Lo mejor del Congreso ESC 2012 de Múnich

Lo mejor sobre insuficiencia cardiaca (IC)

Dr. JJ. Gómez Doblas

H.U. Virgen de la Victoria, Málaga

SOCIEDAD ESPAÑOLA DE Cardiología

www.nejm.org

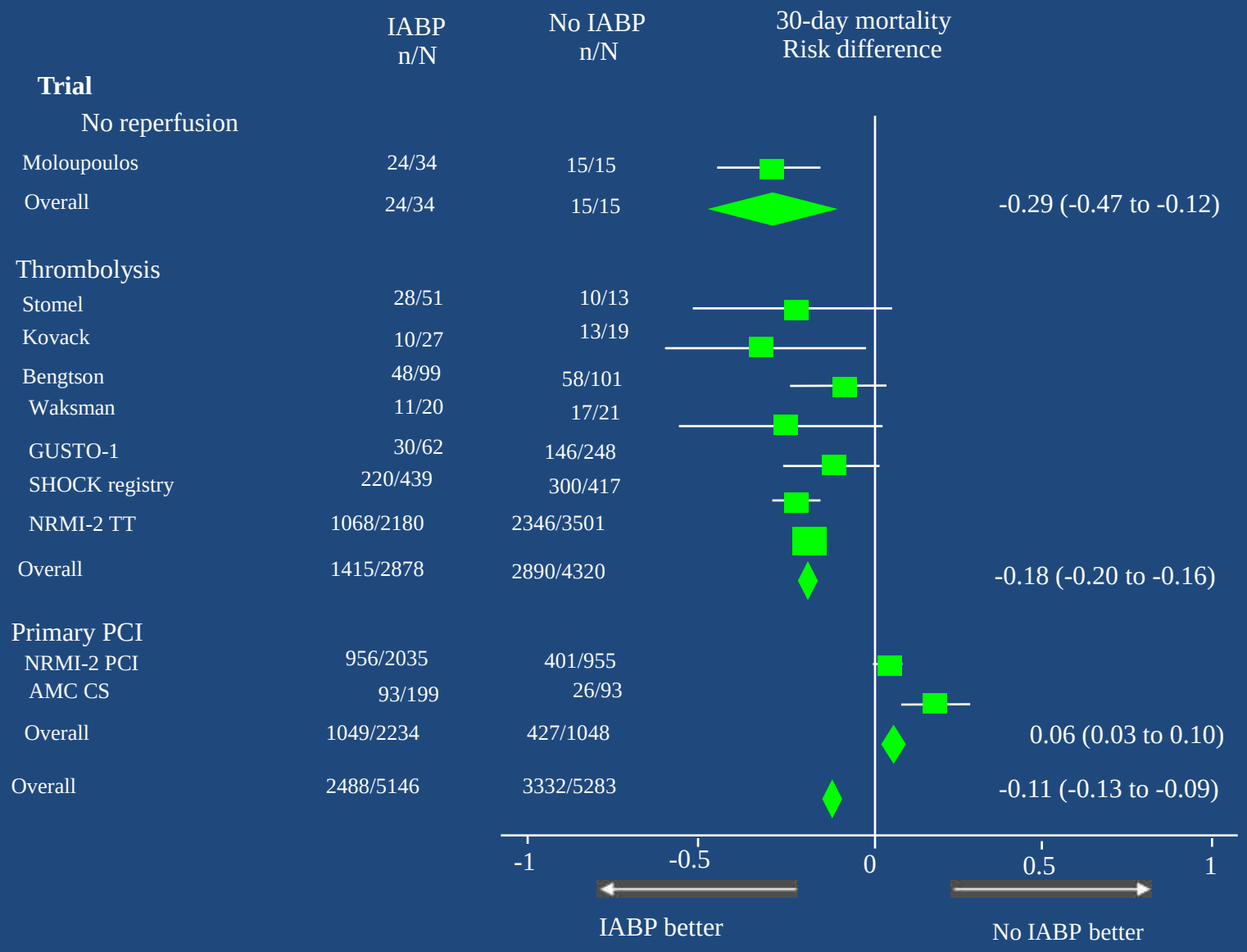
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intraaortic Balloon Support for Myocardial Infarction with Cardiogenic Shock

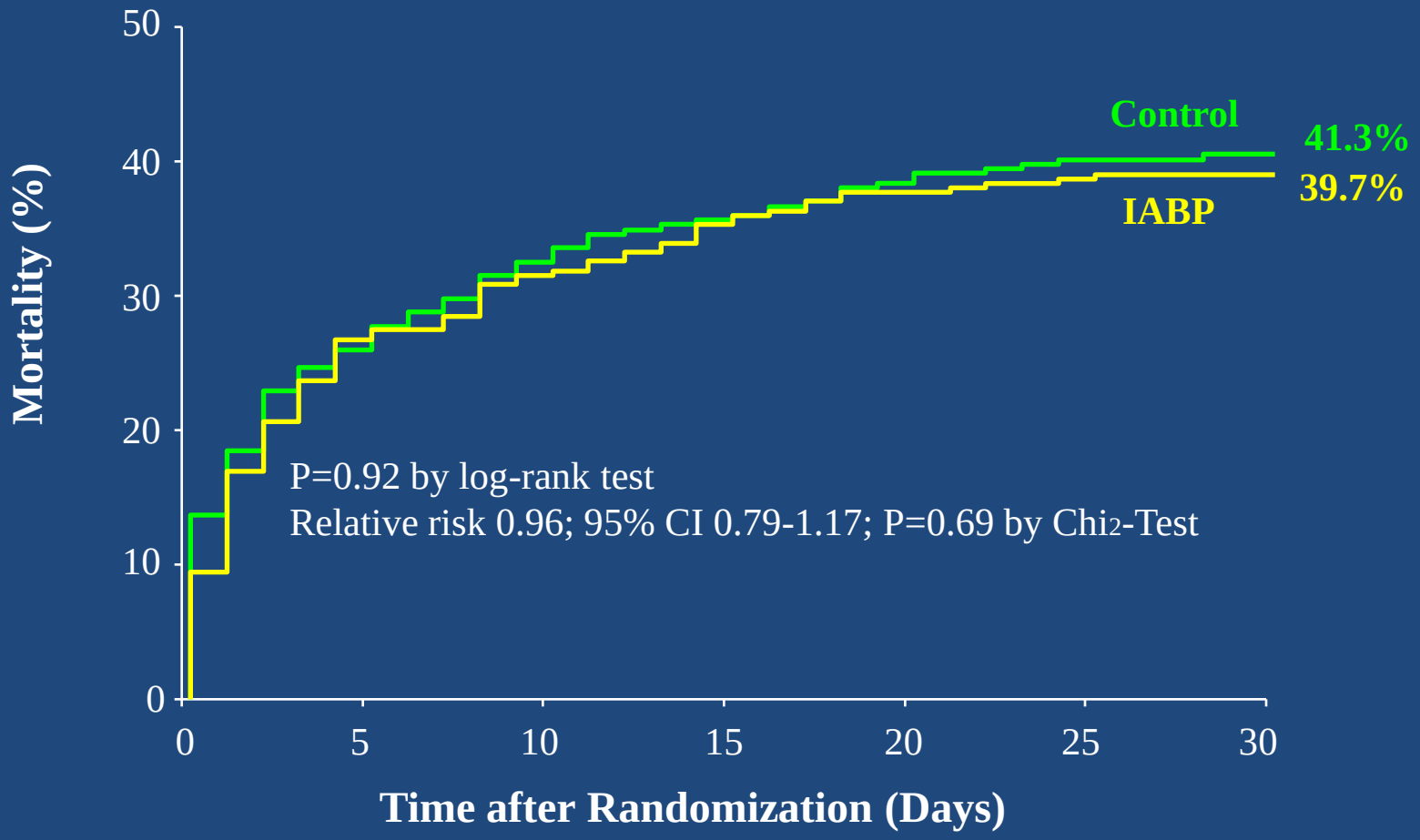
Holger Thiele, M.D., Uwe Zeymer, M.D., Franz-Josef Neumann, M.D., Miroslaw Ferenc, M.D., Hans-Georg Olbrich, M.D., Jörg Hausleiter, M.D., Gert Richardt, M.D., Marcus Hennersdorf, M.D., Klaus Empen, M.D., Georg Fuernau, M.D., Steffen Desch, M.D., Ingo Eitel, M.D., Rainer Hambrecht, M.D., Jörg Fuhrmann, M.D., Michael Böhm, M.D., Henning Ebelt, M.D., Steffen Schneider, Ph.D., Gerhard Schuler, M.D., and Karl Werdan, M.D., for the IABP-SHOCK II Trial Investigators*

MortalityIABP vs no IABP – Metaanalysis



Sjauw et al. Eur Heart J 2009;30:459-468

Primary endpoint study(30-Day mortality)



Summary+ Conclusions

- IABP support in cardiogenic shock is safe without significant inherent complications.
- However, IABP support did not reduce 30-day mortality in this large, randomized, multicenter trial in cardiogenic shock patients complicating myocardial infarction undergoing early revascularization
- The primary study endpoint results are supported by a lack of benefit in secondary endpoints.

The angiotensin receptor neprilysin inhibitor LCZ696 in heart failure with preserved ejection fraction: a phase 2 double-blind randomised controlled trial

*Scott D Solomon, Michael Zile, Burkert Pieske, Adriaan Voors, Amil Shah, Elisabeth Kraigher-Krainer, Victor Shi, Toni Bransford, Madoka Takeuchi, Jianjian Gong, Martin Lefkowitz, Milton Packer, John J V McMurray, for the Prospective comparison of ARNI with ARB on Management Of heart failUre with preserved ejectioN fraction (PARAMOUNT) Investigators**

Summary

Background Heart failure with preserved ejection fraction is associated with substantial morbidity and mortality, but effective treatments are lacking. We assessed the efficacy and safety of LCZ696, a first-in-class angiotensin receptor neprilysin inhibitor, in patients with this disorder.

Methods PARAMOUNT was a phase 2, randomised, parallel-group, double-blind multicentre trial in patients with New York Heart Association (NYHA) class II–III heart failure, left ventricular ejection fraction 45% or higher, and NT-proBNP greater than 400 pg/mL. Participants were randomly assigned (1:1) by central interactive voice response system to LCZ696 titrated to 200 mg twice daily or valsartan titrated to 160 mg twice daily, and treated for 36 weeks. Investigators and participants were masked to treatment assignment. The primary endpoint was change in NT-proBNP, a marker of left ventricular wall stress, from baseline to 12 weeks; analysis included all patients randomly assigned to treatment groups who had a baseline and at least one postbaseline assessment. This trial is registered at Clinicaltrials.gov, number NCT00887588.

www.lancet.com

Background

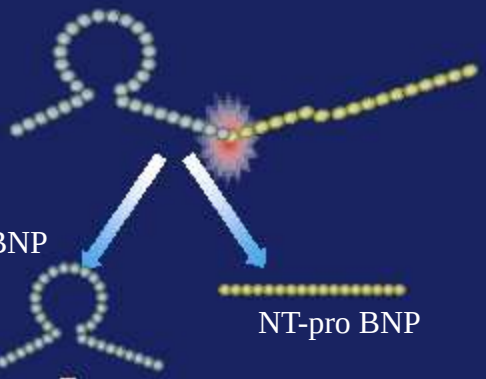
- Heart failure with preserved ejection fraction (HFpEF) accounts for up to half of heart failure cases, and is associated with substantial morbidity and mortality.
- Pharmacologic therapies that have been tested in clinical trials include beta-blockers, calcium-channel blockers, angiotensin converting enzyme (ACE) inhibitors, and angiotensin receptor blockers; to date no therapies have been shown to improve clinical outcomes in this condition.
- Several pathophysiologic mechanisms have been implicated in this disorder, including abnormalities of diastolic function and impaired natriuretic response to acute volume expansion.

