2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

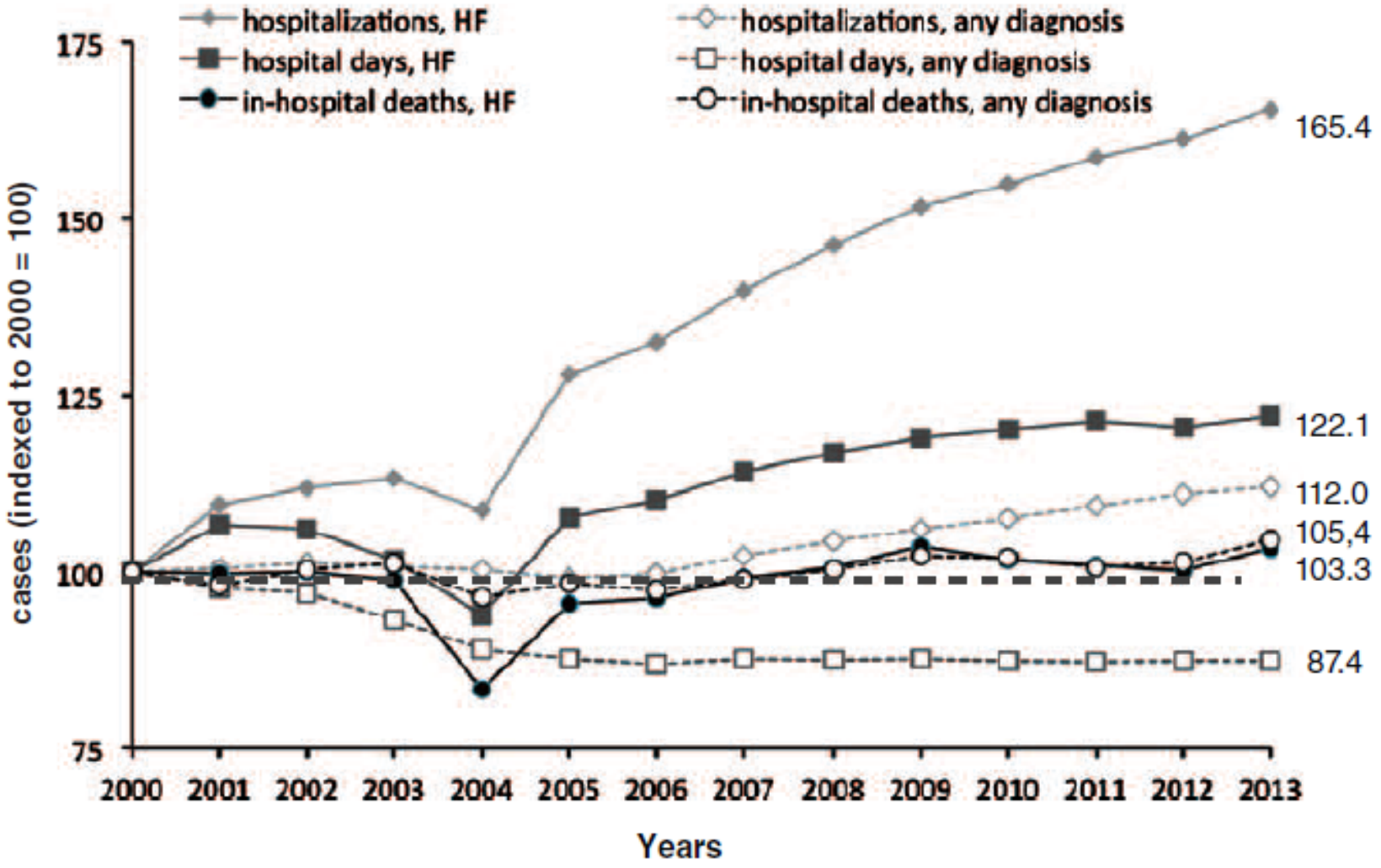
Discussió

Unitat d'Insuficiència Cardíaca

i Trasplantament Cardíac

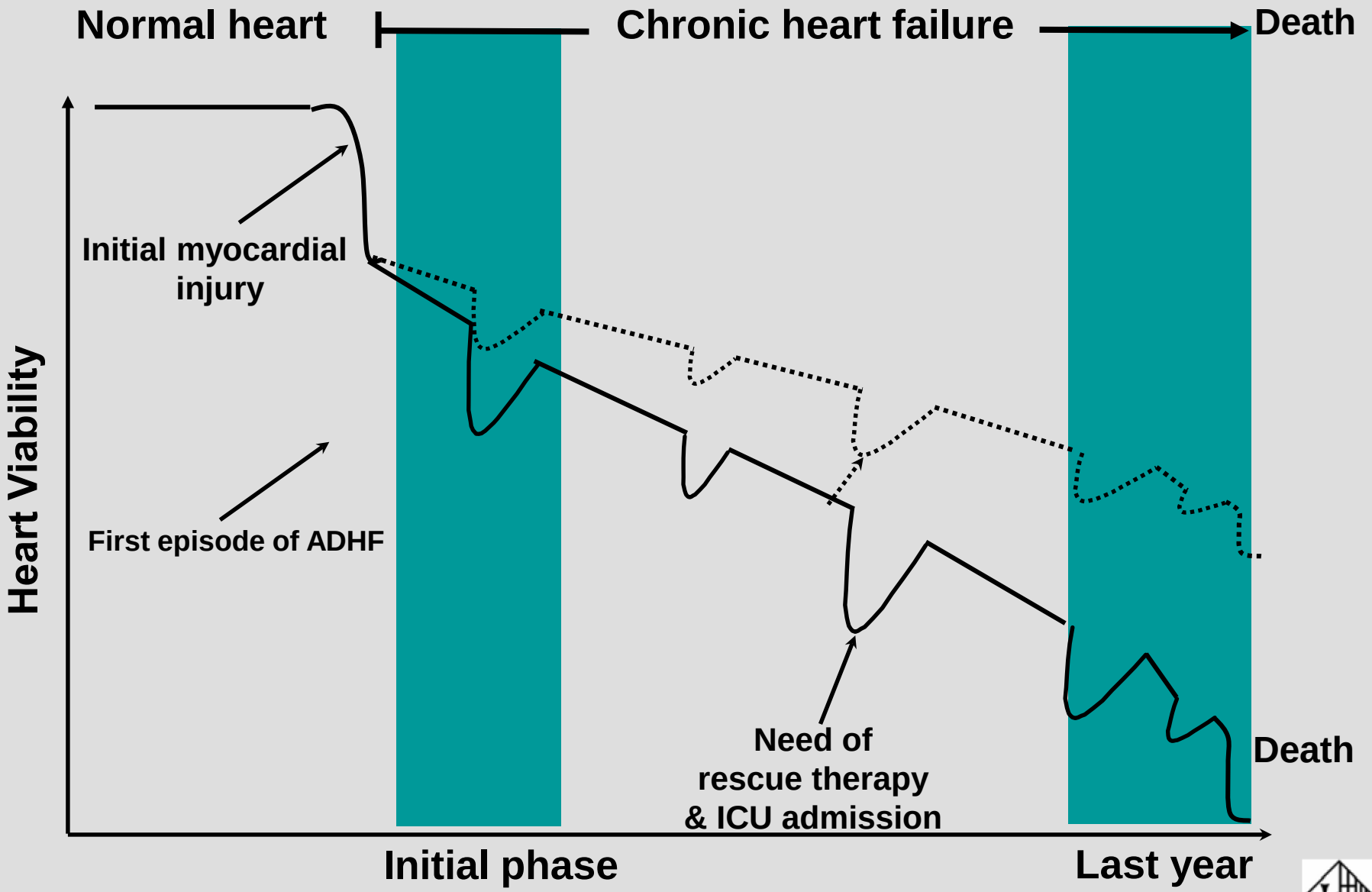
Hospital de la Santa Creu i Sant Pau

