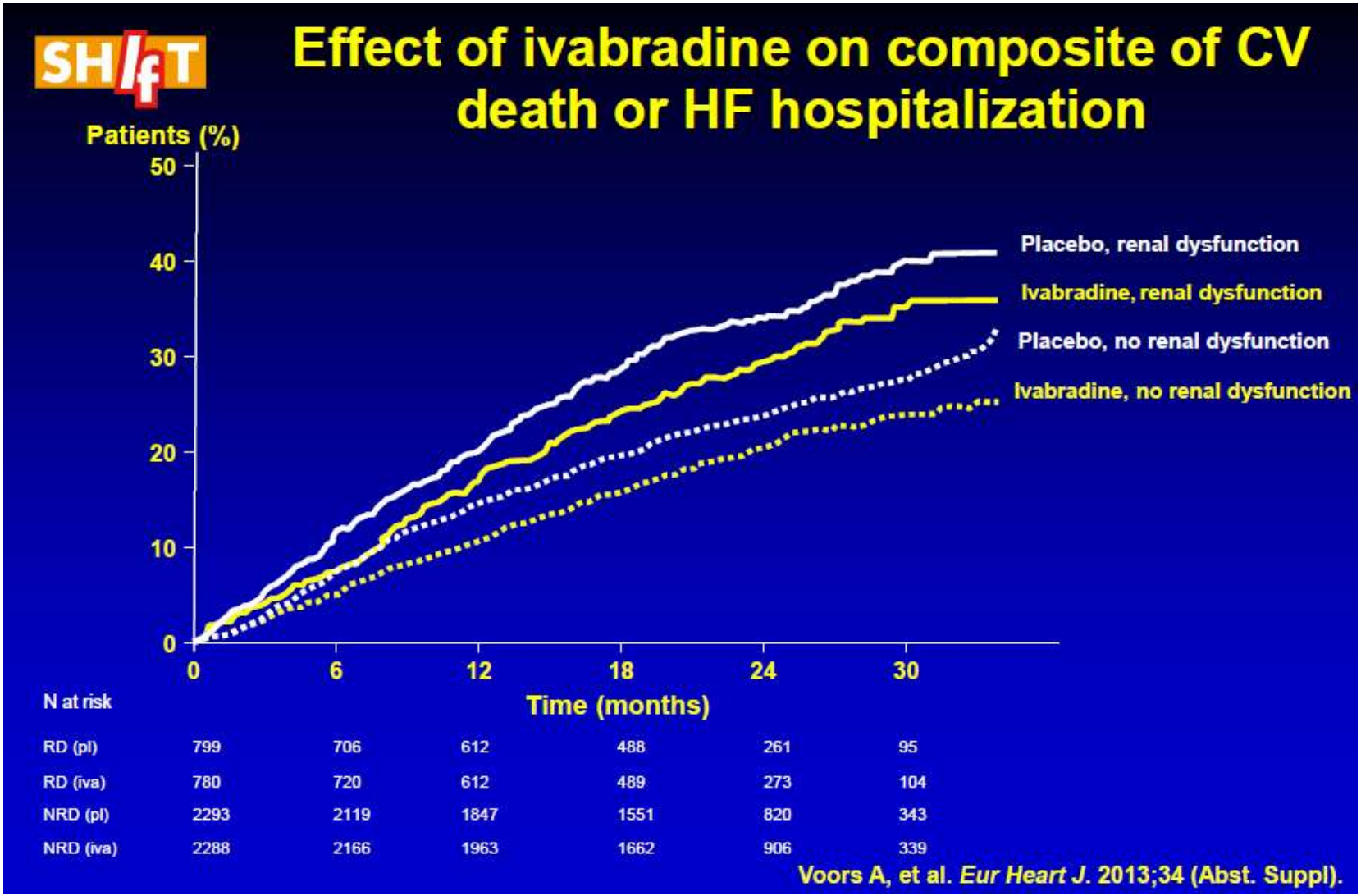
IABP SHOCK II

	Univariable		Stepwise multivariable	
Variable	Hazard Ratio (95% CI)	P-Value	Hazard Ratio (95% CI)	P-Value
Single vessel coronary artery disease	0.68 (0.51-0.92)	0.01	-	-
Mechanical ventilation	1.23 (0.98-1.55)	0.07	-	-
Cold, clammy skin and extremities	1.55 (1.11-2.17)	0.01	-	-
Current smoking	0.63 (0.49-0.81)	<0.001	-	-
History of arterial hypertension	1.33 (1.03-1.72)	0.03	-	-
Hemoglobin, mmol/l	0.87 (0.81-0.94)	<0.001	-	-
Hematocrit, %	0.15 (0.04-0.63)	0.01	-	-
Sinus rhythm	0.78 (0.60-1.01)	0.06	-	-
ST-elevation myocardial infarction	0.76 (0.60-0.95)	0.02	-	-
Age, per 10 years	1.33 (1.20-1.47)	<0.001	1.25 (1.12-1.39)	<0.001
History of stroke	2.18 (1.53-3.11)	<0.001	2.00 (1.37-2.93)	<0.001
Baseline serum lactate, per 10 mmol/l	1.43 (1.29-1.57)	<0.001	1.24 (1.10-1.39)	<0.001
Baseline creatinine, per 100 µmol/l	1.38 (1.24-1.54)	<0.001	1.23 (1.08-1.40)	0.002
Altered mental status	1.73 (1.30-2.30)	<0.001	1.57 (1.15-2.16)	0.005
Oliguria (<30 ml/h)	1.73 (1.38-2.18)	<0.001	1.40 (1.08-1.82)	0.010
pH <7.36 at admission	1.58 (1.24-2.01)	<0.001	1.35 (1.02-1.79)	0.036
Left bundle branch block	1.84 (1.37-2.47)	<0.001	1.41 (1.01-1.98)	0.042