LCZ696 – A First-in-Class Angiotensin Receptor Neprilysin Inhibitor

Heart Failure

Natriuretic Peptide System

pro-BNP



BNP

NT-pro BNP

Neprilysin

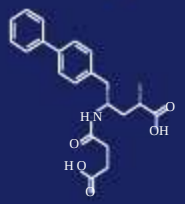
X

Inactive fragments

Vasodilation
- ↓ blood pressure
- ↓ sympathetic tone
- ↓aldosterone levels
- ↓ fibrosis
- ↓ hypertrophy

Natriuresis/Diuresis

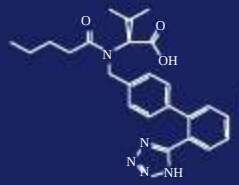
LCZ696



AHU377

↓

LBQ657



Valsartan

Renin Angiotensin System

Angiotensinogen (liver secretion)

Angiotensin I

Angiotensin II

X

AT_1 receptor

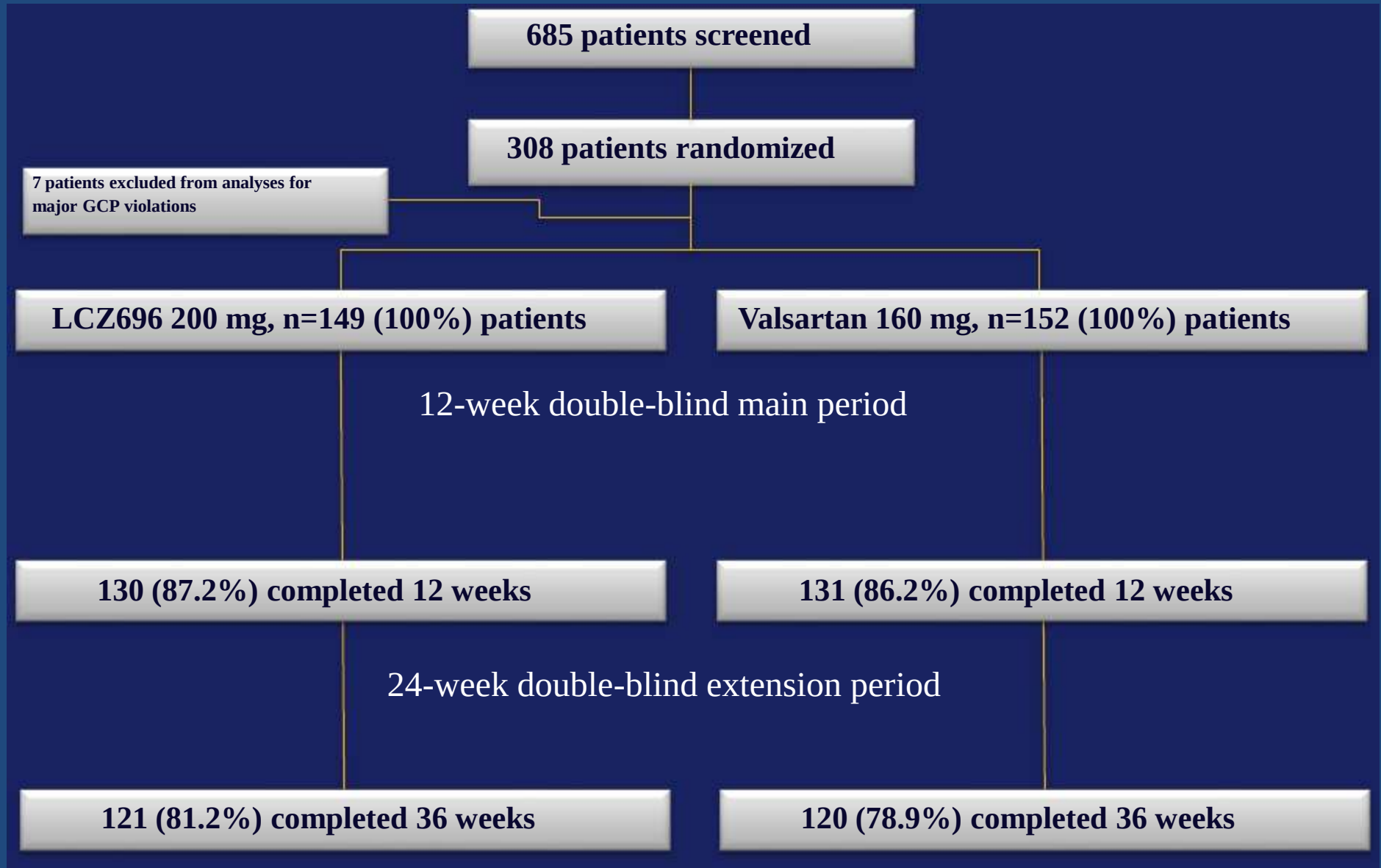
Vasoconstriction
- ↑ blood pressure
- ↑ sympathetic tone
- ↑ aldosterone
- ↑ fibrosis
- ↑ hypertrophy

Objectives and Hypothesis

- The PARAMOUNT trial was designed to test the safety and efficacy of LCZ696 in patients with HFpEF.

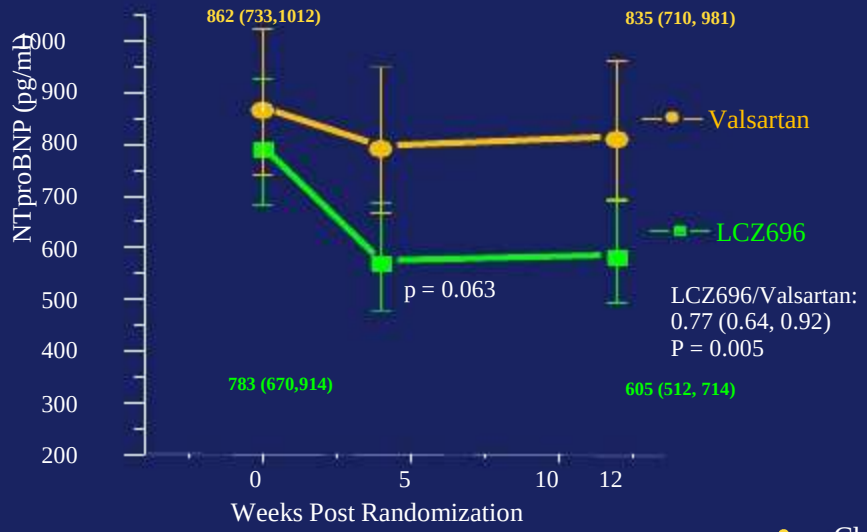
- We hypothesized that LCZ696 would reduce NT-proBNP to a greater extent than the ARB valsartan at 12 weeks, and would be associated with favorable changes in cardiac structure and function at 36 weeks

Patient Flow

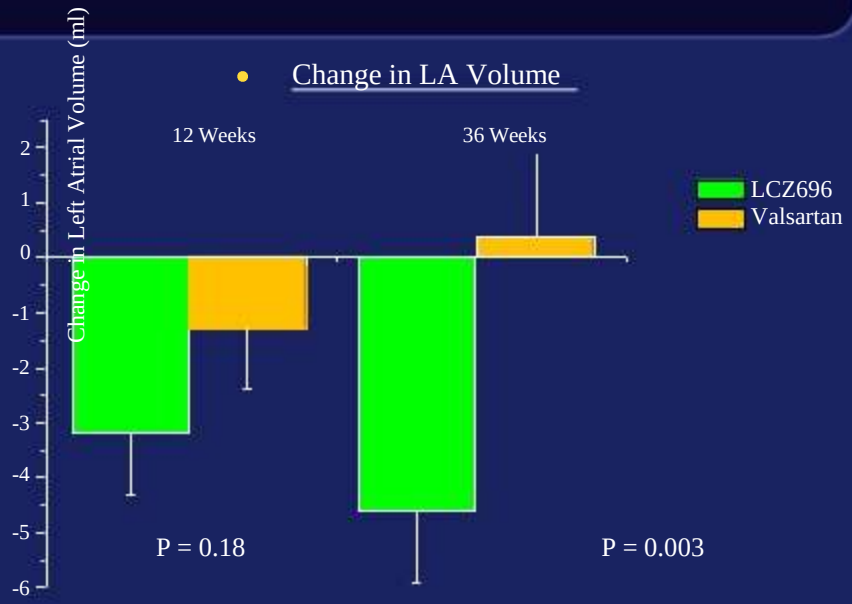


Paramount: LCZ696 reduces NT-ProBNP at 12 weeks, and Reverses Left atrial Remodeling and Improves NYHA Class at 36 weeks