Epidemiologia



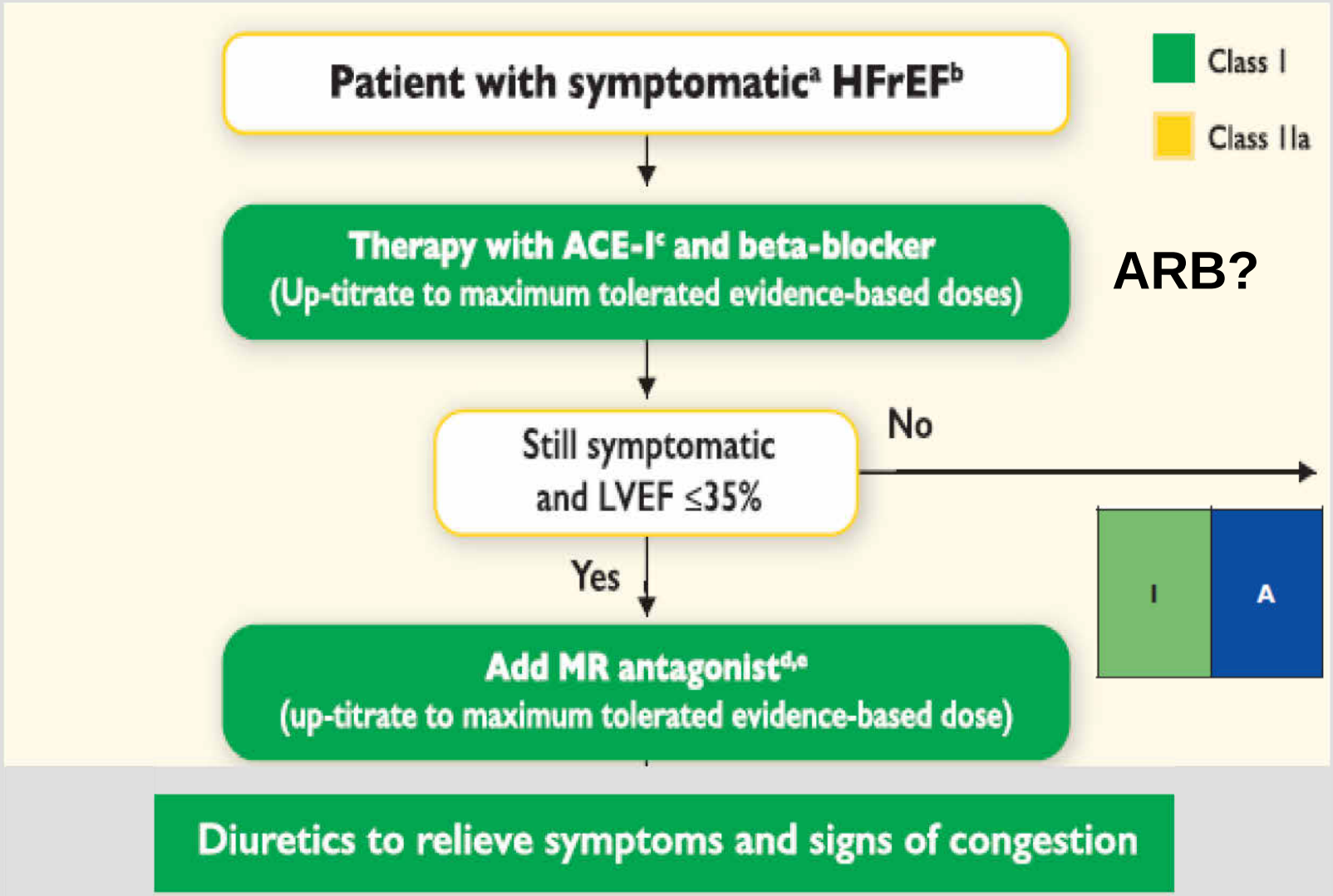
M Christ Eur J Heart Fail 2016:18;1009-18

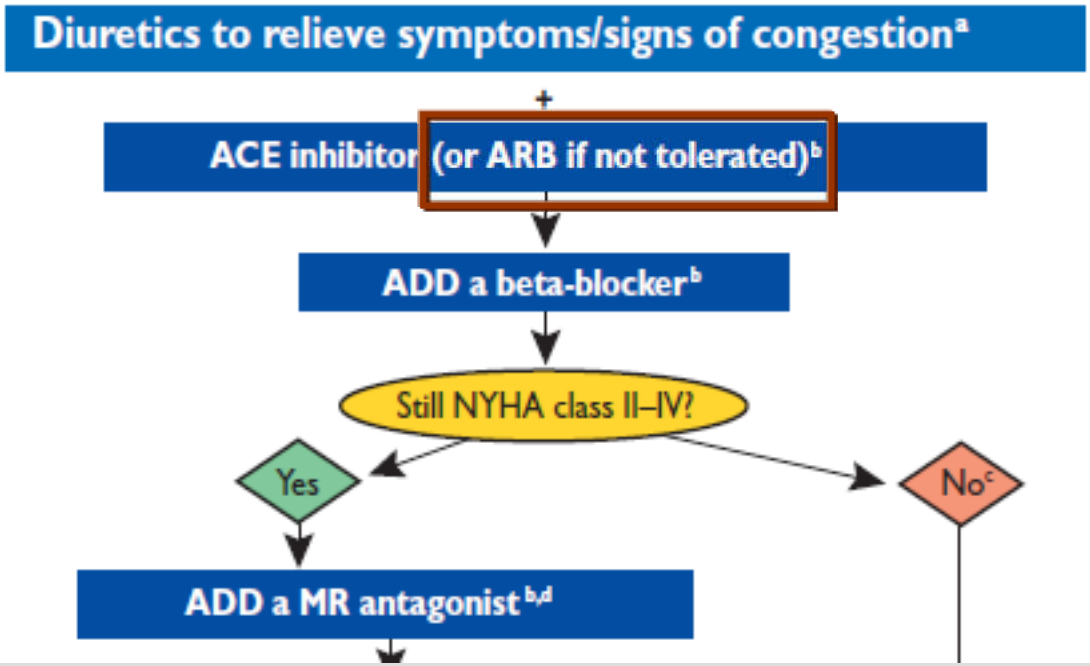
Prognosis of Heart Failure



Gheorghiade M, Am J Cardiology 2005;96(suppl 6A).