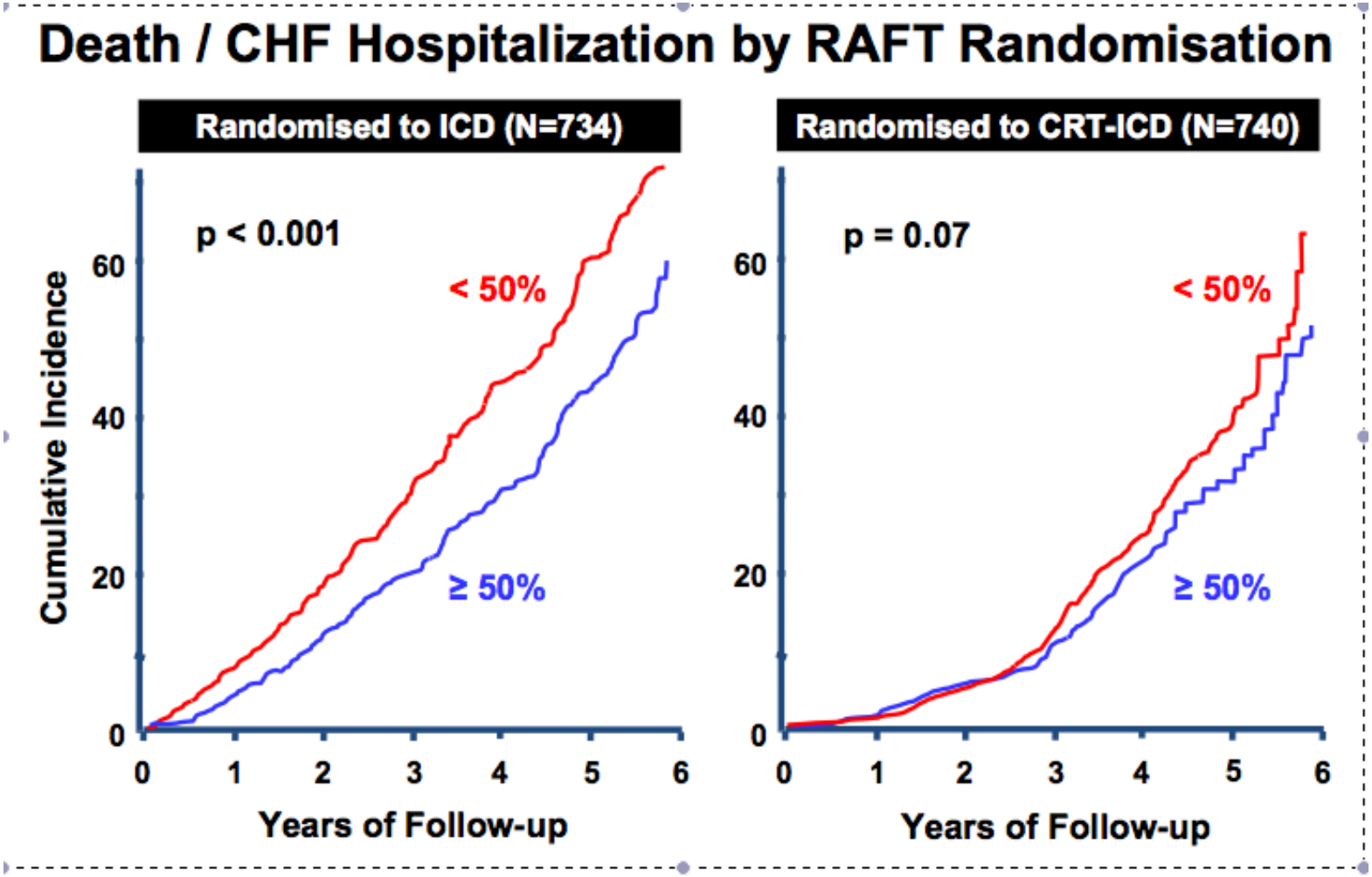
Clinical profiles and outcomes of patients with chronic heart failure and chronic obstructive pulmonary disease: eficacy and safety of Ivabradine: a SHIFT study analysis



SHIFT: The effect of heart rate reduction with ivabradine on renal function in patients with chronic heart failure: an analysis from SHIFT

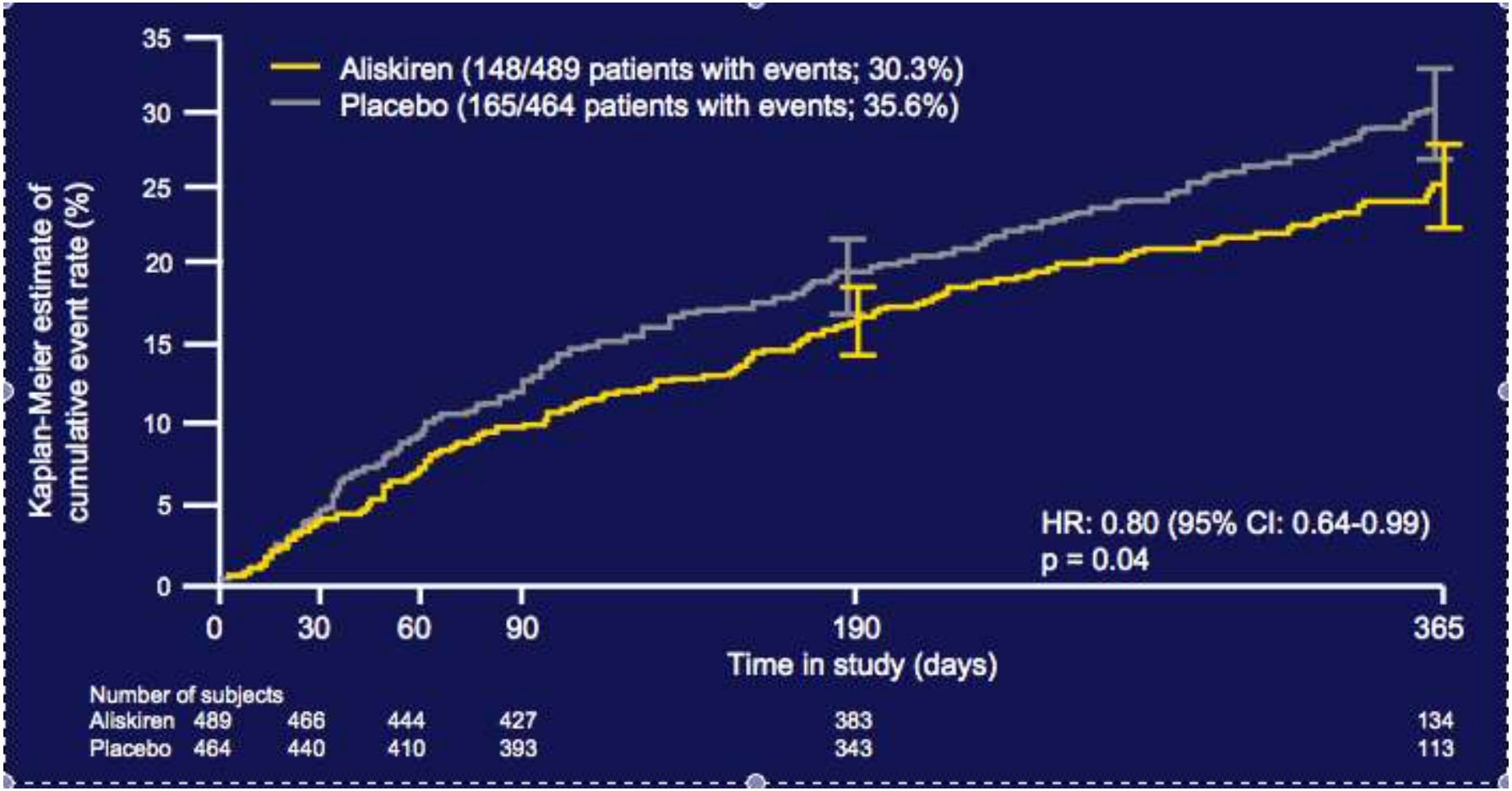


The Importance of Beta-Blockers in Patients with Heart Failure : A Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT) Analysis