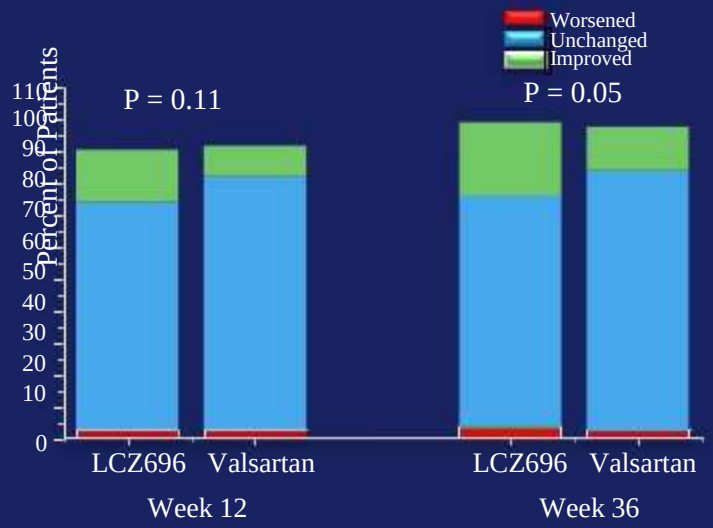
- Change in NT-proBNP at 12 weeks



- Change in LA Volume

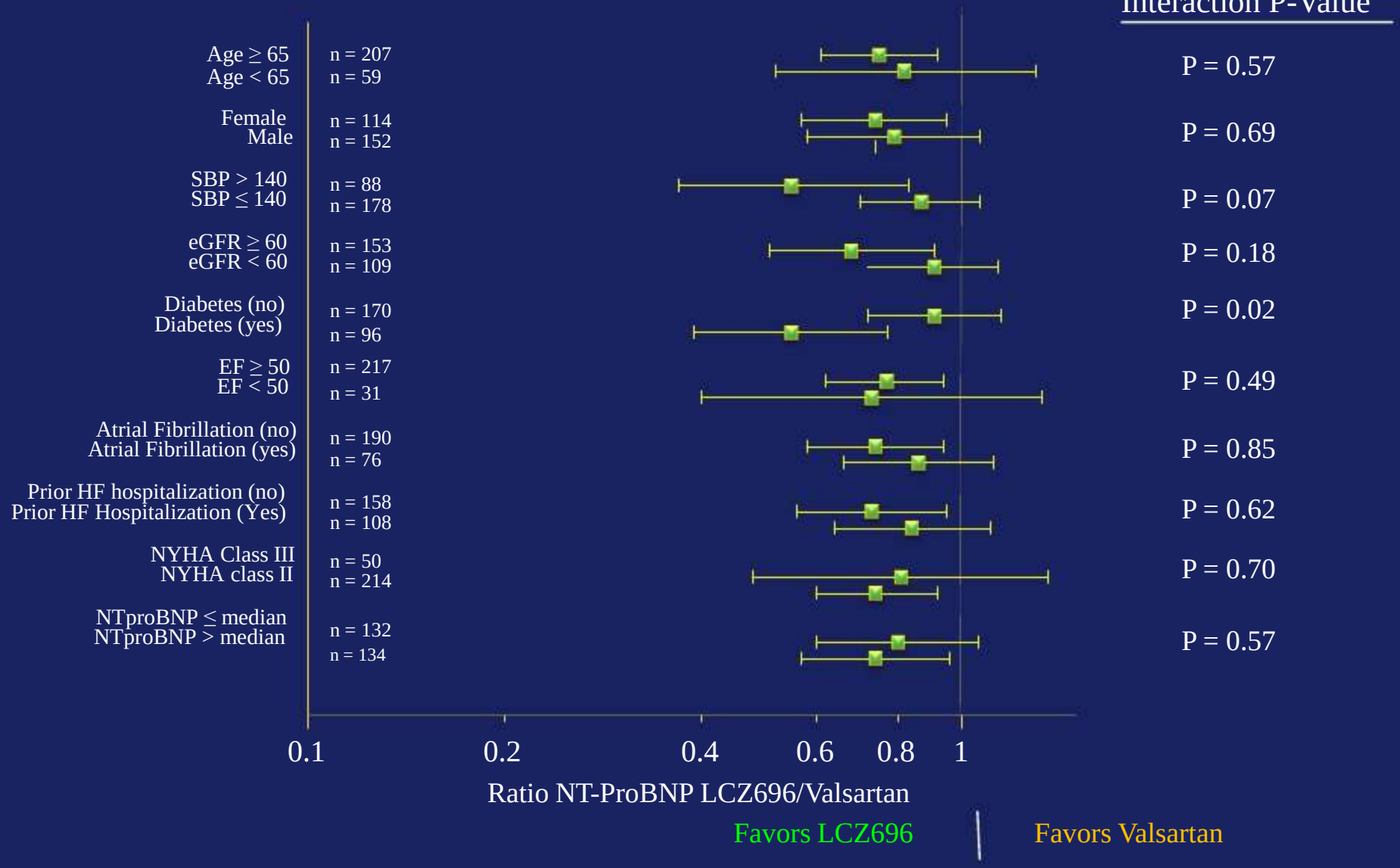


- Change in NYHA Class

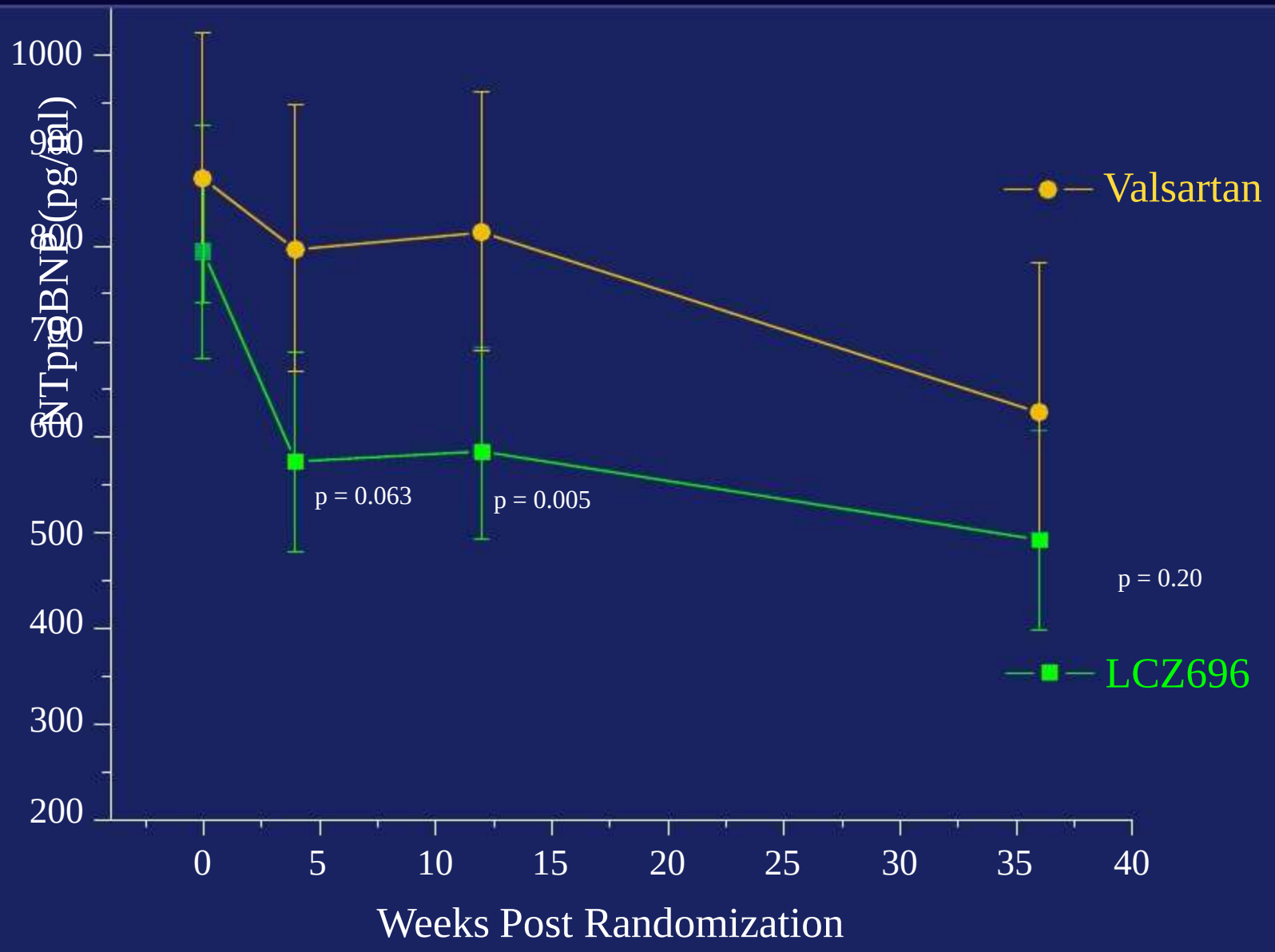


Solomon et al. Lancet 2012

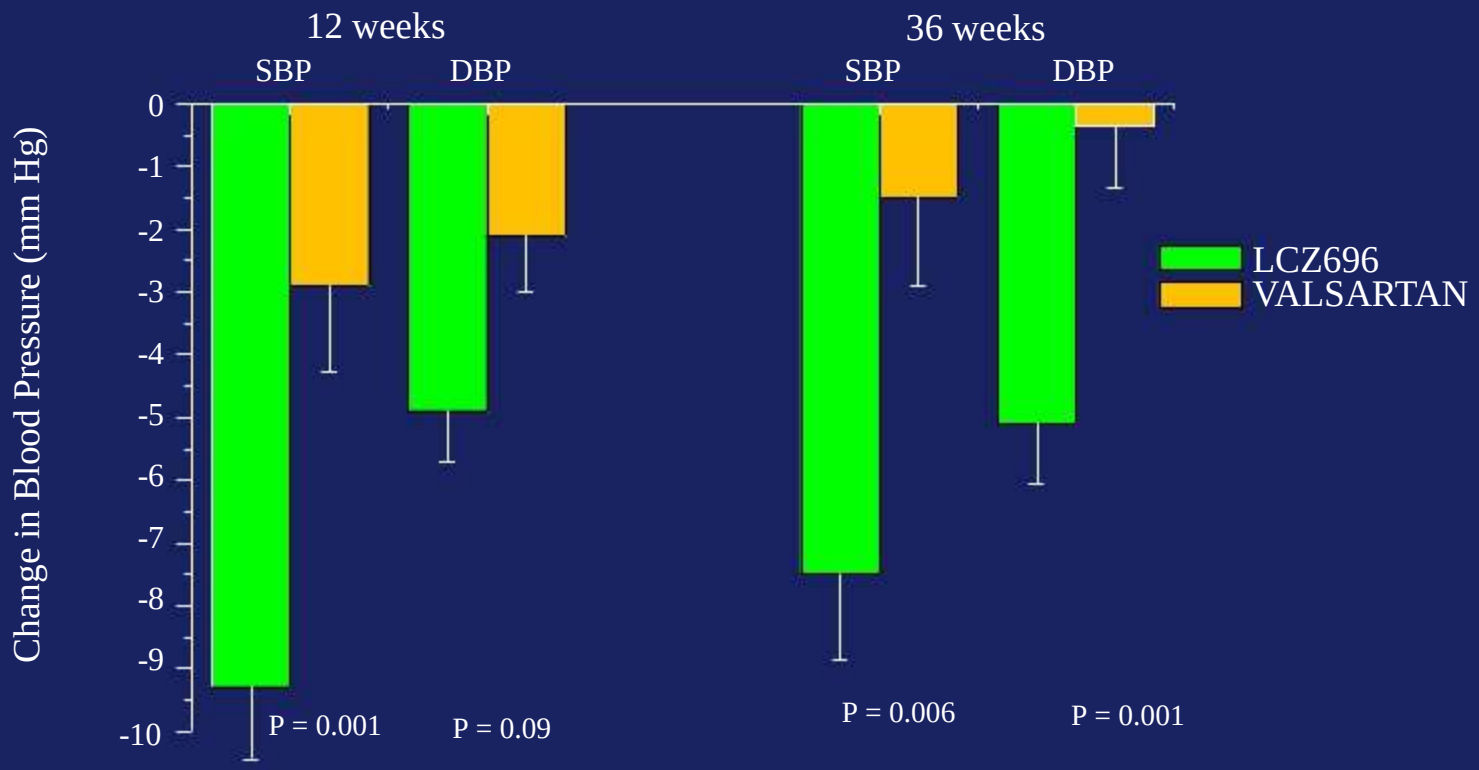
Similar Treatment Effect in All Predefined Subgroups



Change in NT-proBNP over 36 weeks



Blood Pressure Reduction



Note: Change in BP correlated poorly with change in NT-proBNP (r = 0.104, p=0.1). After adjustment for change in BP, the reduction in NT-proBNP between groups remained statistically significant (p=0.01).

Conclusiones

- We found that in patients with HFpEF, the angiotensin receptor neprilysin inhibitor LCZ696 reduced NT-proBNP, a marker associated with worse outcomes in HFpEF, to a greater extent than valsartan after 12 weeks of therapy. This reduction became evident at 4 weeks and was sustained to 36 weeks, though the between group difference was no longer significant.

- We further observed a reduction in left atrial size, indicative of reverse left atrial remodeling, and improvement in NYHA class in patients randomized to LCZ696 after 36 weeks, compared with those randomized to valsartan.

- LCZ696 was well tolerated.

- These hypothesis generating findings suggest that LCZ696 may have beneficial effects in patients with HFpEF and that further testing of this compound may be warranted in patients with this condition.

Disponible online

European Heart Journal Advance Access published August 27, 2012

European Heart Journal
doi:10.1093/eurheartj/ehs259

FASTTRACK
CLINICAL TRIAL & REGISTRY UPDATE

Efecto de ivabradina sobre la hospitalización recurrente por empeoramiento de la insuficiencia cardiaca en pacientes con insuficiencia cardiaca sistólica crónica: Estudio SHIFT

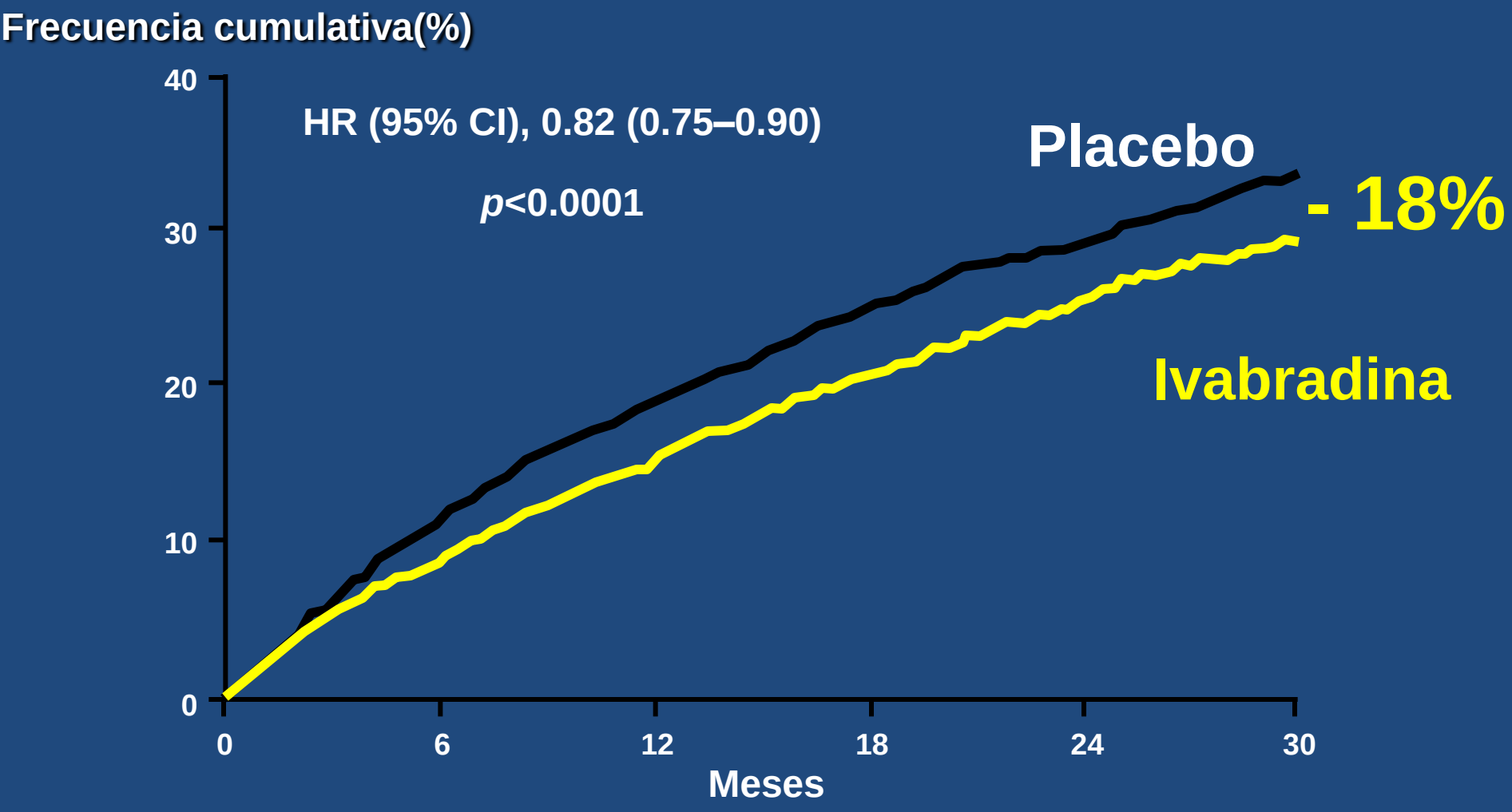
Jeffrey S. Borer[1*], Michael Böhm[2], Ian Ford[3], Michel Komajda[4], Luigi Tavazzi[5], José López Sendón[6], Marco Alings[7], Esteban López-de-Sa[6] y Karl Swedberg[8], en representación de los investigadores del SHIFT