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure





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
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

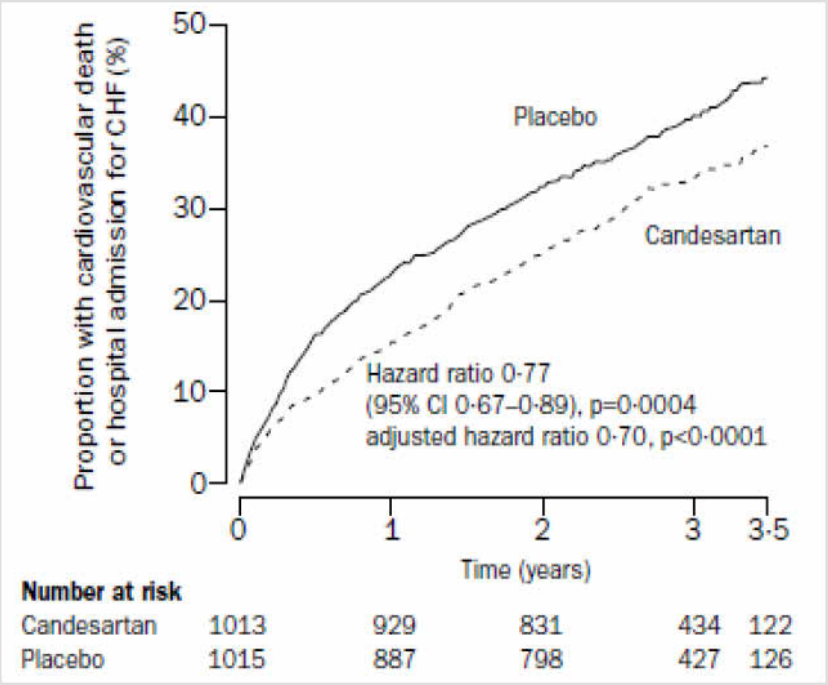
ESC HF-Guidelines 2012

ARB		
An ARB is recommended to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients unable to tolerate an ACE-I (patients should also receive a beta-blocker and an MRA).	I	B
An ARB may be considered to reduce the risk of HF hospitalization and death in patients who are symptomatic despite treatment with a beta-blocker who are unable to tolerate an MRA.	IIb	C

ESC HF-Guidelines 2016

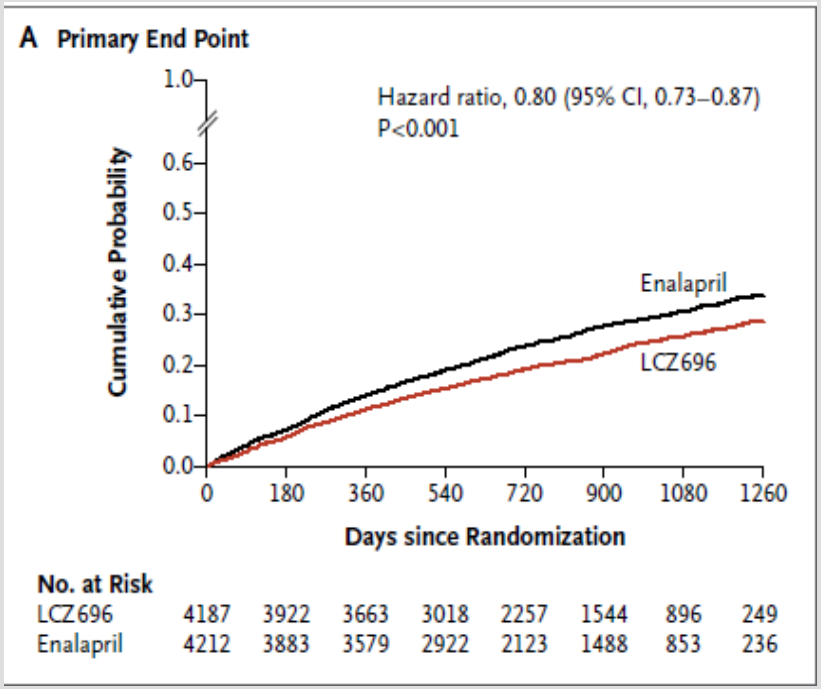
Intolerància a IECAS

CHARM-Alternative trial



RR 23%, BB 55%, ARM 24%

PARADIGM-HF trial

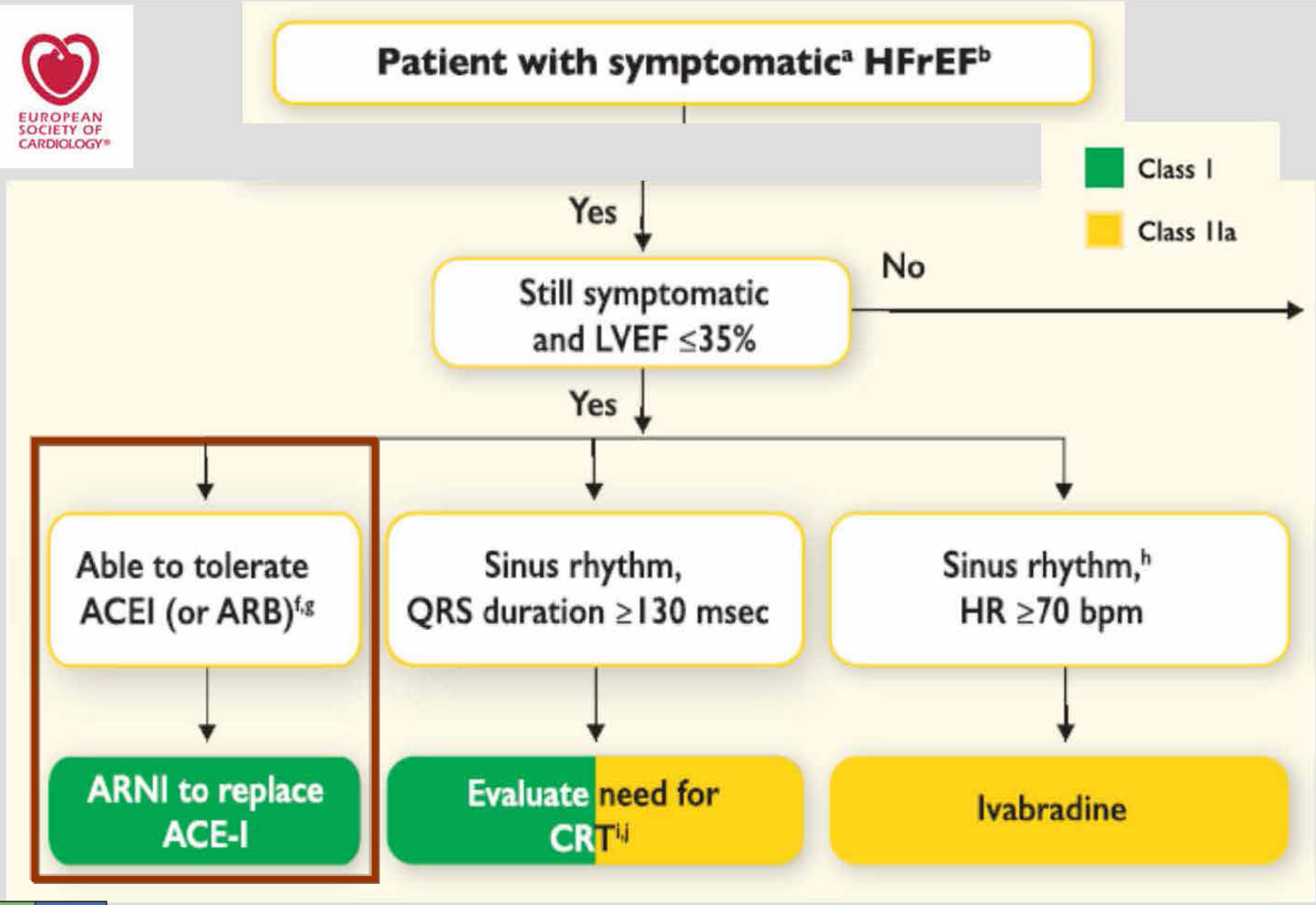


RR 21%, BB 93%, ARM 54%

Sacubitril+Valsartan

Lancet 2003; 362: 772–776

J McMurray NEJM 2014;371:993



I B **Sacubitril/valsartan**

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Angiotensin receptor neprilysin inhibitor		
Sacubitril/valsartan is recommended as a replacement for an ACE-I to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACE-I, a beta-blocker and an MRA[d]	I	B

2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

I	ARNI: B-R	In patients with chronic symptomatic HF*r*EF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality (19).