OBJETIVO SECUNDARIO EN PACIENTES NO DIABÉTICOS

MORTALIDAD CARDIOVASCULAR O REHOSPITALIZACIÓN A 12 MESES



PULMONARY CONGESTION EVALUATED BY LUNG ULTRASOUND PREDICTS ADMISION IN PATIENTS WITH HEART FAILURE

- 97 pacientes seguidos durante un periodo de 106 ±12 dias
- 21 hospitalizaciones por EAP
- El análisis multivariado mostró que la congestión pulmonar evaluada por eco pulmonar era el predictor más potente de ingresos hospitalario

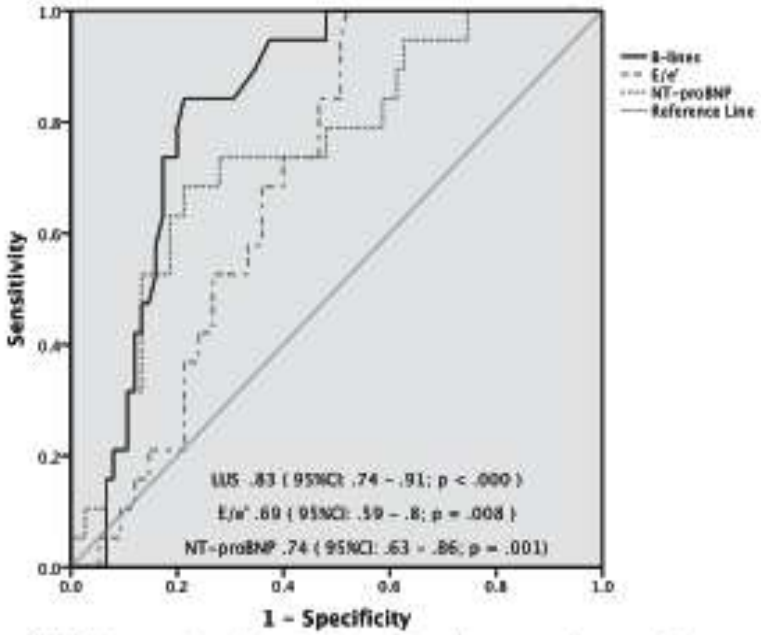


Figure 11: ROC curve using admission due acute pulmonary oedema as reference

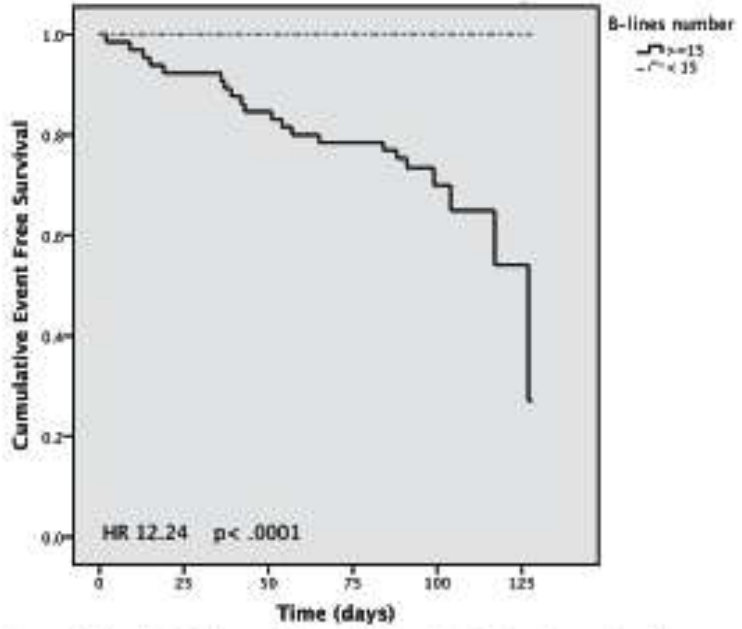
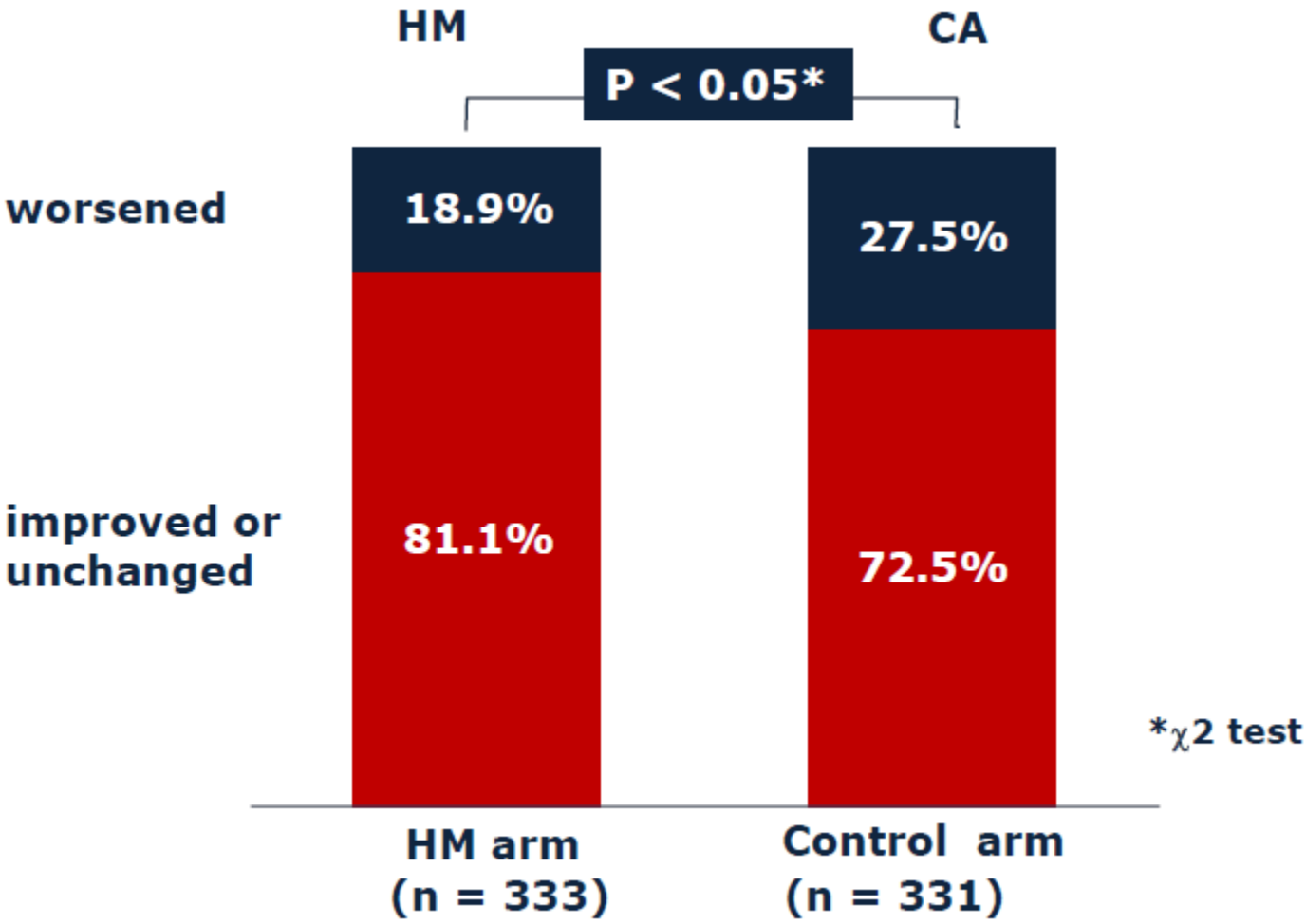