Diseño estudio

- Randomizado, doble ciego, ensayo placebo-controlado en 6.505 pacientes para evaluar la hipótesis de que reducir la FC con Ivabradina, inhibidor I_f, mejora los eventos CV en pacientes con insuficiencia cardiaca crónica (IC)
  - Hospitalización por empeoramiento de la IC en los 12 últimos meses previos a la randomización
  - FEVI≤35%
  - Ritmo sinusal y FC≥70 lpm
  - Recibiendo terapia de fondo basada en las guías

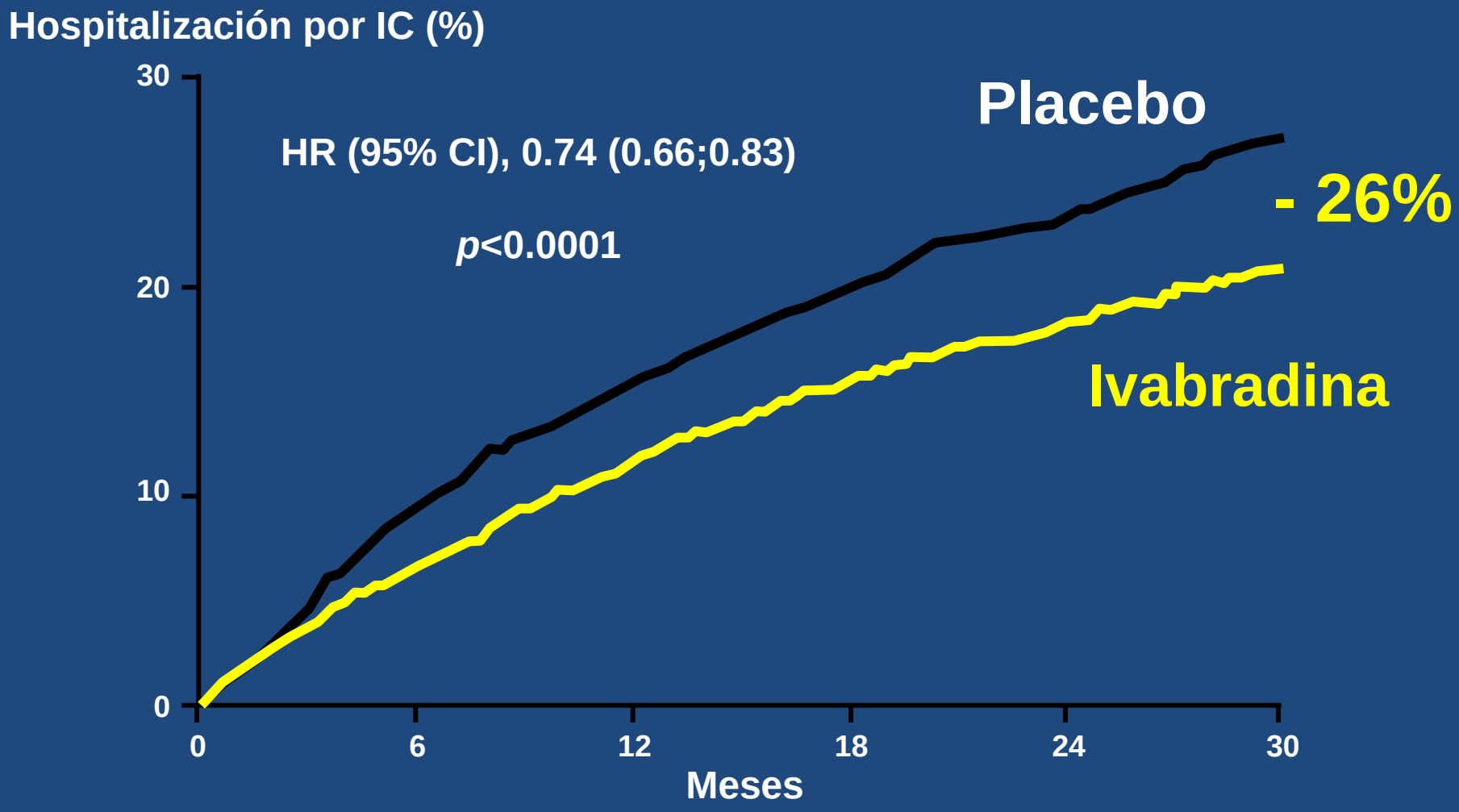
Swedberg K, et al. *Lancet* 2010;376: 875-885.

Objetivo primario: muerte CV o hospitalización por IC



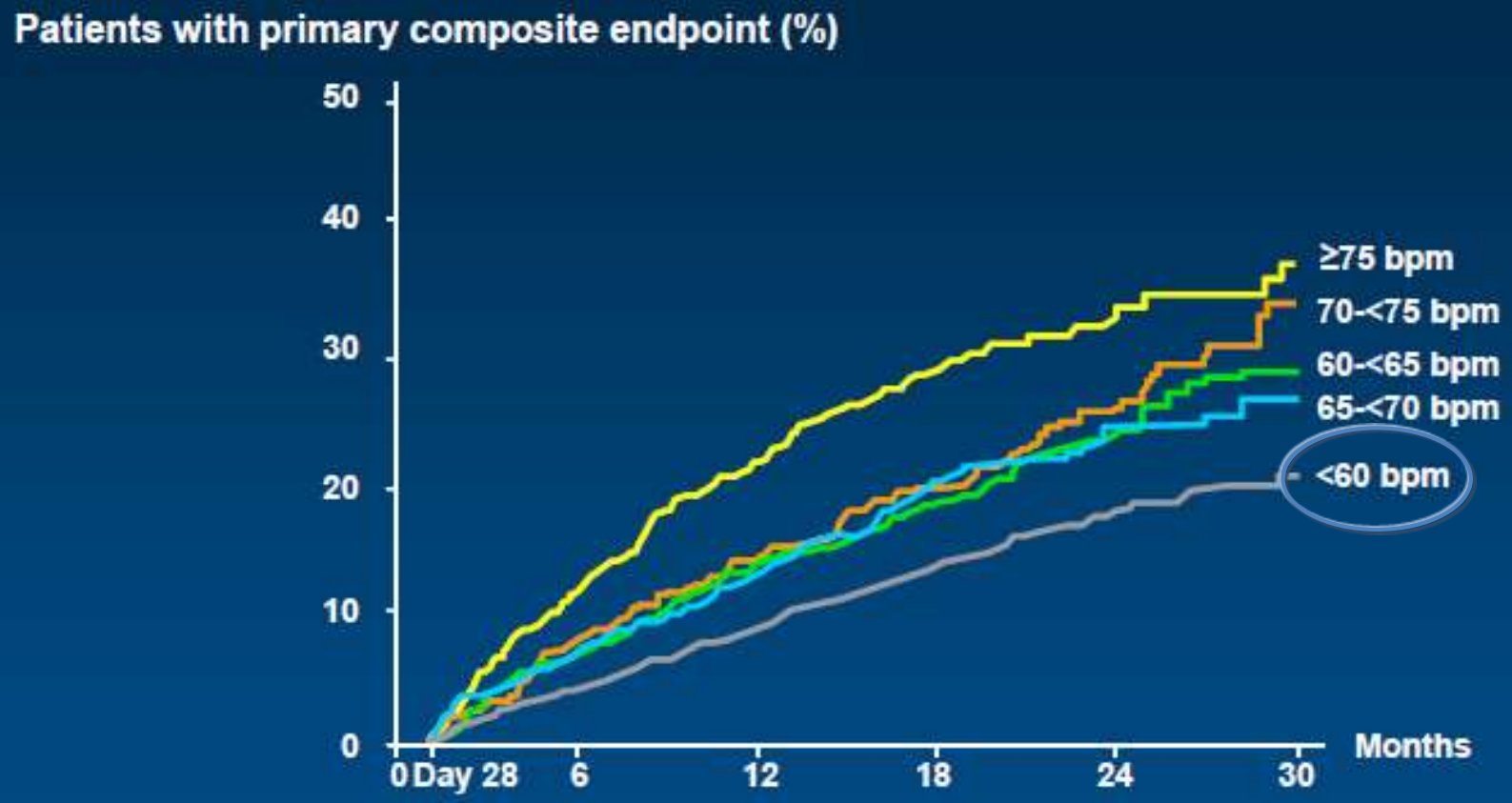
Swedberg K, et al. *Lancet* 2010;376: 875-885.

Objetivo secundario preespecificado: Hospitalización por IC



Swedberg K, et al. *Lancet* 2010;376: 875-885.

Objetivo primario según la FC alcanzada a los 28 días en el grupo de Ivabradina



*Data exclude patients reaching primary composite endpoint in the first 28 days

Lancet. Online 29-08-2010

Objetivo del presente análisis

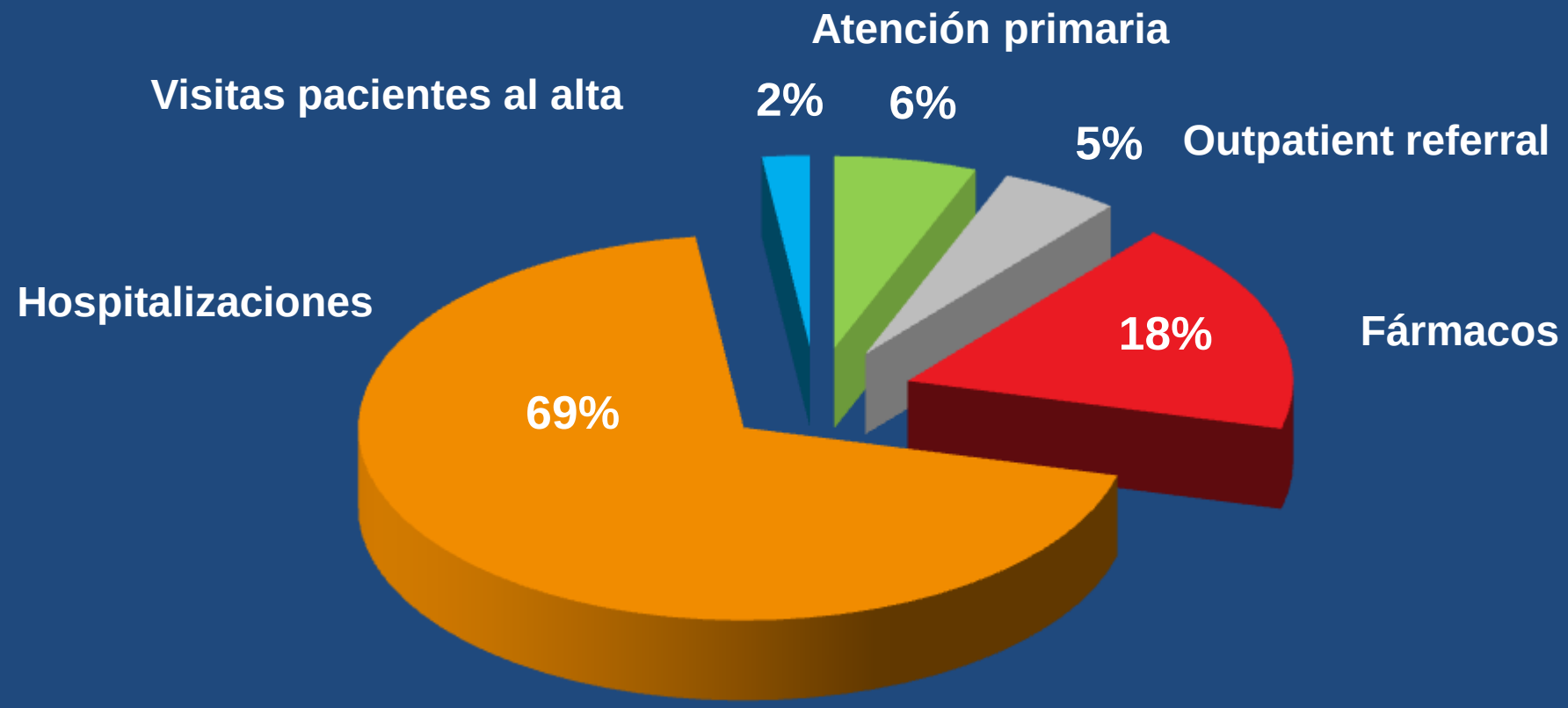
- Evaluar el efecto de reducir la FC con Ivabradina en las hospitalizaciones recurrentes por empeoramiento de la IC

Racional: carga de la hospitalización por IC

- Principal razón de hospitalizaciones en pacientes con IC = agravamiento de la IC
- Elevada tasa de readmisión después de la primera hospitalización:
  - 20% al cabo de un mes
  - 50% al cabo de 6 meses
  - 17% son reingresados 2 o más veces
  - Hospitalización = mayor contribución al coste del tratamiento de la IC

Centers for Medicare and Medicaid Services. 2000 MedPAR data. DRG 127; Fonarow, GC. *Rev Cardiovasc Med*. 2002;3
(suppl 4):S3; Krumholz HM et al. *R Arch Intern Med*. 1997 Jan 13;157(1):99-104; Roger VL, *Circulation*. 2012;125(1):e2-e220.