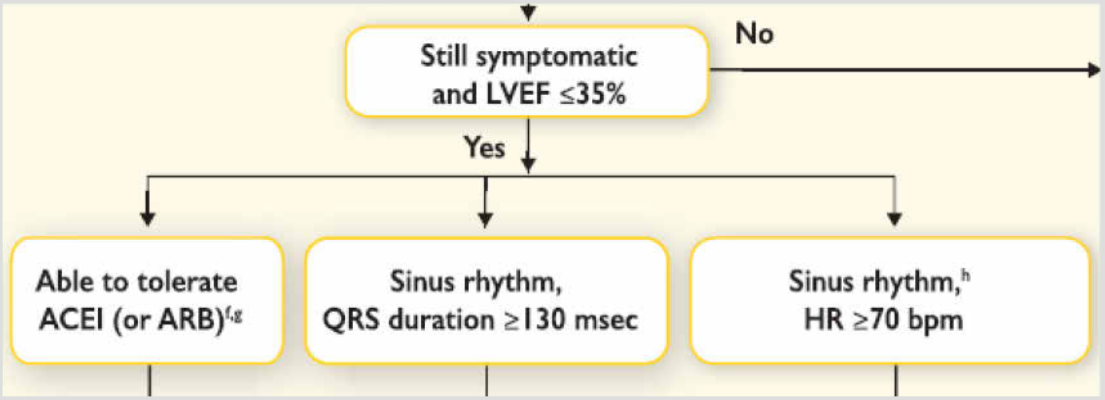
ESC HF-Guidelines 2016

AHA HF-Guidelines 2016

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

HF Classification

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).



ARNI indication according to HF-Guidelines

- **Ambulatory symptomatic HFrEF**
- **LVEF ≤ 40% - 35%**
- **BNP >150 pg/mL or NT-proBNP ≥600 pg/mL**

  (with a prior hospitalization in the preceding 12 m)
- **BNP ≥100 pg/mL or NT-proBNP ≥400 pg/mL**
- **Able to tolerate a dose of enalapril (10mg/12h)**
- **SBP ≥100 mmHg**
- **Estimated GFR ≥30 mL/min/1.73 m^2**

AHA HF-Guidelines 2016

Angiotensin receptor neprilysin inhibitor		
Sacubitril/valsartan is recommended as a replacement for an ACE-I to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACE-I, a beta-blocker and an MRA[d]	I	B

- **Ambulatoty symptomatic HFrEF (LVEF < 40%)**
- **BNP >150 pg/mL or NT-proBNP ≥600 pg/mL**
- **BNP ≥100 pg/mL or NT-proBNP ≥400 pg/mL**

  (with a prior hospitalization in the preceding 12 m)
- **SBP ≥100 mmHg**
- **Estimated GFR ≥30 mL/min/1.73 m^2**
- **Able to tolerate a dose of enalapril (10mg/12h)**

- **Sacubitril/Valsartan 24 mg / 26 mg /12h**
- **Sacubitril/Valsartan 49 mg / 51 mg /12h**
- **Sacubitril/Valsartan 97 mg / 103 mg /12h**

AHA HF-Guidelines 2016

Adverse Events during Randomized Treatment.

Event	LCZ696 (N=4187)	Enalapril (N=4212)	P Value
	no. (%)		
Hypotension			
Symptomatic	588 (14.0)	388 (9.2)	<0.001
Symptomatic with systolic blood pressure <90 mm Hg	112 (2.7)	59 (1.4)	<0.001
Elevated serum creatinine			
≥2.5 mg/dl	139 (3.3)	188 (4.5)	0.007
≥3.0 mg/dl	63 (1.5)	83 (2.0)	0.10
Elevated serum potassium			
>5.5 mmol/liter	674 (16.1)	727 (17.3)	0.15
>6.0 mmol/liter	181 (4.3)	236 (5.6)	0.007
Cough	474 (11.3)	601 (14.3)	<0.001
Angioedema†			
No treatment or use of antihistamines only	10 (0.2)	5 (0.1)	0.19
Use of catecholamines or glucocorticoids without hospitalization	6 (0.1)	4 (0.1)	0.52

Suspendre enalapril 36h abans del canvi

J McMurray NEJM 2014;371:993

Recommendations for the management of ventricular arrhythmias in heart failure

Recommendations	Class[a]	Level[b]
It is recommended that potential aggravating/precipitating factors (e.g. electrolyte disorders, use of proarrhythmic drugs, myocardial ischaemia) should be sought and corrected in patients with ventricular arrhythmias.	I	C
It is recommended that treatment with an ACE inhibitor (or ARB), beta-blocker, and MRA should be optimized in patients with ventricular arrhythmias.	I	A
It is recommended that coronary revascularization is considered in patients with ventricular arrhythmias and coronary artery disease (see Section 13.2).	I	C
It is recommended that an ICD is implanted in a patient with symptomatic or sustained ventricular arrhythmia (ventricular tachycardia or ventricular fibrillation), reasonable functional status, and in whom a goal of treatment is to improve survival.	I	A
Amiodarone is recommended in patients with an ICD, who continue to have symptomatic ventricular arrhythmias or recurrent shocks despite optimal treatment and device re-programming.	I	C
Catheter ablation is recommended in patients with an ICD who continue to have ventricular arrhythmias causing recurrent shocks not preventable by optimal treatment device re-programming and amiodarone.	I	C
Amiodarone may be considered as a treatment to prevent recurrence of sustained symptomatic ventricular arrhythmias in otherwise optimally treated patients in whom an ICD is not considered appropriate.	IIb	C
Routine use of amiodarone is not recommended in patients with non-sustained ventricular arrhythmias because of lack of benefit and potential drug toxicity.	III	A

Recommendations for the management of ventricular tachyarrhythmias in heart failure

Recommendations	Class [a]	Level [b]
Potential aggravating/precipitating factors (e.g. low serum potassium/ magnesium, ongoing ischaemia) should be sought and corrected in patients with ventricular arrhythmias.	IIa	C
Treatment with beta-blocker, MRA and sacubitril/valsartan reduces the risk of sudden death and is recommended for patients with HFrEF and ventricular arrhythmias (as for other patients)(see Section 7).	I	A
Implantation of an ICD or CRT-D device is recommended for selected patients with HFrEF (see Section 8).	I	A
Several strategies should be considered to reduce recurrent symptomatic arrhythmias in patients with an ICD (or in those who are not eligible for ICD), including attention to risk factors and optimal pharmacological treatment of HF, amiodarone, catheter ablation and CRT.	IIa	C

frequent, recurrent ventricular tachyarrhythmias

162-Paradigm-HF
170-3 .. 4 BB
174-5 .. 2 MRA

Gaps Guies - ARNI

- **HFrEF definició EF<40% (EF 35 - 40% ?)**
- **Paper del NT-proBNP?**
- **Pts que no toleren dosis de IECA 10mg/12h?**
- **Pts que no toleren ARM per hiperK?**
- **Pts de novo?**
- **Altres fàrmacs hipotensors (amiodarona)?**
- **Efectes cerebrals a llarg-termini?**
- **Cal esperar empitjorament dels símptomes pel canviar a ARNI?**