Figure 12: Kaplan-Meier survival analysis for admission due acute pulmonary oedema

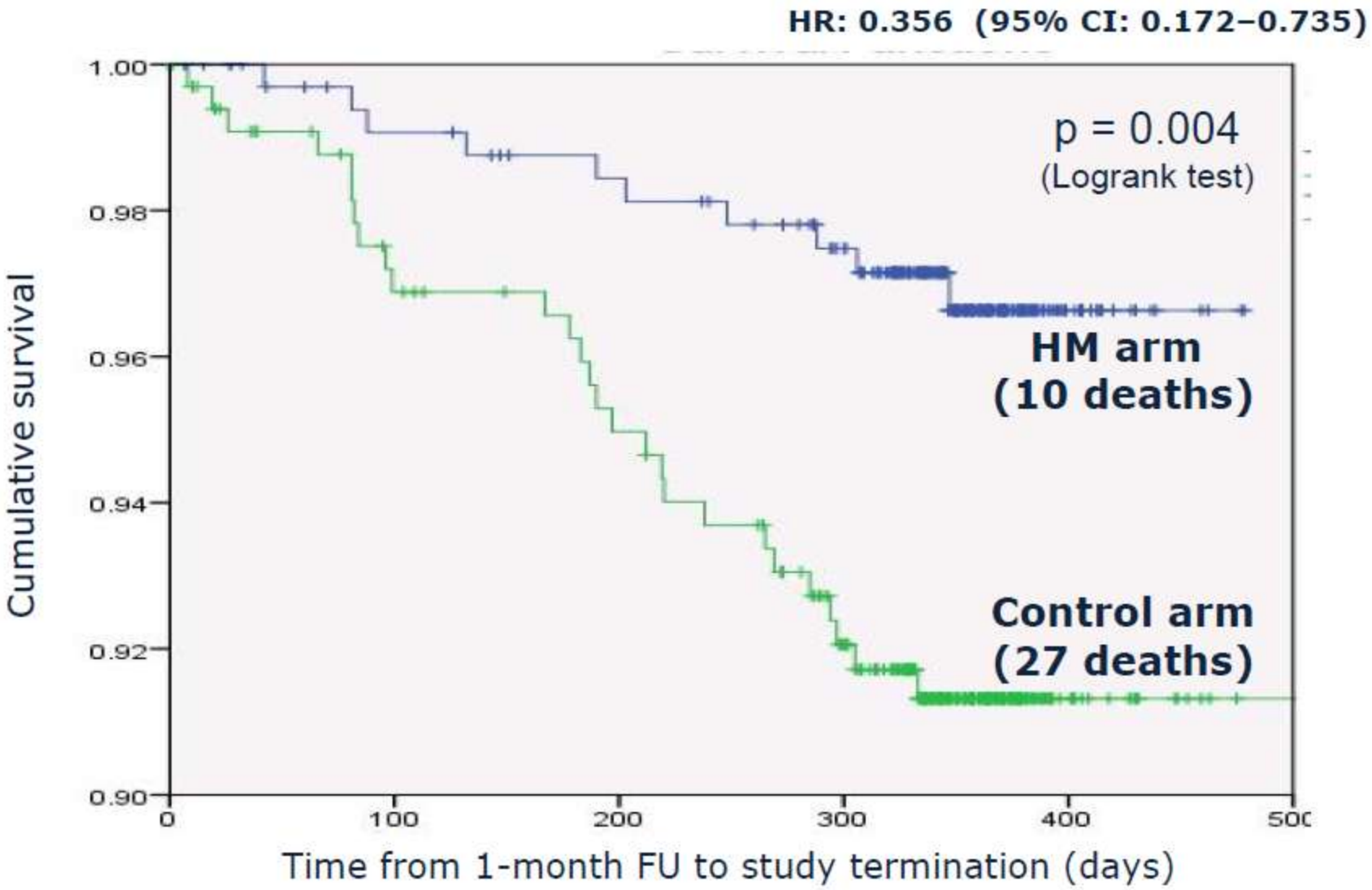
CONCLUSION

In a HF outpatient setting, B-lines assessment by LUS may help to identify patients most likely to develop acute pulmonary oedema. This simple evaluation could help in identifying decompensated patients, whose treatment should be intensified.