Carga económica de la IC



- Hospitalización está relacionada con los mayores costes de la IC

Stewart S et al. *Eur J Heart Fail* 2002;4:361–71.

Características basales pre-randomización

	Nº de hospitalizaciones por IC durante el ensayo				
	Ninguna (n=5319)	**Una** (n=714)	**Dos** (n=254)	**3 o >** (n=218)	*p*-valor
Edad (años)	60.0	62.3	61.8	62.4	<0.0001
Sexo (%)	77	74	77	81	0.18
Fc (bpm)	79.3	82.2	83.4	82.2	<0.0001
PAS (mmHg)	122.3	119.8	118.1	117.6	<0.0001
PAD(mmHg)	76.0	75.0	73.4	73.3	<0.0001
FEVI (%)	29.3	27.6	27.8	27.1	<0.0001
NYHA clase II (%)	51	38	38	34	<0.0001
NYHA clase III/IV (%)	49	62	62	66	
Duración de la IC (years)	3.3	4.2	4.3	4.6	<0.0001
Diabetes (%)	29	35	35	40	<0.0001

Borer J, Böhm M, Ford I, et al. Effect of ivabradine on recurrent hospitalization for worsening heart failure in patients with chronic systolic heart failure: the SHIFT study. Eur Heart J. 2012; doi: 10.1093/eurheartj/ehs259

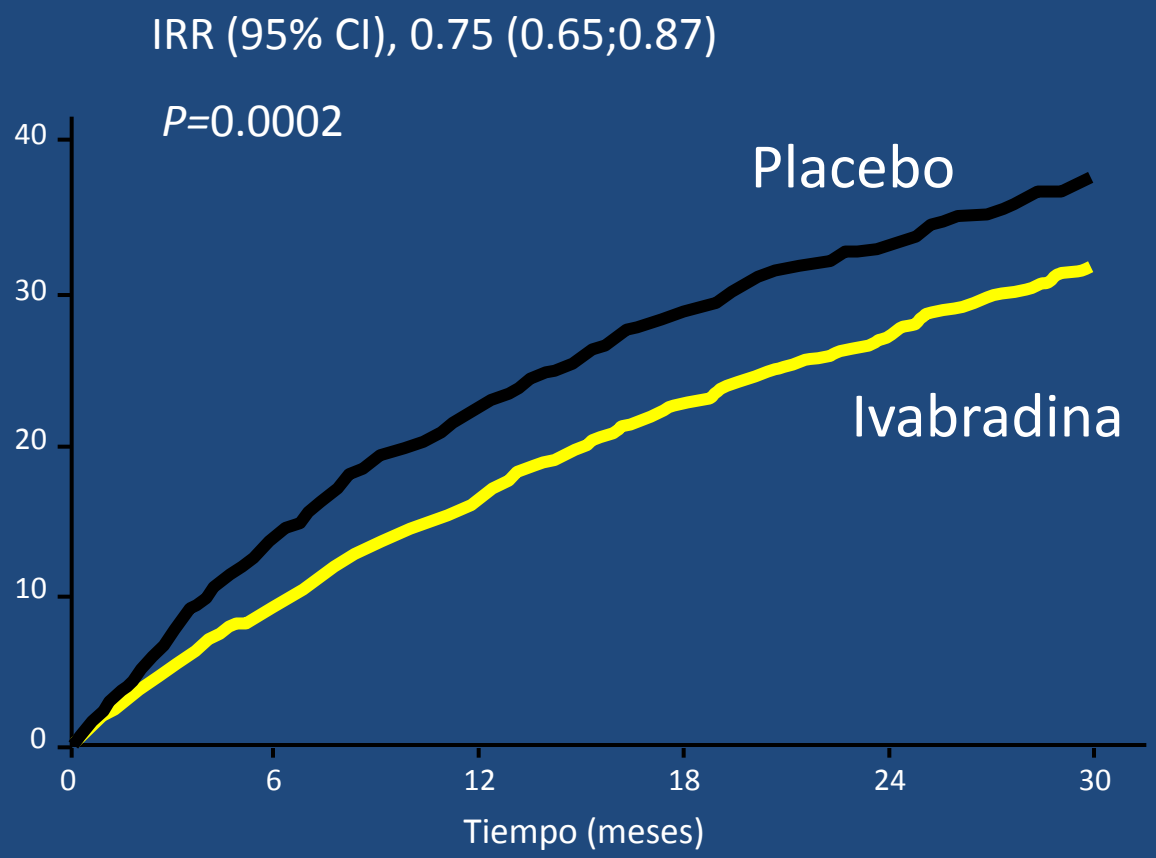
Pre-randomización tratamiento de fondo

	Nº de hospitalizaciones por IC durante el ensayo				
	Ninguna (n=5319)	**Una** (n=714)	**Dos** (n=254)	**Tres o >** (n=218)	*p*-valor
Beta-bloqueantes (%)	90	89	80	86	<0.0001
IECAs y/o ARAII (%)	91	89	90	93	0.13
Antialdosterónicos (%)	58	69	67	73	<0.0001
Diuréticos (%)	82	90	90	95	<0.0001
Digitálicos (%)	20	30	33	35	<0.0001

Borer J, Böhm M, Ford I, et al. Effect of ivabradine on recurrent hospitalization for worsening heart failure in patients with chronic systolic heart failure: the SHIFT study. Eur Heart J. 2012; doi: 10.1093/eurheartj/ehs259

Efecto de Ivabradina en las hospitalizaciones totales por IC

Incidencia cumulativa de hospitalizaciones por IC (primera y repetidas)



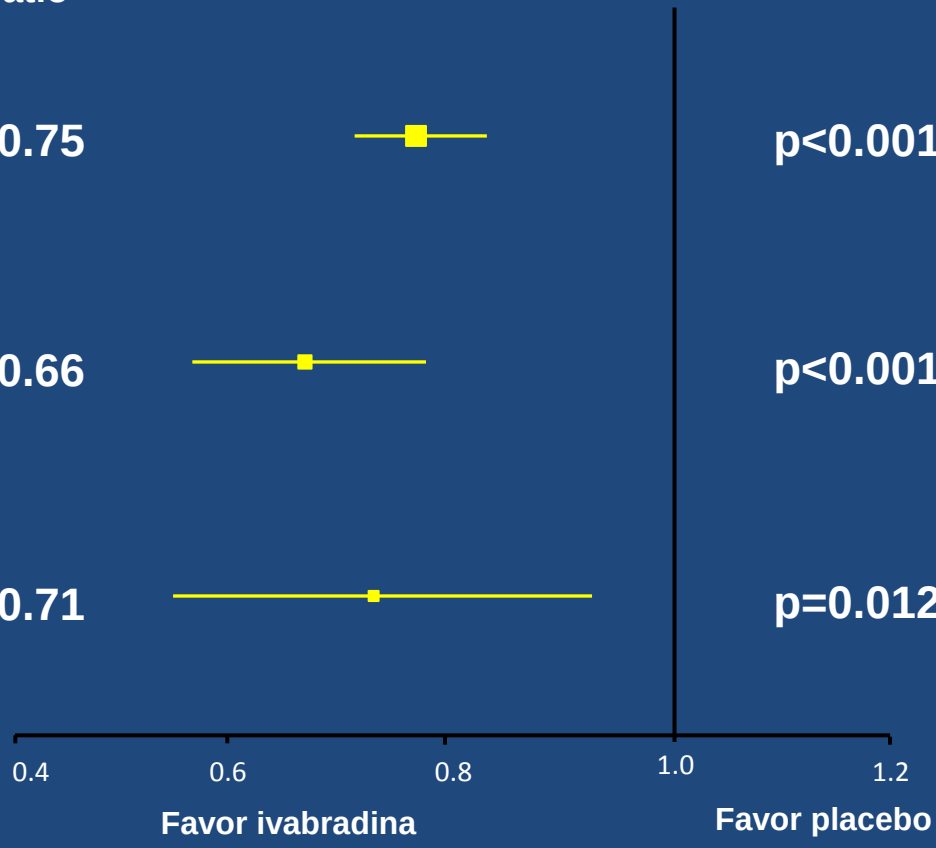
- 25%

Borer J, Böhm M, Ford I, et al. Effect of ivabradine on recurrent hospitalization for worsening heart failure in patients with chronic systolic heart failure: the SHIFT study. Eur Heart J. 2012; doi: 10.1093/eurheartj/ehs259

Efecto de Ivabradina en las hospitalizaciones recurrentes por IC

Total-time approach

	Ivabradina (n=3241)	Placebo (n=3264)	Hazard ratio	*p*-valor
Primera hospitalización	514 (16%)	672 (21%)	0.75	p<0.001
Segunda hospitalización	189 (6%)	283 (9%)	0.66	p<0.001
Tercera hospitalización	90 (3%)	128 (4%)	0.71	p=0.012

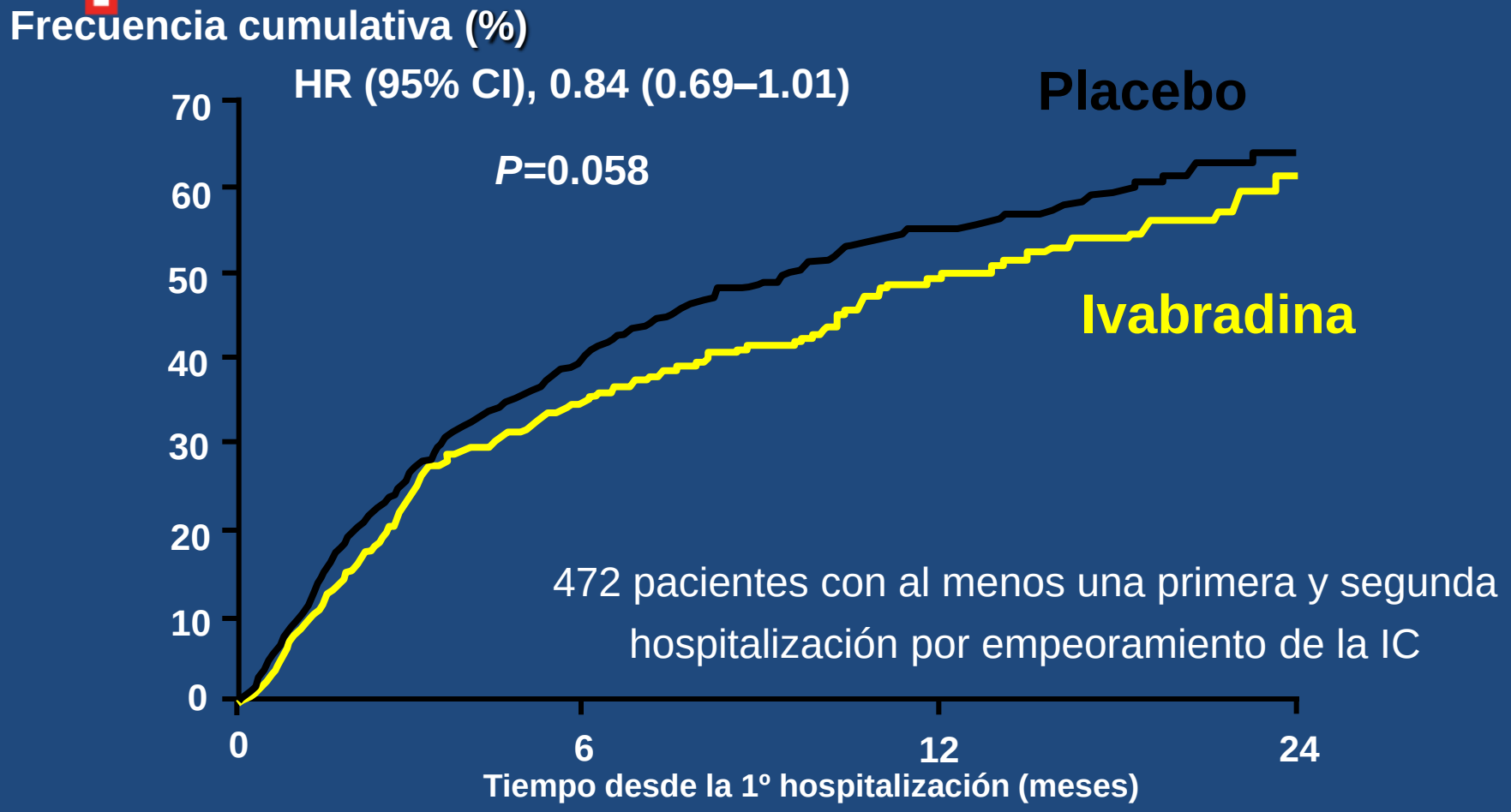


Borer J, Böhm M, Ford I, et al. Effect of ivabradine on recurrent hospitalization for worsening heart failure in patients with chronic systolic heart failure: the SHIFT study. Eur Heart J. 2012; doi: 10.1093/eurheartj/ehs259