Gaps - ARNI

- **HFrEF definició** **EF < 40%**
- **Paper del NT-proBNP?** **No necessari**
- **Pts que no toleren dosis de IECA 10 mg/12h?**

Individualitzar, iniciar amb la dosi baixa si TA≥100 mmHg

- **Pts que no toleren ARM per hiperK?** **Desconegut**
- **Pts de novo?** **No, de moment ....**
- **Altres fàrmacs hipotensors (amiodarona)** **?**
- **Efectes cerebrals a llarg-termini** **?**
- **Cal esperar empitjorament dels símptomes pel canviar a ARNI** **No cal esperar**

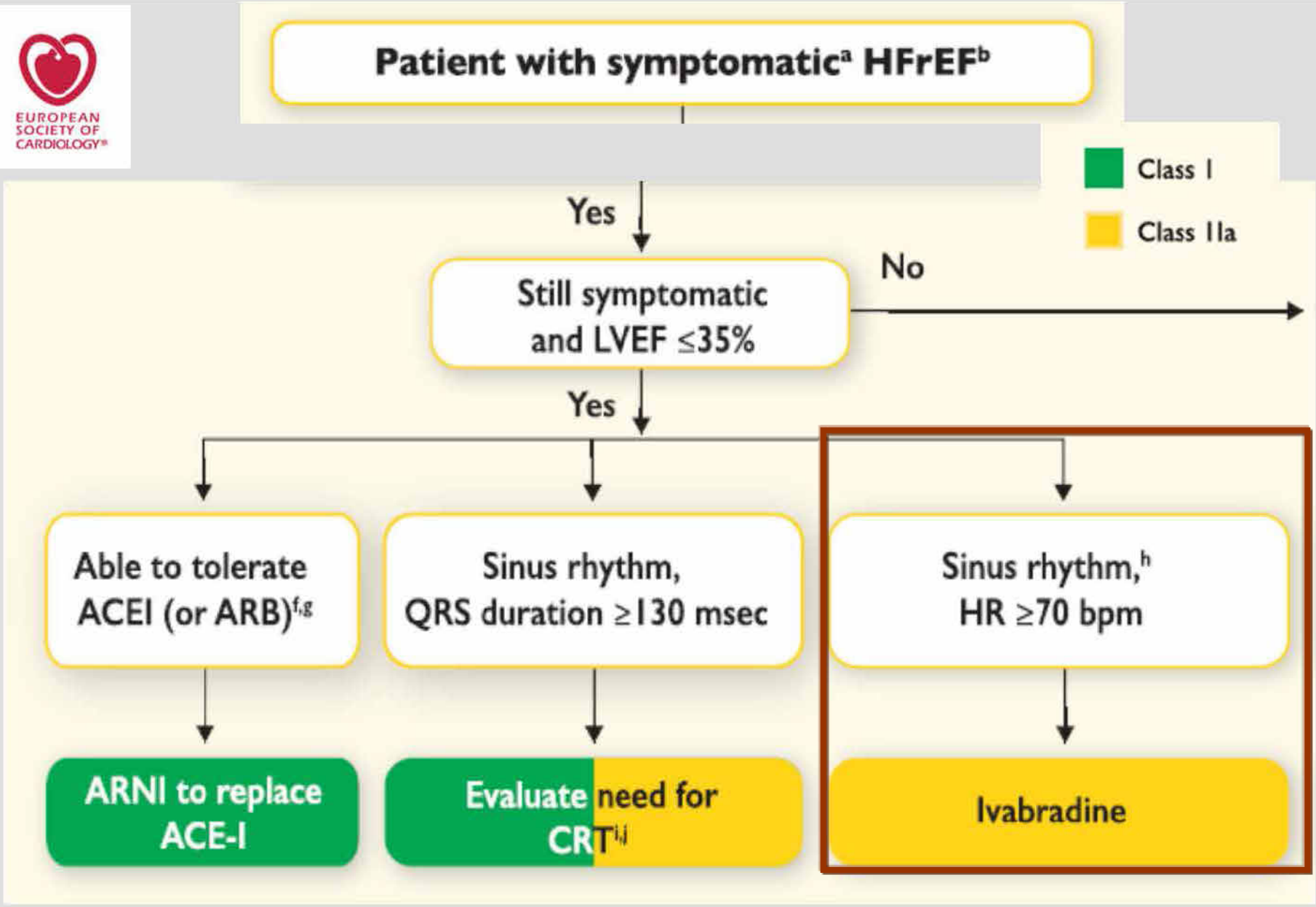
Clinical events associated with worse prognosis

Repeated (≥2) hospitalizations or ED visits for HF in the past year
Progressive deterioration in renal function (e.g., rise in BUN and creatinine)
Weight loss without other cause (e.g., cardiac cachexia)
Intolerance to ACE inhibitors due to hypotension and/or worsening renal function
Intolerance to beta blockers due to worsening HF or hypotension
Frequent systolic blood pressure <90 mm Hg
Persistent dyspnea with dressing or bathing requiring rest
Inability to walk 1 block on the level ground due to dyspnea or fatigue
Recent need to escalate diuretics to maintain volume status,
Progressive decline in serum sodium, usually to <133 mEq/L
Frequent ICD shocks

Població exclosa - ARNI

- **IC avançada**
- **HipoTA**
- **Insuf. Renal – Sdr Cardiorenal**

C Yancy AHA/ACC Circulation 2013;128:1-163



Sacubitril/valsartan

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

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).[a]	IIa	B
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).[a]	IIb	C

ESC HF-Guidelines 2012

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

If-channel inhibitor		
Ivabradine should be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE-I (or ARB), and an MRA (or ARB).	IIa	B
Ivabradine should be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm who are unable to tolerate or have contra-indications for a beta-blocker. Patients should also receive an ACE-I (or ARB) and an MRA (or ARB).	IIa	C

ESC HF-Guidelines 2016

Pooled data from BEAUTIFUL and SHIFT Trials

LVEF 30±6%, (87% beta-blockers, 90% RAS inhibitors)

Table 4 Heart failure outcomes in patients with left-ventricular dysfunction and heart rate ≥75 b.p.m. (*n* = 7632; 3812 ivabradine, 3820 placebo)

	Event rates, *n* (%)		HR (95% CI)	*P*-value
	Ivabradine group (*n* = 3812)	Placebo group (*n* = 3820)		
CV mortality or hospitalization for HF	858 (23%)	1003 (26%)	0.82 (0.75–0.90)	<0.0001
CV mortality	492 (13%)	548 (14%)	0.88 (0.78–1.00)	0.049
Hospitalization for HF	568 (15%)	704 (18%)	0.78 (0.70–0.87)	<0.0001
Total mortality	577 (15%)	636 (17%)	0.89 (0.80–1.00)	0.048