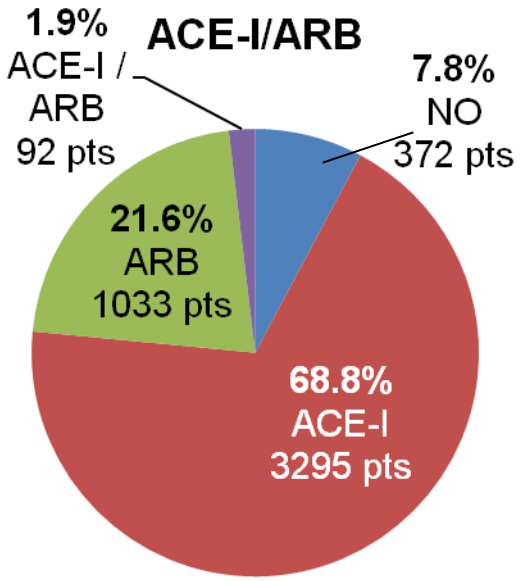
In-Time Study: The Influence of Implant-Based Home Monitoring on the Clinical Status of Heart Failure Patients with Impaired Left Ventricular Function

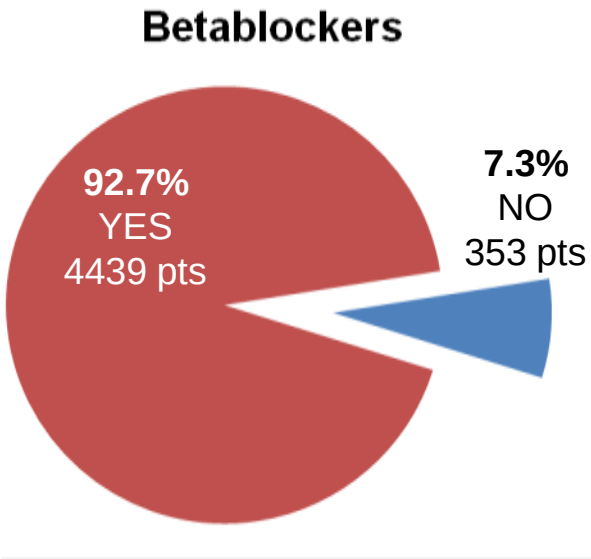


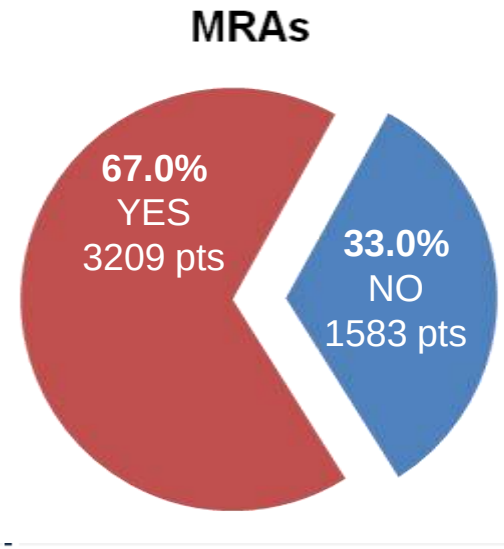
All-cause mortality



Reason for non use of recommended treatments in outpatients patients with reduced EF





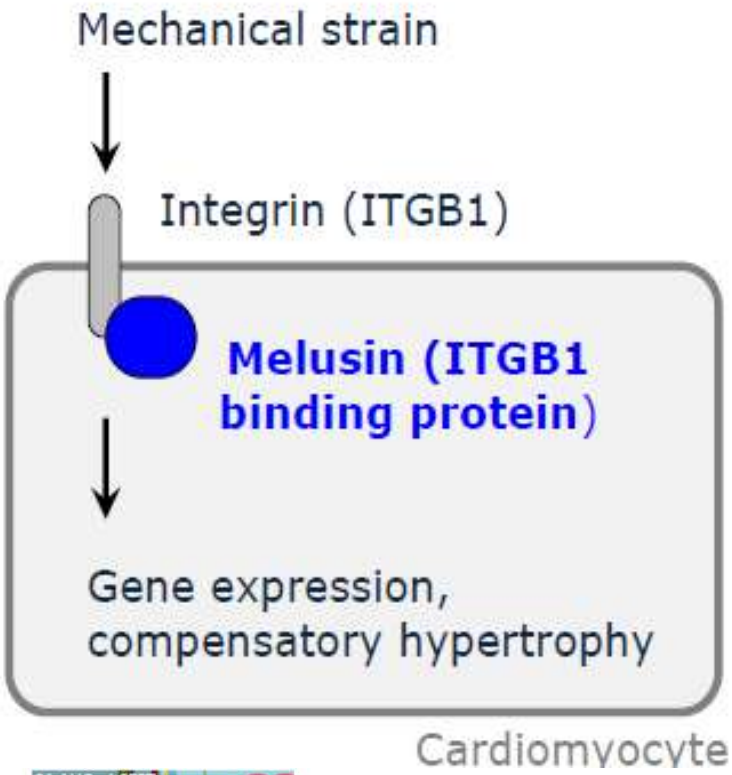


Rate of patients at target dosage of recommended pharmacological treatments

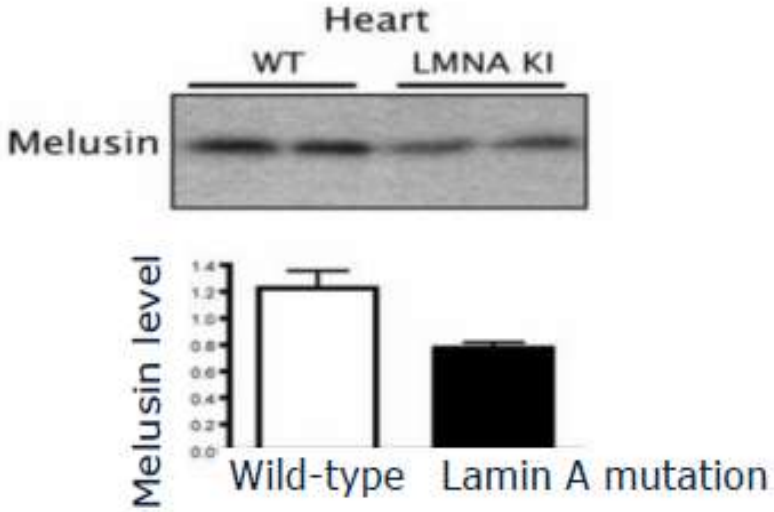
ACE-I (4710 pts)	**1380 (29.3)**	**B-blockers** (6468 pts)	**1130 (17.5)**	**MRAs** (4226 pts)	**1290 (30.5)**
ARBs (1500 pts)	**362 (24.1)**				

Melusin gene therapy: a novel approach to fight familial cardiomyopathy

- **Melusin transduces mechanical strain signals and mediates compensatory hypertrophy**