Hospitalizaciones recurrentes por IC

Gap-time approach = efecto en la 2º hospitalización

Tiempo desde la 1º hospitalización hasta la 2º hospitalización



Borer J, Böhm M, Ford I, et al. Effect of ivabradine on recurrent hospitalization for worsening heart failure in patients with chronic systolic heart failure: the SHIFT study. Eur Heart J. 2012; doi: 10.1093/eurheartj/ehs259

Nº total de hospitalizaciones

	Ivabradina (N=3241)	Placebo (N=3264)	IRR	95% CI	*p*-valor
Hospitalización por empeoramiento de la IC	902	1211	0.75	0.65-0.87	0.0002
Hospitalización por cualquier causa	2661	3110	0.85	0.78-0.94	0.001
Hospitalización CV	1909	2272	0.84	0.76-0.94	0.002
Hospitalización por otra causa que no sea empeoramiento de la IC	1759	1899	0.92	0.83-1.02	0.12

Borer J, Böhm M, Ford I, et al. Effect of ivabradine on recurrent hospitalization for worsening heart failure in patients with chronic systolic heart failure: the SHIFT study. Eur Heart J. 2012; doi: 10.1093/eurheartj/ehs259

Conclusión

- La reducción de la FC con Ivabradina en pacientes con IC, ritmo sinusal, con FC ≥70 lpm y ya tratados con las terapias que indican las guías reduce de una manera substancial el riesgo de una deterioración clínica reflejada por:
  - Reducción de las hospitalizaciones totales por empeoramiento de la IC
  - Reducción de la incidencia de las hospitalización recurrentes
  - Aumento del tiempo entre la primera y la hospitalización subsecuente

- Este beneficio reduce la carga total del paciente con IC y puede reducir substancialmente los costes en el sistema de salud

CRT Produces Long-term Improvements in Disease Progression in Mildly Symptomatic Heart Failure Patients:

Five-year results from the **RE**synchronization re**VE**rses **R**emodeling in **S**ystolic left v**E**ntricular dysfunction (REVERSE) study

Cecilia Linde, MD, PhD, Stockholm, Sweden

Michael R. Gold, MD, PhD, Charleston, U.S.

William T. Abraham, MD, Columbus, U.S

Martin St John Sutton, MD, Philadelphia, U.S.

Stefano Ghio, MD, Pavia, Italy

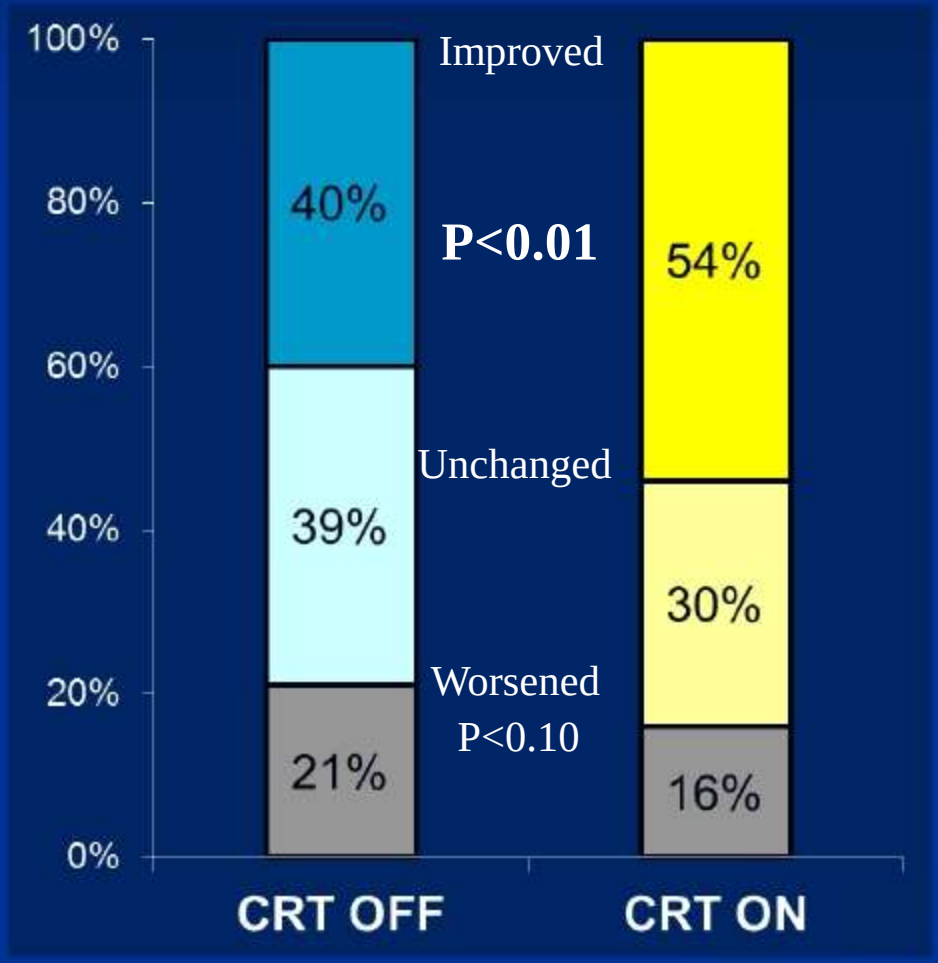
Jeff Cerkvenik, MS, Minneapolis, U.S.

Jean-Claude Daubert, MD, Rennes, France

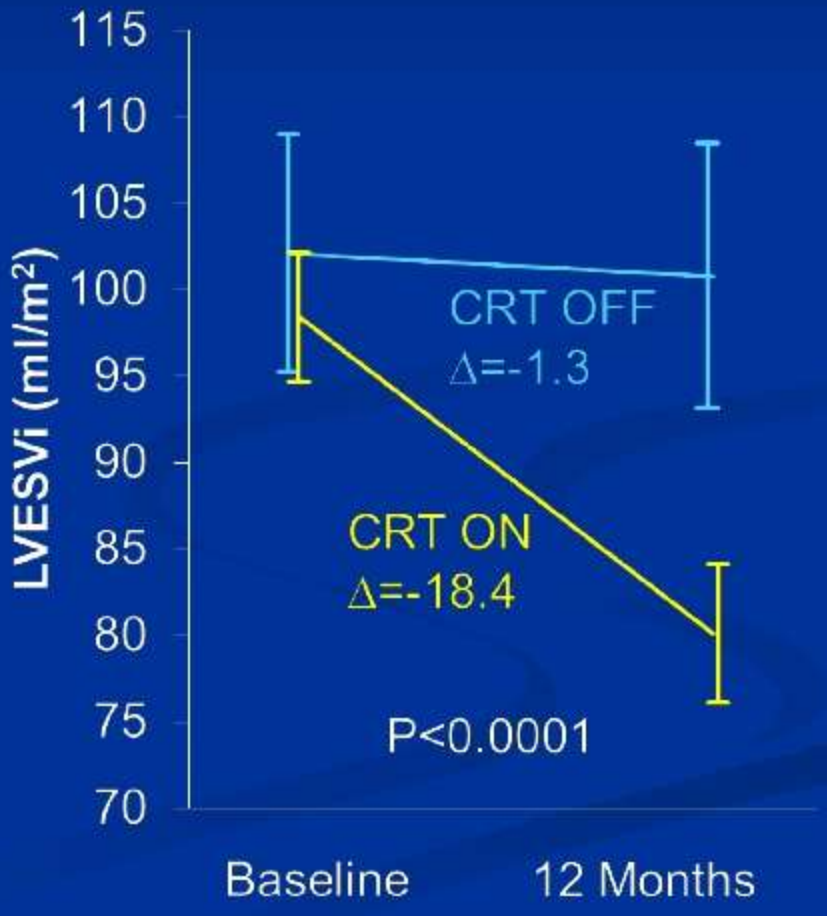
On Behalf of the REVERSE Study Group

Results of REVERSE main study

Primary Objective:
Clinical Composite Score



Powered Secondary Objective:
Change in LVESVi



Linde C, et al. *JACC*. 2008;52;1834-43

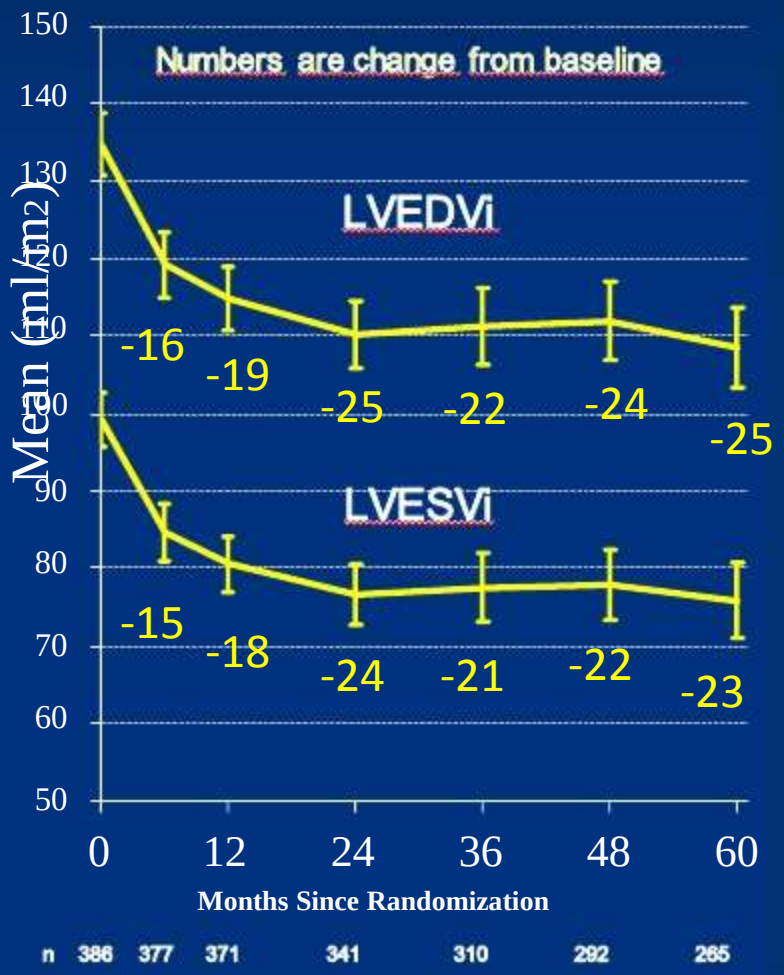
Purpose of present 5 years study

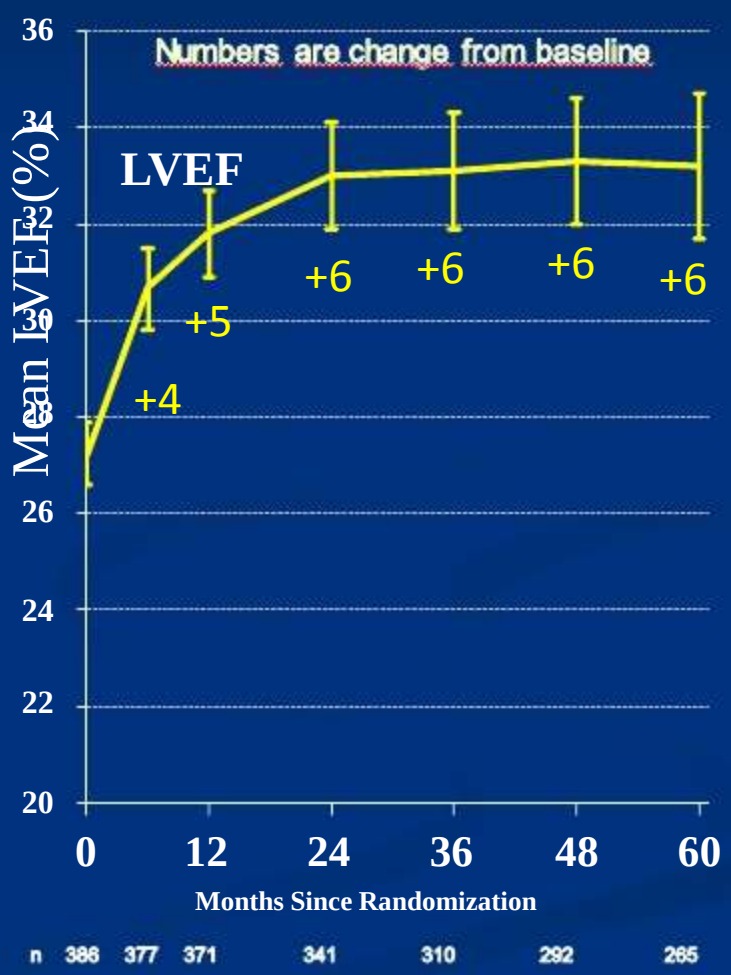
To evaluate if the benefits regarding :