Fox K Eur Heart J 2013;34:2263

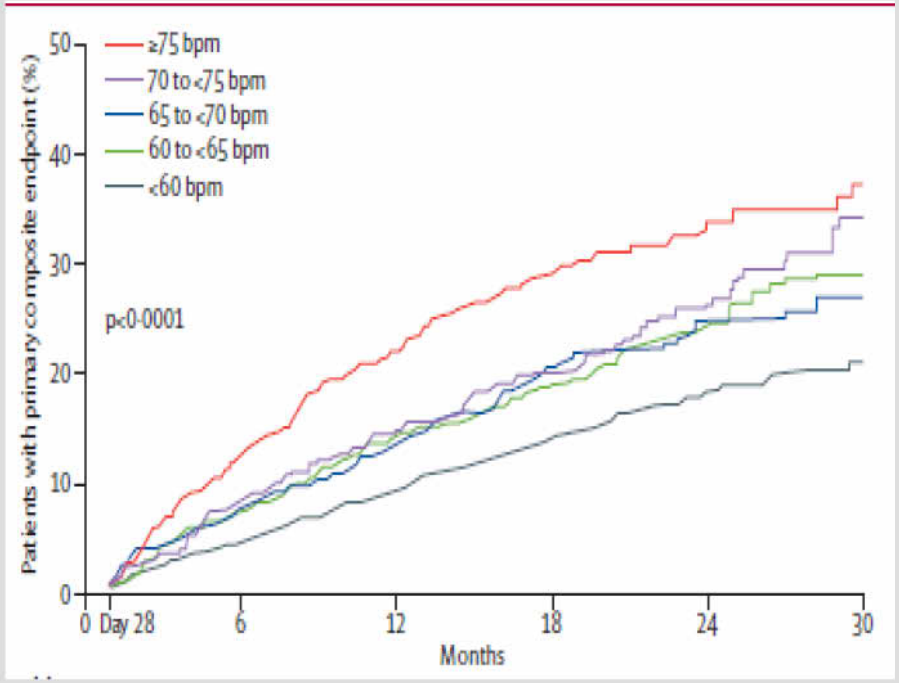
2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA

Recommendation for Ivabradine		
COR	LOE	Recommendation
IIa	B-R	Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HF*r*EF (LVEF ≤35%) who are receiving GDEM, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest (37-40).

Heart rate as a risk factor in chronic heart failure (SHIFT): the association between heart rate and outcomes in a randomised placebo-controlled trial

In the ivabradine group, heart rate achieved at 28 days was analyzed in relation to subsequent outcomes

Primary endpoint

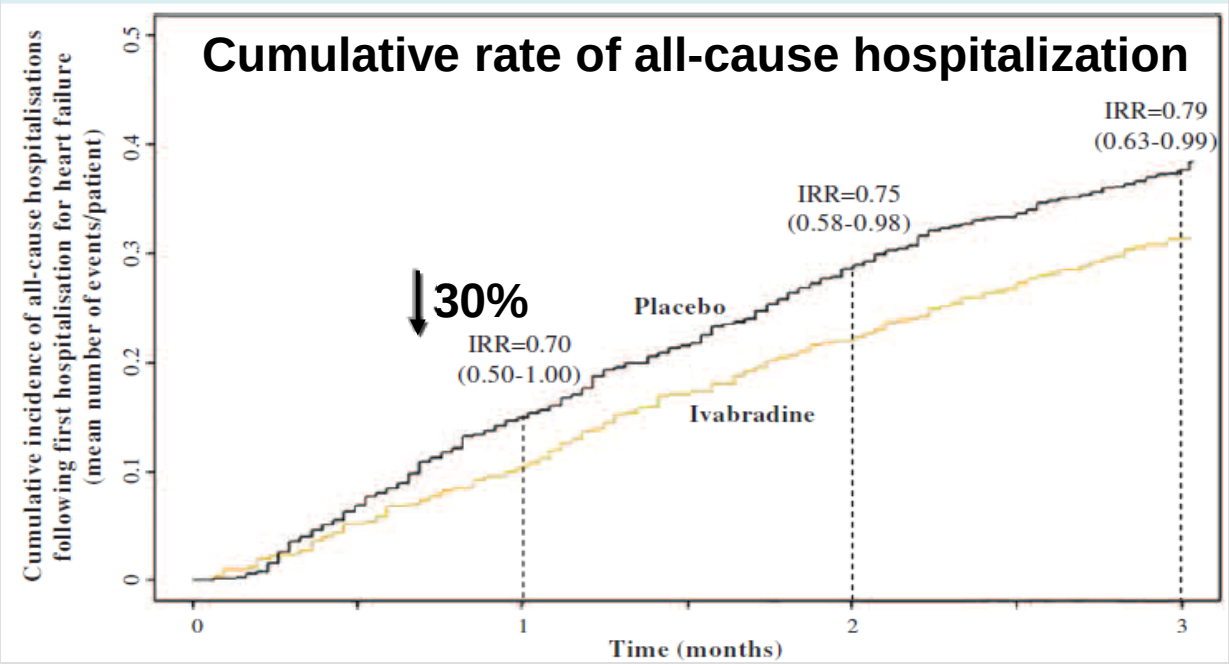


Pts with HR < 60 bpm at 28 days on treatment had fewer composite endpoint events (n=1192, event rate of 17%, 95%CI 15–19) than did patients with higher HR