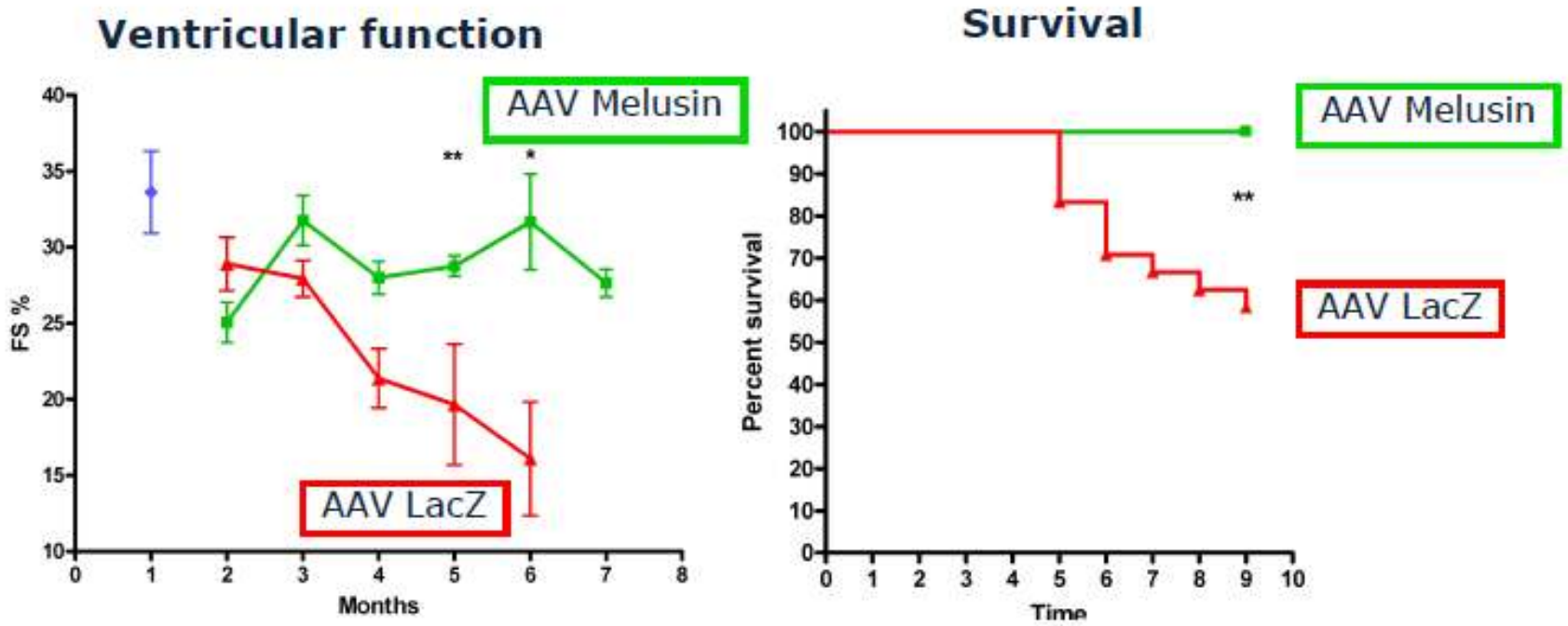
- **Melusin is downregulated in a genetic model of cardiac failure (Lamin A mutant mice)**



- **Aim of the current study**

Test therapeutic applicability of restoration of melusin levels in heart failure model

AAV9-Melusin gene therapy prevented cardiomyopathy in LaminA-mutant mice



Early detection of cardiotoxicity in patients on cancer therapy

The role of myocardial deformation imaging and biomarkers

(*GECAME REGISTRY.* Study Group for Cardiotoxicity due to Chemotherapy)

S. Valbuena[1], D. Iglesias[2], T. López[1], O. Rodríguez[1], D. Gemma[1], F. De Torres[1], O. Salvador[1], A. Buño[1], M. Moreno[1], J. López-Sendón[1]

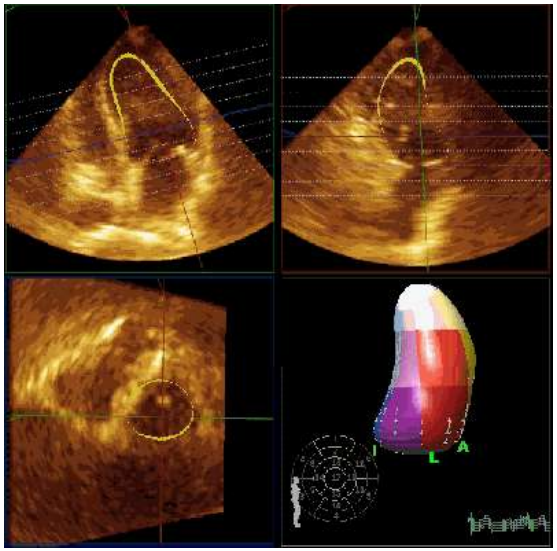
(1) Hospital Universitario La Paz, Madrid

(2) Hospital Infanta Sofía, Madrid

N=119, fw 1 año: 99

- IE33
  - 2D and 3D LVEF
  - Global longitudinal Strain (GLS)

- Postprocessing for 3D and Strain analysis with QLAB software



RESULTS

We observed a significant decrease in LVEF, GLS, ESV and MAPSE early after start of chemotherapy. This decrease was maintained along the study period.

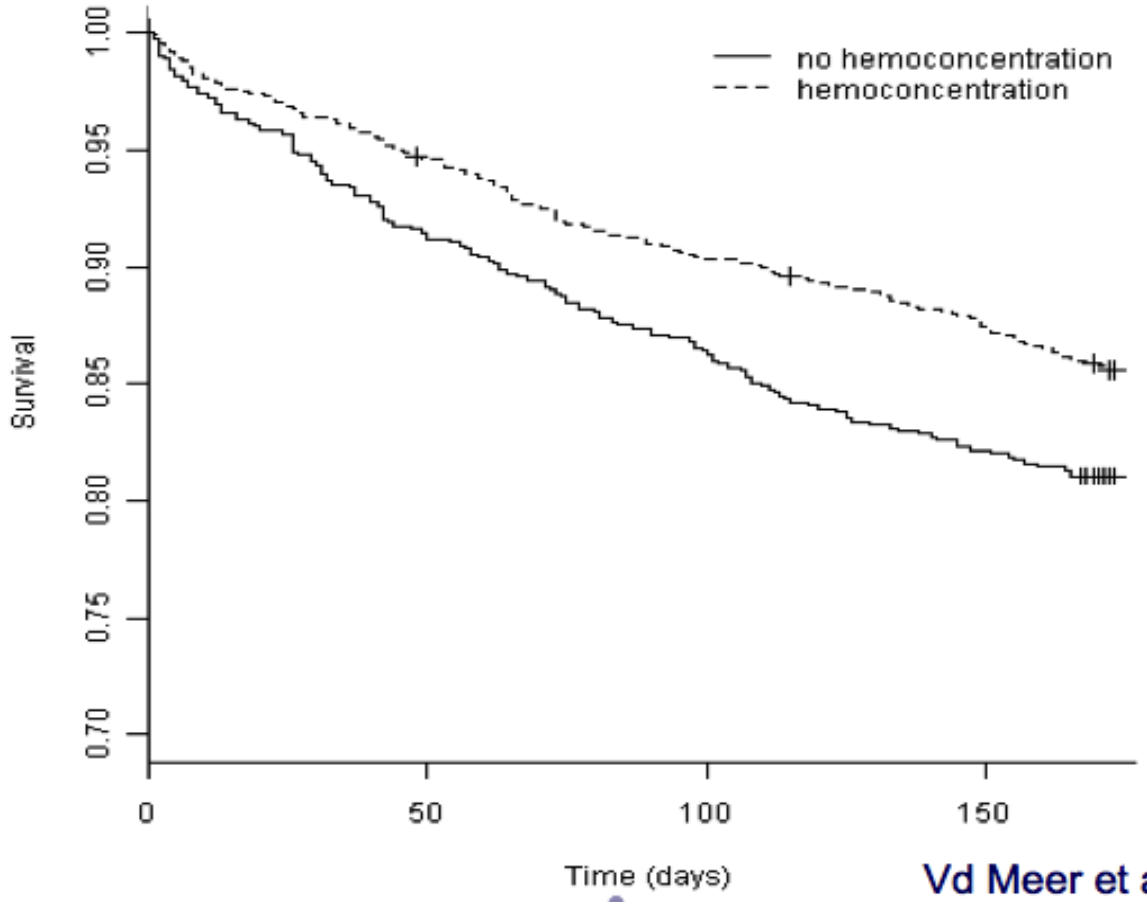
Cardiotoxicity (%)