Reverse remodeling, functional status, mortality and HF hospitalizations are maintained over

5 years in the 419 pts assigned to CRT ON

LV Reverse Remodeling





Error bars represent 95% confidence intervals

Conclusions

CRT produced sustained reverse remodeling accompanied by low mortality and need for heart failure hospitalizations

Benefits of CRT persisted indicating that CRT attenuates disease progression in mildly symptomatic heart failure patients with wide QRS over at least 5 years

The 2012 ESC heart failure guidelines

European Heart Journal (2012) **33**, 1787–1847
doi:10.1093/eurheartj/ehs104

ESC GUIDELINES

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

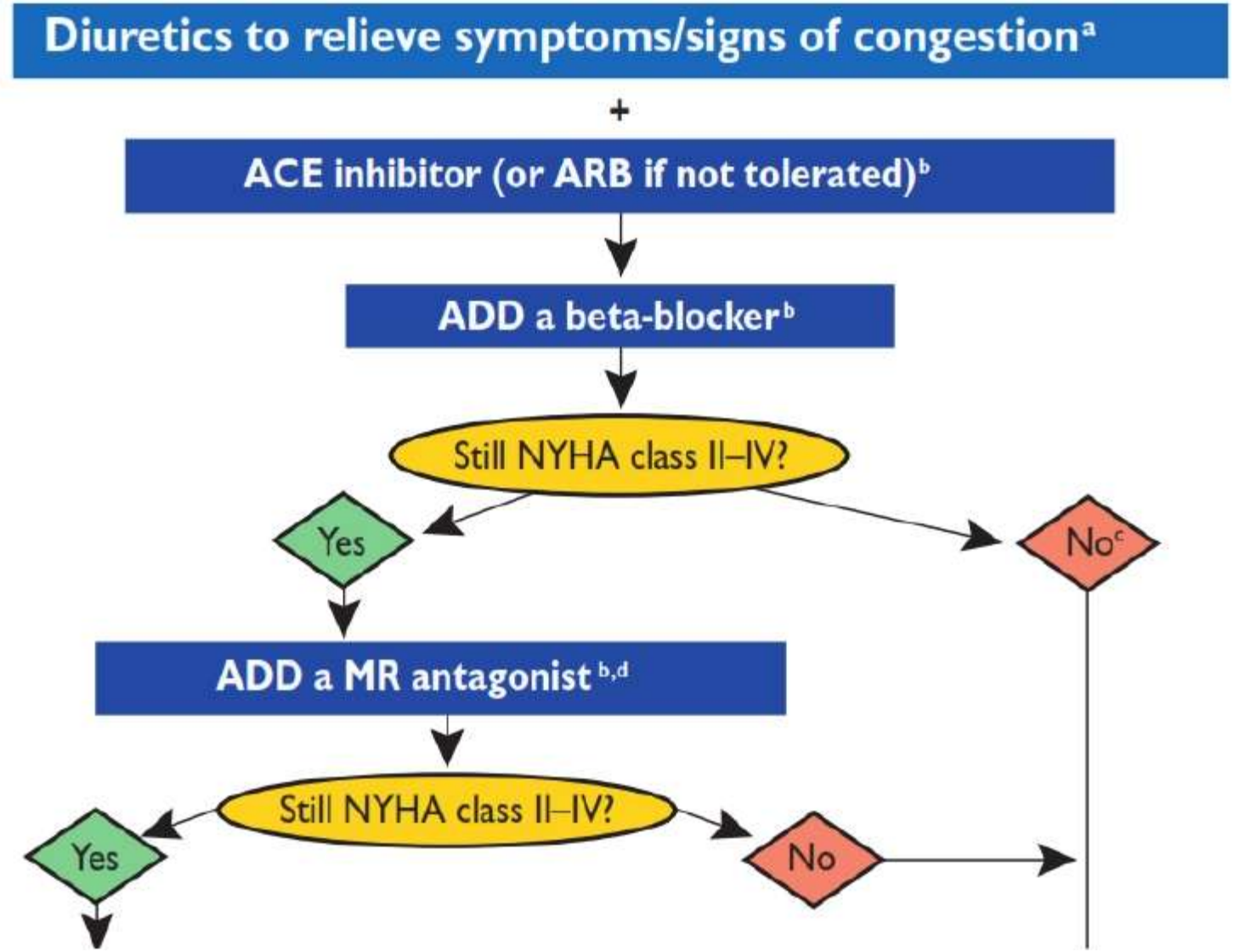
The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC

Authors/Task Force Members: John J.V. McMurray (Chairperson) (UK)*, Stamatis Adamopoulos (Greece), Stefan D. Anker (Germany), Angelo Auricchio (Switzerland), Michael Böhm (Germany), Kenneth Dickstein (Norway), Volkmar Falk (Switzerland), Gerasimos Filippatos (Greece), Cândida Fonseca (Portugal), Miguel Angel Gomez-Sanchez (Spain), Tiny Jaarsma (Sweden), Lars Køber (Denmark), Gregory Y.H. Lip (UK), Aldo Pietro Maggioni (Italy), Alexander Parkhomenko (Ukraine), Burkert M. Pieske (Austria), Bogdan A. Popescu (Romania), Per K. Rønnevik (Norway), Frans H. Rutten (The Netherlands), Juerg Schwitter (Switzerland), Petar Seferovic (Serbia), Janina Stepinska (Poland), Pedro T. Trindade (Switzerland), Adriaan A. Voors (The Netherlands), Faiez Zannad (France), Andreas Zeiher (Germany).

Main changes from 2008 guidelines: Treatment

1. **An expanded indication for mineralocorticoid (aldosterone) receptor antagonists (MRAs).**
2. **A new indication for the sinus node inhibitor ivabradine.**
3. **An expanded indication for cardiac resynchronization therapy (CRT).**
4. **New information on the role of coronary revascularization in systolic HF.**
5. **Recognition of the growing use of ventricular assist devices (VADs).**
6. **The emergence of transcatheter valve interventions.**

Initial pharmacological therapy



Pharmacological therapy indicated in potentially all patients with systolic HF

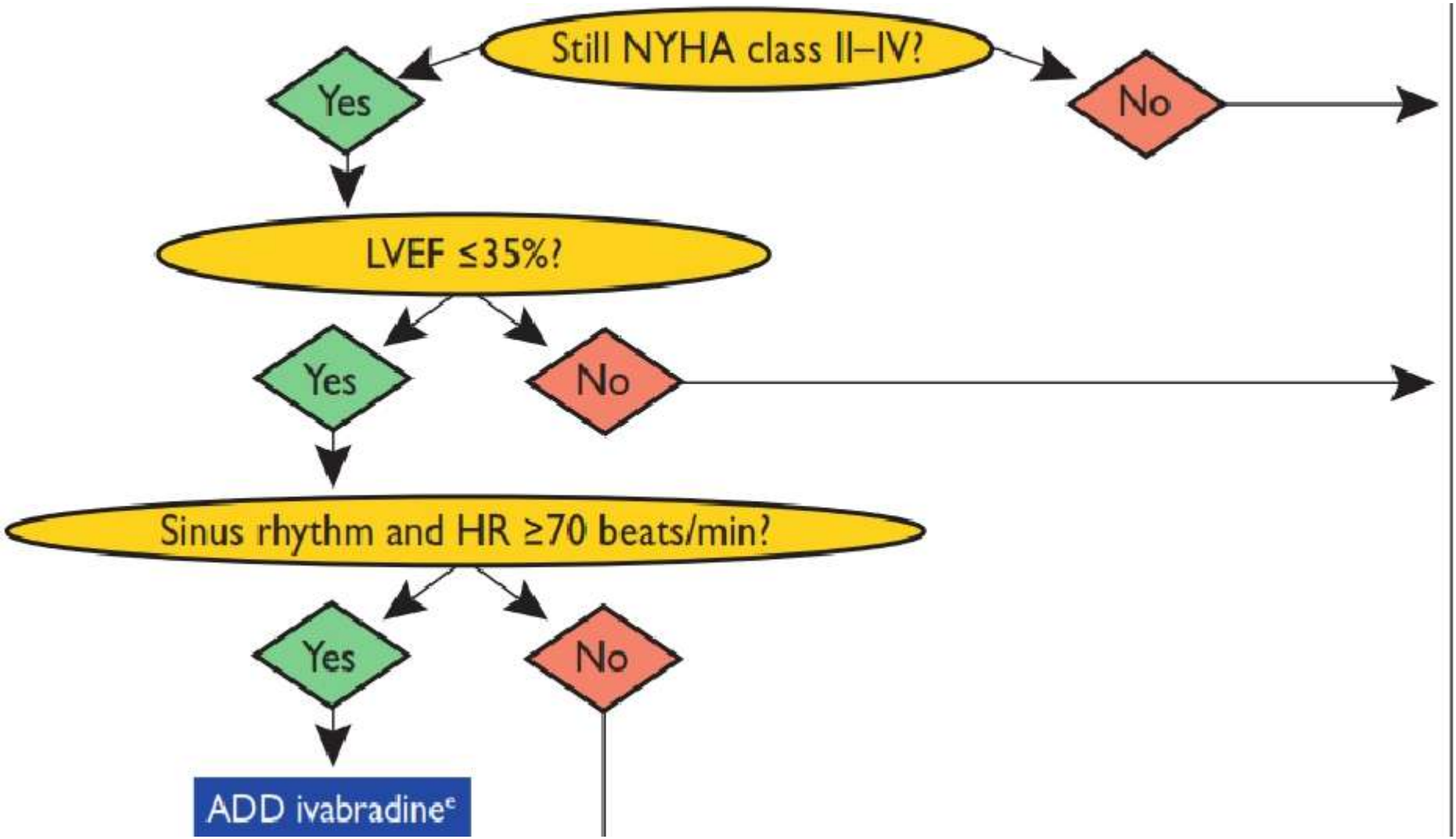
ACE inhibitor

Beta-blocker

MRA

An ACE inhibitor is recommended, in addition to a beta-blocker, for all patients with an EF ≤40% to reduce the risk of HF hospitalization and the risk of premature death.	I	A	87–91
A beta-blocker is recommended, in addition to an ACE inhibitor (or ARB if ACE inhibitor not tolerated), for all patients with an EF ≤40% to reduce the risk of HF hospitalization and the risk of premature death.	I	A	92–98
An MRA is recommended for all patients with persisting symptoms (NYHA class II–IV) and an EF ≤35%, despite treatment with an ACE inhibitor (or an ARB if an ACE inhibitor is not tolerated) and a beta-blocker, to reduce the risk of HF hospitalization and the risk of premature death.	I	A	99, 100

Pharmacological therapy – next step



Pharmacological therapy – other treatments with less certain benefits in systolic HF

ARB			
Recommended to reduce the risk of HF hospitalization and the risk of premature death in patients with an EF ≤40% and unable to tolerate an ACE inhibitor because of cough (patients should also receive a beta-blocker and an MRA).	I	A	108, 109
Recommended to reduce the risk of HF hospitalization in patients with an EF ≤40% and persisting symptoms (NYHA class II–IV) despite treatment with an ACE inhibitor and a beta-blocker who are unable to tolerate an MRA.[d]	I	A	110, 111
Ivabradine			
Should be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35%, a heart rate remaining ≥70 b.p.m., and persisting symptoms (NYHA class II–IV) despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE inhibitor (or ARB), and an MRA (or ARB).[e]	IIa	B	112
May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35% and a heart rate ≥70 b.p.m. who are unable to tolerate a beta-blocker. Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB).[e]	IIb	C	–
Digoxin			
May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤45% who are unable to tolerate a beta-blocker (ivabradine is an alternative in patients with a heart rate ≥70 b.p.m.). Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB).	IIb	B	113
May be considered to reduce the risk of HF hospitalization in patients with an EF ≤45% and persisting symptoms (NYHA class II–IV) despite treatment with a beta-blocker, ACE inhibitor (or ARB), and an MRA (or ARB).	IIb	B	113
H-ISDN			
May be considered as an alternative to an ACE inhibitor or ARB, if neither is tolerated, to reduce the risk of HF hospitalization and risk of premature death in patients with an EF ≤45% and dilated LV (or EF ≤35%). Patients should also receive a beta-blocker and an MRA.	IIb	B	114, 115
May be considered to reduce the risk of HF hospitalization and risk of premature death in patients in patients with an EF ≤45% and dilated LV (or EF ≤35%) and persisting symptoms (NYHA class II–IV) despite treatment with a beta-blocker, ACE inhibitor (or ARB), and an MRA (or ARB).	IIb	B	116
An *n*-3 PUFA[f] preparation may be considered to reduce the risk of death and the risk of cardiovascular hospitalization in patients treated with an ACE inhibitor (or ARB), beta-blocker, and an MRA (or ARB).	IIb	B	117

Ivabradine

Ivabradine		
Should be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35%, a heart rate remaining ≥70 b.p.m., and persisting symptoms (NYHA class II–IV) despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE inhibitor (or ARB), and an MRA (or ARB).[e]	IIa	B

Should be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with a heart rate remaining ≥70 beats per minute and persisting symptoms (NYHA class II–IV) despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE inhibitor (or ARB) and an MRA (or ARB).