Böhm M Lancet 2010;376:886

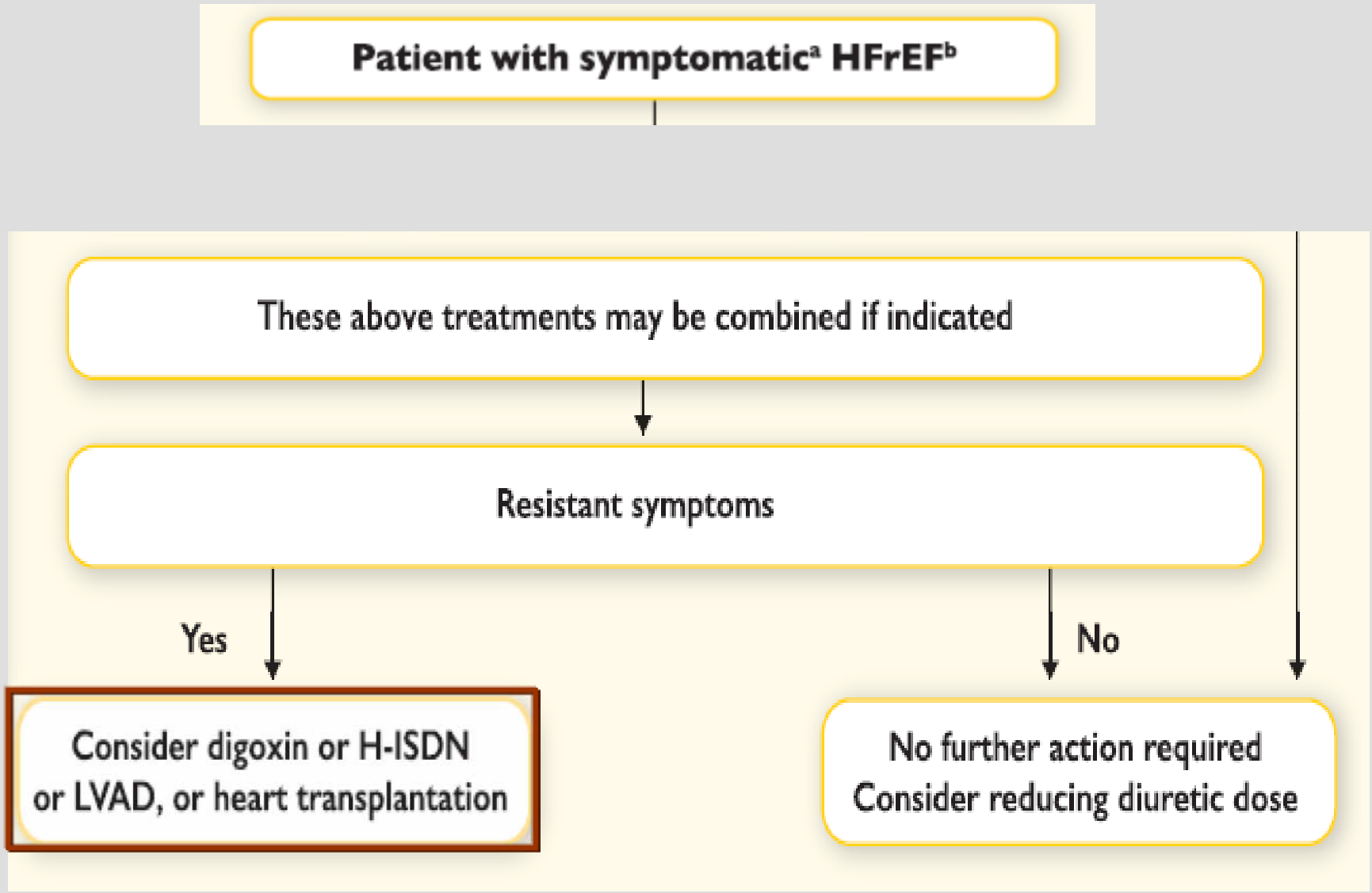
Ivabradine and HF readmmission

1186 pts of 6505 required HF-H, 334 patients (28%) were re-H within 3m for CV causes (86%), including HF-H (61%).



	Cumulative number of events		IRR (95% CI) (adjusted for prognostic factors)
	Ivabradine ($n = 514$)	Placebo ($n = 672$)	
Cardiovascular hospitalizations			
1 month	38	76	0.66 (0.44–1.01)
2 months	90	155	0.77 (0.57–1.02)
3 months	131	221	0.79 (0.62–1.01)
Heart failure hospitalizations			
1 month	21	42	0.67 (0.40–1.13)
2 months	56	97	0.77 (0.55–1.09)
3 months	86	148	0.78 (0.59–1.02)

Komajda M, Eur J Heart Fail 2016


Patient with symptomatic[a] HFrEF[b]
These above treatments may be combined if indicated
Resistant symptoms
Yes
No
Consider digoxin or H-ISDN
or LVAD, or heart transplantation
No further action required
Consider reducing diuretic dose

Patient with symptomatic[a] HFrEF[b]

Hydralazine and isosorbide dinitrate		
Hydralazine and isosorbide dinitrate should be considered in self-identified black patients with LVEF ≤35% or with an LVEF <45% combined with a dilated LV in NYHA Class III–IV despite treatment with an ACE-I or beta-blocker and an MRA to reduce the risk of HF hospitalizat	IIa	B
Hydralazine and isosorbide dinitrate nor an ARB (or they are contra-indic either an ACE-I	IIb	B
Other treatments with less-certai		
Digoxin		
Digoxin may be considered in sympt and an MRA, to reduce the risk of h), a beta-blocker	IIb	B

Recommendations for implantation of mechanical circulatory support in patients with refractory heart failure

Recommendations	Class[a]	Level[b]	Ref[c]
An LVAD should be considered in patients who have end- stage HFrEF despite optimal medical and device therapy and who are eligible for heart transplantation in order to improve symptoms, reduce the risk of HF hospitalization and the risk of premature death (Bridge to transplant indication).	IIa	C	
An LVAD should be considered in patients who have end-stage HFrEF despite optimal medical and device therapy and who are not eligible for heart transplantation to, reduce the risk of premature death.	IIa	B	605, 612, 613

HFrEF – Diabetis Mellitus

1. Metformin is safe to use in patients with HFrEF, and it should be the treatment of choice in patients with HF. IIa-C

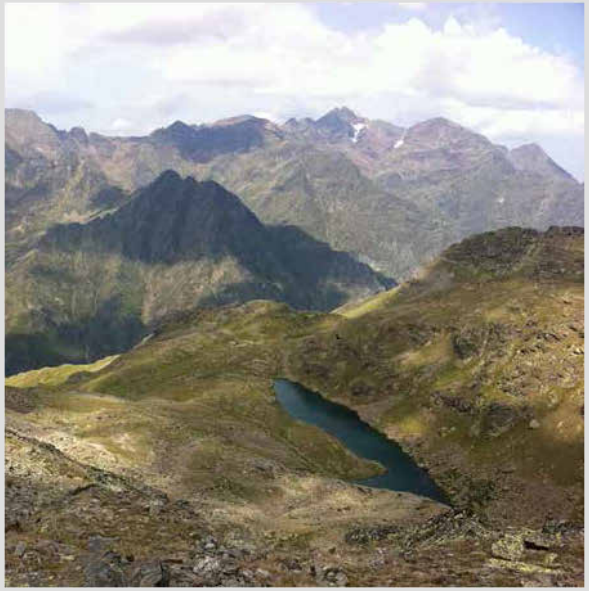
2.Thiazolidinediones (glitazones) cause Na and water retention and increased risk of HF and hospitalization and are not recommended in patients with HF.

3. Empagliflozin, (an inhibitor of sodium-glucose cotransporter 2), EMPA-REG reduced hospitalization for HF and mortality, but not AMI or stroke, in patients with diabetes at high cardiovascular risk, some of whom had HF