	Baseline	3 months	6 months	12 months
LVEF	--	**8.7**	**7.1**	**11.4**
3D LVEF	--	**12.0**	**15.6**	**20.4**
GLS	--	**40.7**	**40.5**	**44.6**
hs-TnT *(> p99=14 Pg/ml)*	**9.5**	**50.0**	**38.1**	--

GLS and 3D LVEF are more sensitive than LVEF to detect CT.

Hemoconcentration in AHF: lower 180 day mortality

1,969 AHF patients and mild to moderate impaired renal function

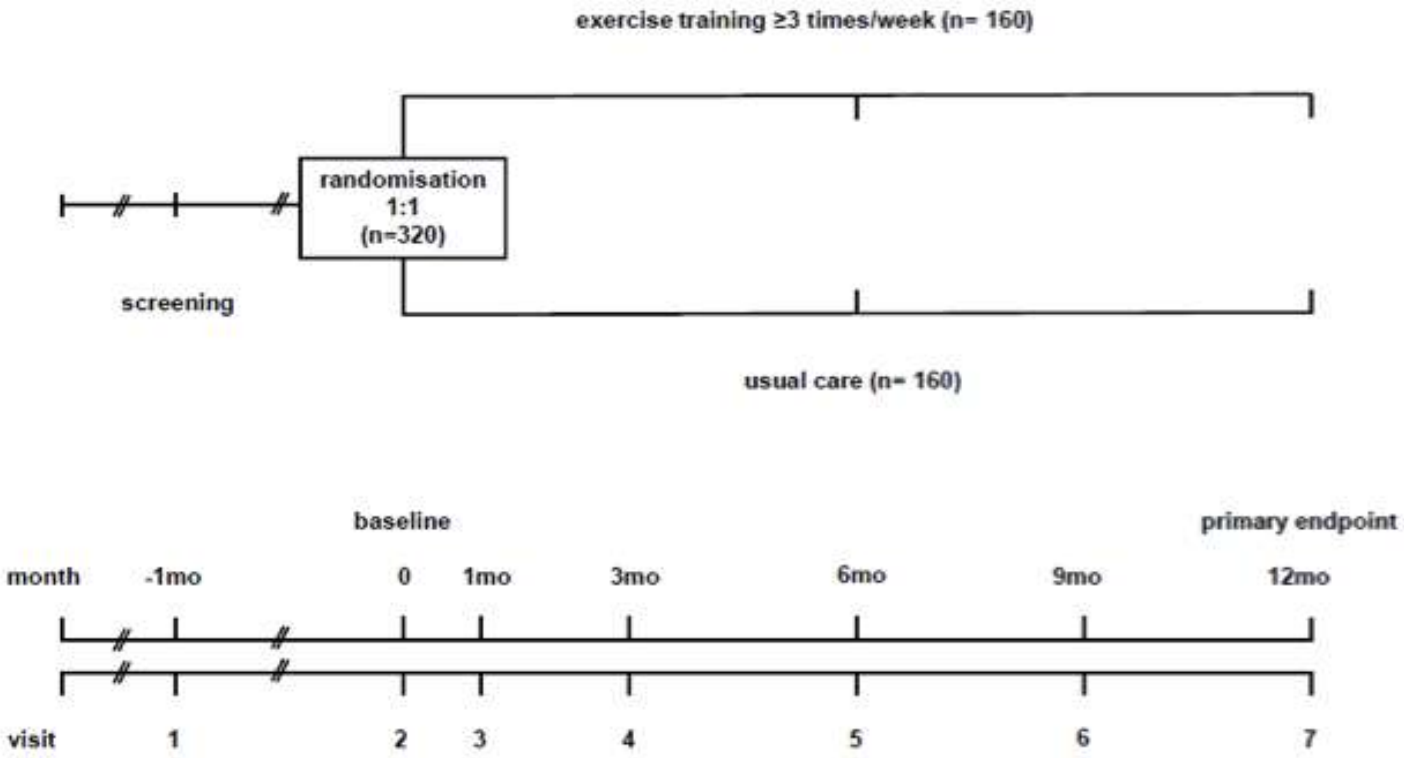


Vd Meer et al. JACC 2013

Effects of Exercise Training on Outcome in HFpEF: The Ex-DHF Trial

multi-center, prospective, randomised, controlled, parallel group study to assess the effects of exercise training in n=320 patients with HFpEF (composite outcome score)