Caveat about EMA labelling: ≥75 b.p.m.

Recommendations for ivabradine: Patients NOT taking a beta-blocker

Recommendations	Class[a]	Level[b]	Ref[c]
Ivabradine			
May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35% and a heart rate ≥70 b.p.m. who are unable to tolerate a beta-blocker. Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB).[e]	IIb	C	–

May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35% and a heart rate remaining ≥70 beats per minute who are unable to tolerate a beta-blocker. Patients should receive an ACE inhibitor (or ARB), and an MRA (or ARB).

Recommendations for ivabradine: Patients with HF and angina: IA

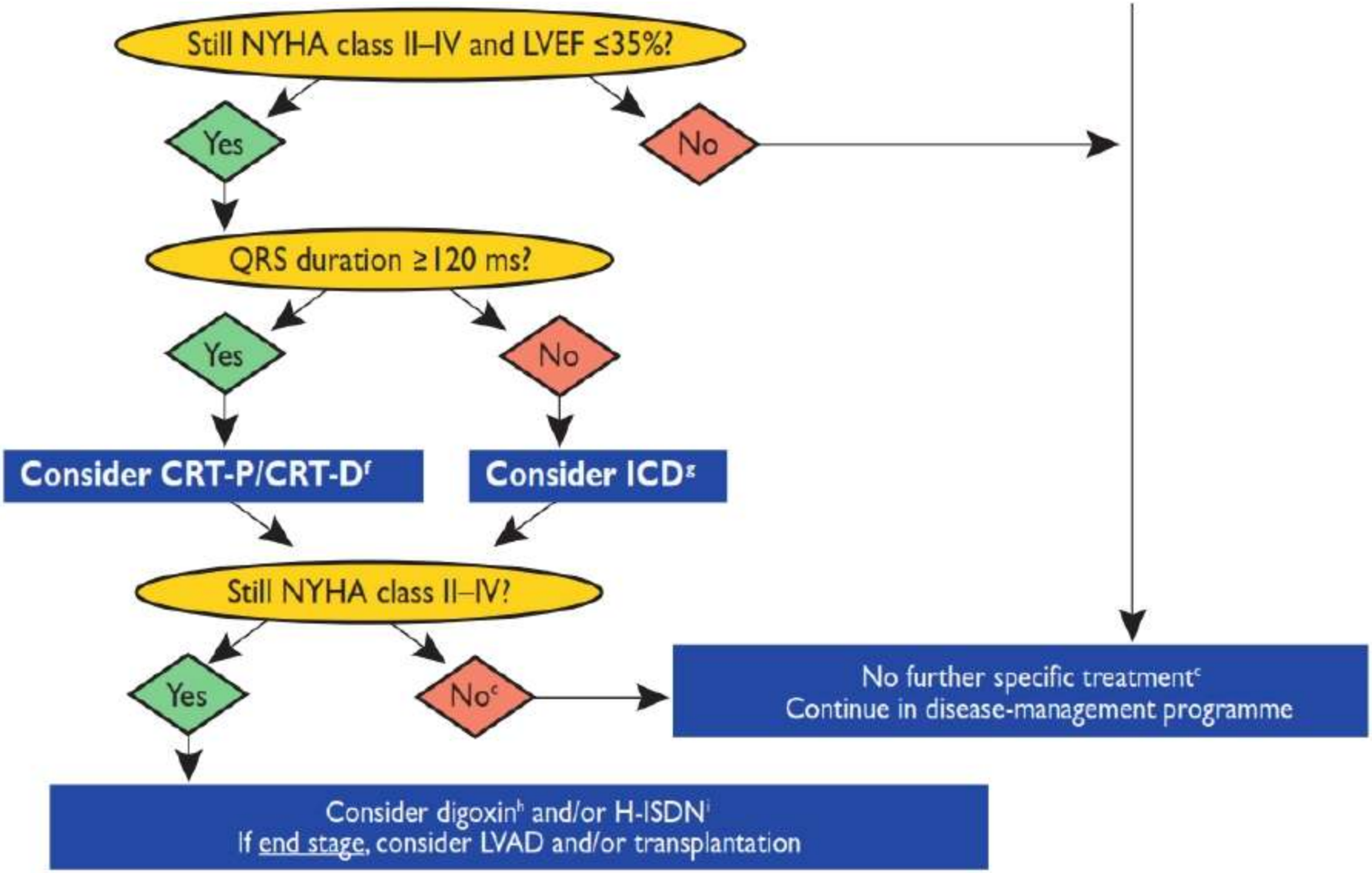
Recommendations for the pharmacological treatment of stable angina pectoris in patients with symptomatic HF (NYHA functional class II–IV) and LV systolic dysfunction

Recommendations	Class[a]	Level[b]	Ref[c]
Step 1: A beta-blocker			
A beta-blocker is recommended as the preferred first-line treatment to relieve angina because of the associated benefits of this treatment (reducing the risk of HF hospitalization and the risk of premature death).	I	A	92–98
Alternatives to a beta-blocker:			
(i) Ivabradine should be considered in patients in sinus rhythm who cannot tolerate a beta-blocker, to relieve angina (effective antianginal treatment and safe in HF).	IIa	A	112, 122
(ii) An oral or transcutaneous nitrate should be considered in patients unable to tolerate a beta-blocker, to relieve angina (effective antianginal treatment and safe in HF).	IIa	A	114–116
(iii) Amlodipine should be considered in patients unable to tolerate a beta-blocker, to relieve angina (effective antianginal treatment and safe in HF).	IIa	A	188, 189
(iv) Nicorandil may be considered in patients unable to tolerate a beta-blocker, to relieve angina (effective antianginal treatment but safety in HF uncertain).	IIb	C	–
(v) Ranolazine may be considered in patients unable to tolerate a beta-blocker, to relieve angina (effective antianginal treatment but safety in HF uncertain).	IIb	C	–
Step 2: Add a second anti-anginal drug			
The following may be added to a beta-blocker (or alternative)—taking account of the combinations not recommended below.			
The addition of ivabradine is recommended when angina persists despite treatment with a beta-blocker (or alternative), to relieve angina (effective antianginal treatment and safe in HF).	I	A	112, 122
The addition of an oral or transcutaneous nitrate is recommended when angina persists despite treatment with a beta-blocker (or alternative), to relieve angina (effective antianginal treatment and safe in HF).	I	A	114–116
The addition of amlodipine is recommended when angina persists despite treatment with a beta-blocker (or alternative), to relieve angina (effective antianginal treatment and safe in HF).	I	A	188, 189
The addition of nicorandil may be considered when angina persists despite treatment with a beta-blocker (or alternative), to relieve angina (effective antianginal treatment but safety in HF uncertain).	IIb	C	–
The addition of ranolazine may be considered when angina persists despite treatment with a beta-blocker (or alternative), to relieve angina (effective antianginal treatment but safety in HF uncertain).	IIb	C	–
Step 3: Coronary revascularization			

Main changes from 2008 guidelines

1. **An expanded indication for mineralocorticoid (aldosterone) receptor antagonists (MRAs).**
2. **A new indication for the sinus node inhibitor ivabradine.**
3. **An expanded indication for cardiac resynchronization therapy (CRT).**
4. **New information on the role of coronary revascularization in systolic HF.**
5. **Recognition of the growing use of ventricular assist devices (VADs).**
6. **The emergence of transcatheter valve interventions.**

When to consider CRT and ICD



Cardiac resynchronization therapy (CRT)

1. **Expanded indication for patients with mild symptoms**
2. **Less certain about patients**

    a) in atrial fibrillation

    b) with right bundle branch-block/IVCD (non-LBBB)

An expanded indication for cardiac resynchronization therapy (CRT)

Recommendations for the use of CRT where the evidence is strong—patients in sinus rhythm with NYHA functional class II heart failure and a persistently reduced ejection fraction, despite optimal pharmacological therapy

Recommendations	Class[a]	Level[b]
LBBB QRS morphology CRT, preferably CRT-D is recommended in patients in sinus rhythm with a QRS duration of ≥130 ms, LBBB QRS morphology, and an EF ≤30%, who are expected to survive for >1 year with good functional status, to reduce the risk of HF hospitalization and the risk of premature death.	I	A
Non-LBBB QRS morphology CRT, preferably CRT-D should be considered in patients in sinus rhythm with a QRS duration of ≥150 ms, irrespective of QRS morphology, and an EF ≤30%, who are expected to survive for >1 year with good functional status, to reduce the risk of HF hospitalization and the risk of premature death.	IIa	A

2 trials: MADIT-CRT and RAFT

QRS morphology, duration and effect of CRT

CRT-D vs. ICD only HR for primary endpoint

Patients		RAFT	MADIT-CRT
All		0.75 (0.64, 0.87)	0.66 (0.52, 0.84)
LBBB	QRS < 150 QRS ≥ 150	0.89 (0.60, 1.32) 0.51 (0.37, 0.69)	0.55 (0.35, 0.86) 0.41 (0.30. 0.56)
Non-LBBB	QRS < 150 QRS ≥ 150	1.24 (0.70, 2.19) 0.83 (0.47, 1.47)	1.41 (0.85, 2.32) 0.92 (0.52, 1.64)

New information on the role of coronary revascularization in systolic HF

CABG is recommended for patients with angina and significant left main stenosis, who are otherwise suitable for surgery and expected to survive >1 year with good functional status, to reduce the risk of premature death.	I	C	–
CABG is recommended for patients with angina and two- or three-vessel coronary disease, including a left anterior descending stenosis, who are otherwise suitable for surgery and expected to survive >1 year with good functional status, to reduce the risk of hospitalization for cardiovascular causes and the risk of premature death from cardiovascular causes.	I	B	191

Recognition of the growing use of ventricular assist devices (VADs) – Bridge to transplantation

An LVAD or BiVAD is recommended in selected patients[d] with end-stage HF despite optimal pharmacological and device treatment and who are otherwise suitable for heart transplantation, to improve symptoms and reduce the risk of HF hospitalization for worsening HF and to reduce the risk of premature death while awaiting transplantation.	I	B	254, 255, 258

Recognition of the growing use of ventricular assist devices (VADs) – Destination therapy

An LVAD should be considered in highly selected patients[d] who have end-stage HF despite optimal pharmacological and device therapy and who are not suitable for heart transplantation, but are expected to survive >1 year with good functional status, to improve symptoms, and reduce the risk of HF hospitalization and of premature death.	IIa	B	254

Lifestyle and non- pharmacological/ device/surgical interventions

Lack of robust evidence for most lifestyle, non-pharmacological, interventions e.g. sodium restriction.

Lifestyle and non- pharmacological/ device/surgical interventions

Recommendations	Class[a]	Level[b]	Ref[C]
It is recommended that regular aerobic exercise is encouraged in patients with heart failure to improve functional capacity and symptoms.	I	A	262, 263
It is recommended that patients with heart failure are enrolled in a multidisciplinary-care management programme to reduce the risk of heart failure hospitalization.	I	A	236, 259, 264

Lo mejor sobre insuficiencia cardiaca (IC)

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