HFmEF - HFpEF

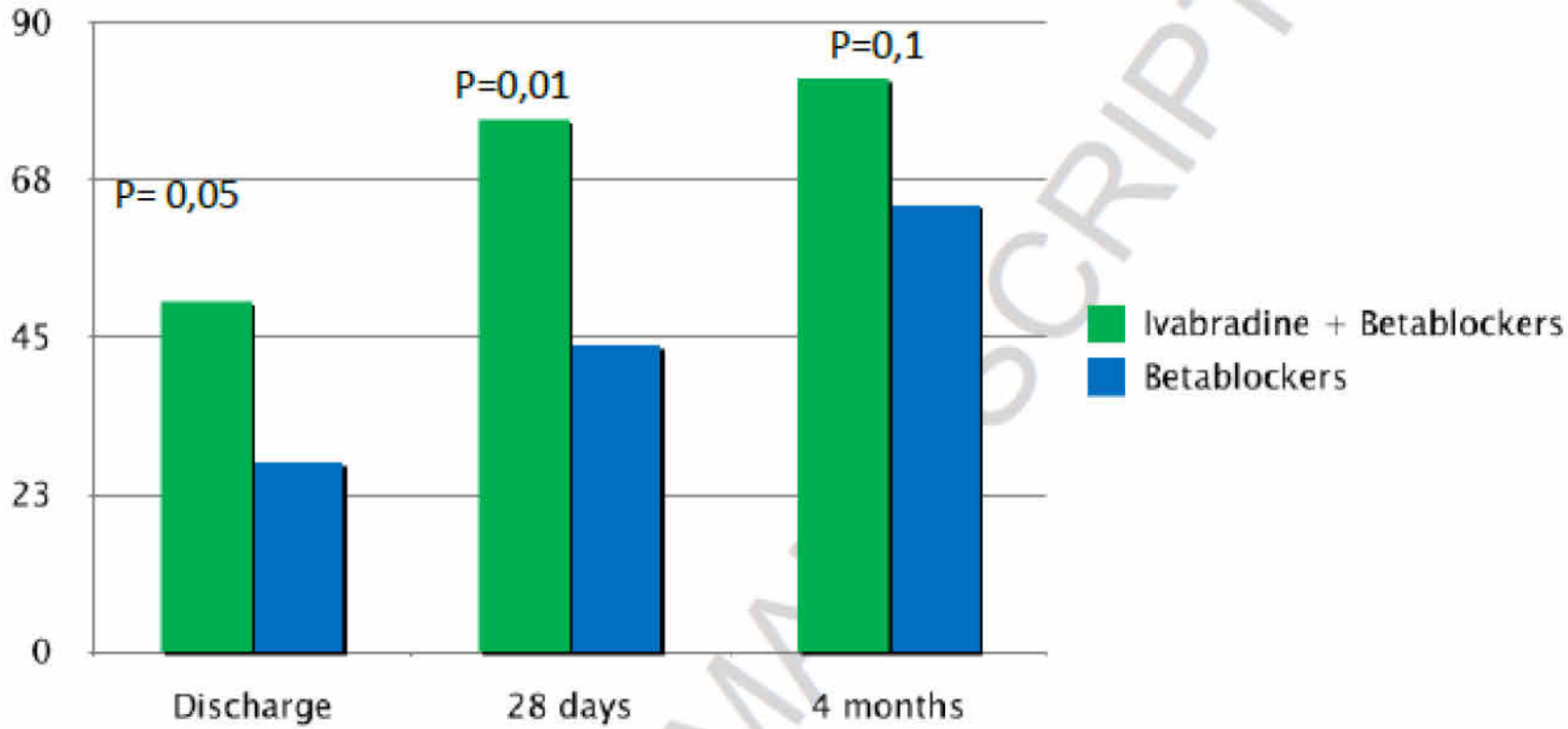
Recommendations for treatment of patients with heart failure with preserved ejection fraction and heart failure with mid-range ejection fraction

Recommendations	Class [a]	Level [b]	Ref [c]
it is recommended to screen patients with HFpEF or HFmrEF for both cardiovascular and non-cardiovascular comorbidities, which, if present, should be treated provided safe and effective interventions exist to improve symptoms, well-being and/or prognosis.	I	C	
Diuretics are recommended in congested patients with HFpEF or HFmrEF in order to alleviate symptoms and signs.	I	B	178, 179



Moltes Gràcies

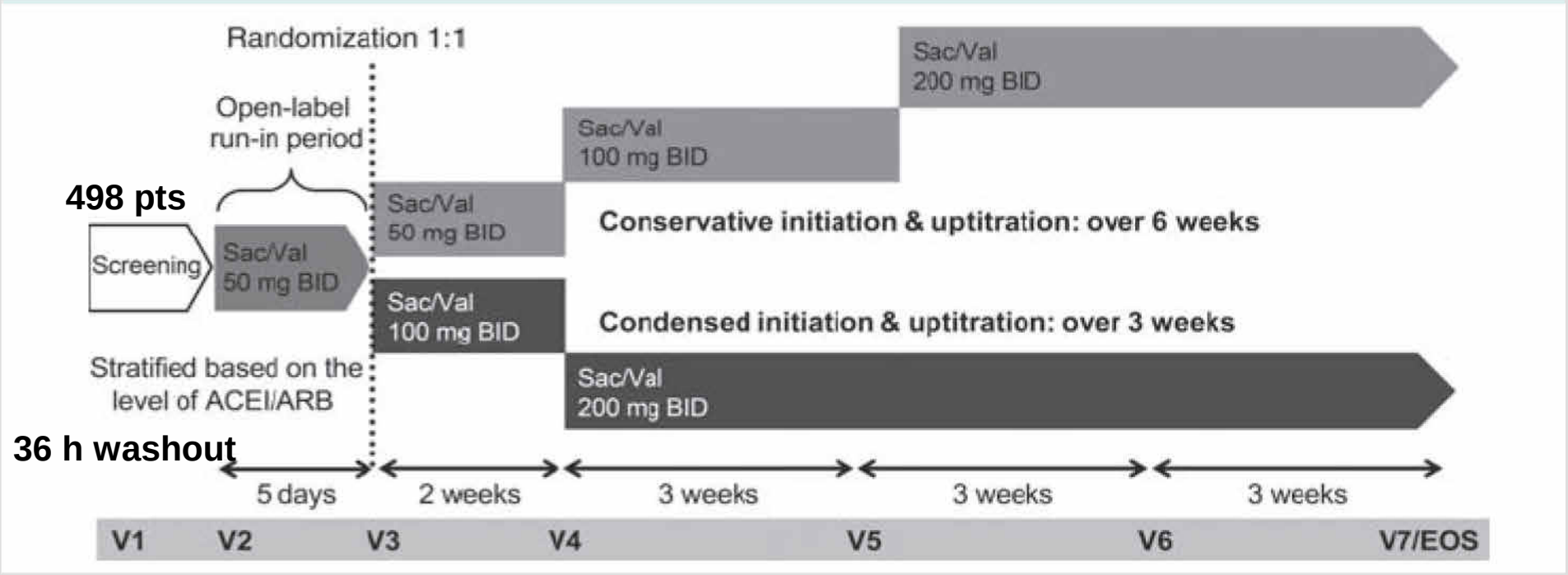
Percentage of patients with heart rate values < 70 bpm. HR: Heart rate.



Hidalgo FJ Int J Cardiol 2016;217;11

TITRATION - ARNI

CF II-IV, FE ≤ 35%, ACEI/ARB stable for 2 w or naive to ACEI/ARB
SBP ≥ 100 mmHg ≤ 180 mmHg



K< 5.4 mmol/L, GFR ≥ 30 mL/min.1.73m^2 o GFR reduction ≤ 35%, SBP ≥ 95 mmHg

- **High-dose si >160 mg Valsartan or >10 mg Enalapril /dia**
- **Low-dose si ≤160 mg Valsartan or ≤ 10 mg Enalapril /dia**

Low-dose SBP<95 mmHg condensed 14% vs conservative 5%, p=0.01

Senni M Eur J Heart Fail 2016

Com iniciar ARNI

- **Suspendre enalapril 36h abans del canvi**
- **Si Enalapril > 10 mg ---- dosi ARNI 49/51mg/12h**
- **Si Enalapril ≤ 10 mg ---- dosi ARNI 24/26 mg/12h**
- **Si Valsartan >160 mg ---- dosi ARNI 49/51mg/12h**
- **Si Valsartan ≤ 160 mg ---- dosi ARNI 24/26 mg/12h**

- **Si TFGe < 30 mL/min/1.73 m^2 contraindicat**
- **Si TFGe entre 60 - 30 mL/min/1.73 m^2 ajustar dosi**

Relevant safety issues of sacubitril/valsartan

- **Symptomatic hipotension**
- **Low risk of angioedema although higher than ACE (ACEi should be withheld for at least 36h before initiating ARNI)**
- **Additional concern about its long-term effects on the degradation of beta-amiloide peptide in the brain**

  (no evidence for increases in cognitive function or dementia)