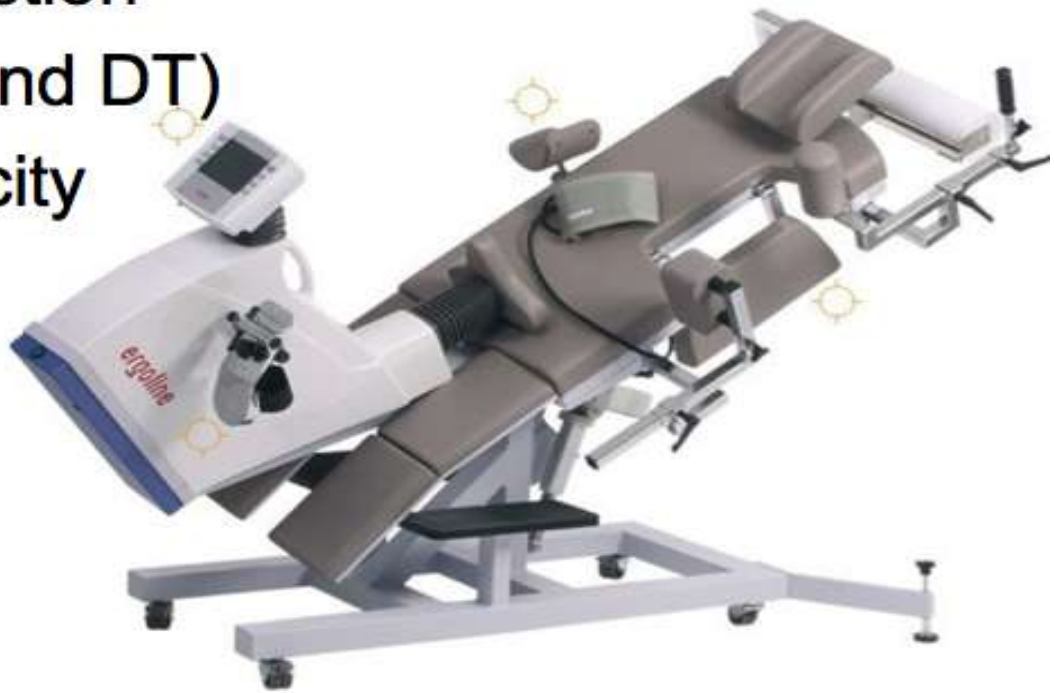
Flow Chart:



(http://www.controlled-trials.com/ ISRCTN86879094)

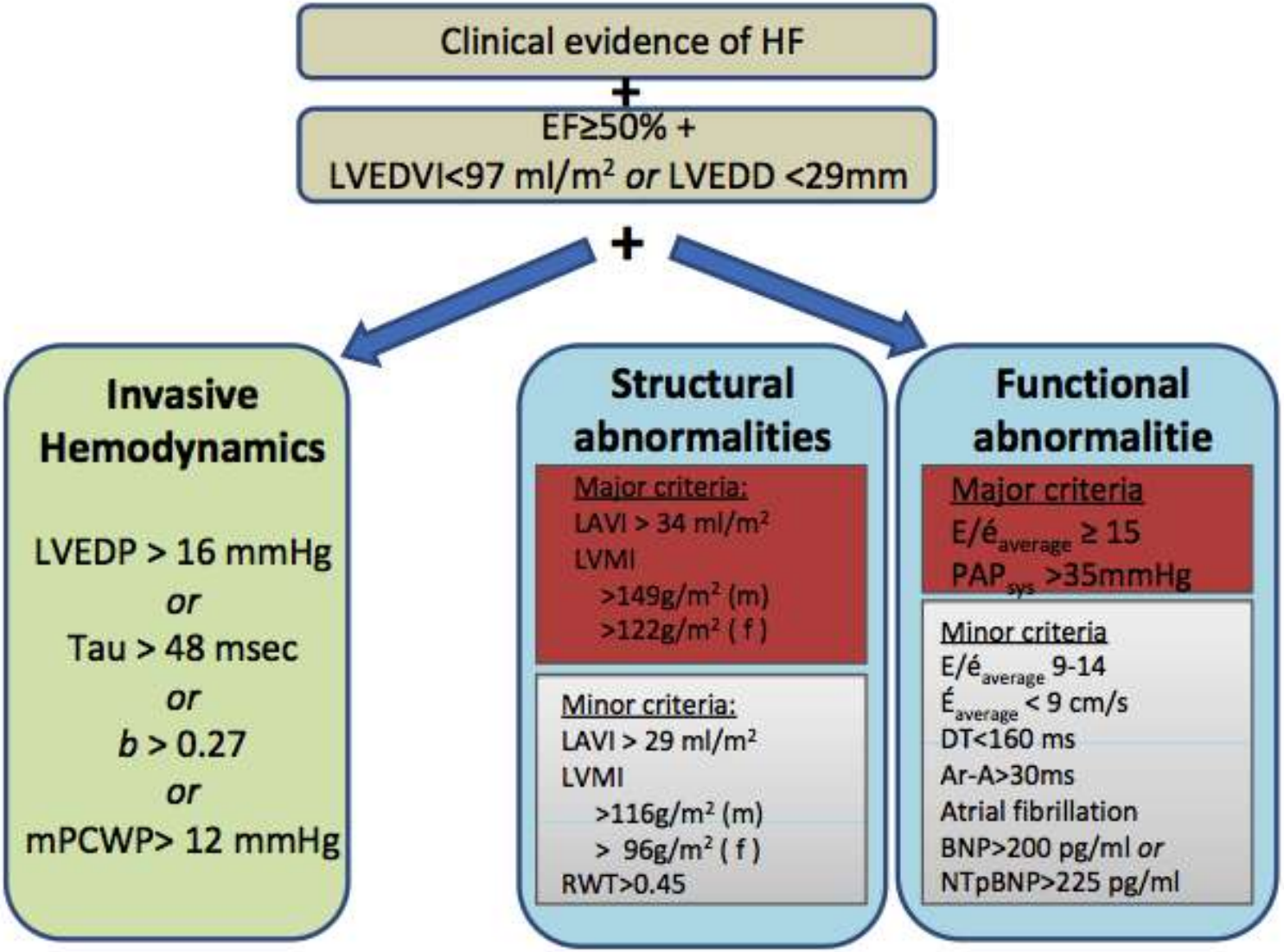
The “Diastolic Stress Test”

- Supine bike
- 25 Watts increments
- Access systolic function
- Mitral inflow (E, A and DT)
- Mitral annulus velocity
- E/e´
- TR velocity
- Recovery



Jae K. Oh et al. (Mayo Clinic, 2005)

HFpEF : NEW DIAGNOSTIC RECOMENDATIONS ?



A diagnostic score, followed by stress test

If ≥4 points: Definite diagnosis of HFpEF

2 major

or

1 major+2minor

or

4 minor

If 1-3 points: HFpEF possible

Diastolic stress test!

If 0 points: HFpEF exluded

Alternative cause for symptoms?

MENSAJES FINALES

- Siguen las novedades en la ICA : omecamtiv mecarbil / serelaxina.
- Hay que seguir avanzando en la implementación de las terapias para la IC según las GPC.
- Tratamiento personalizado según las comorbilidades.
- Detección precoz no invasiva de las descompensaciones de la IC.
- La telemedicina tendrá impacto sobre el pronóstico de la IC.
- Avances en la detección precoz y en el tramiento genético de las miocardiopatias.
- Nuevos biomarcadores: hemoglobina / hemoconcentración
- El ejercicio como elemento clave tanto en el diagnóstico como en el tratamiento de la IC con función sistólica preservada.