

III Jornades d'actualització en Insuficiència cardíaca



CONTROVÈRSIES EN IC: QUÈ FEM EN L'ESTADI B DE LA IC REDUÏDA

ELS TEMPS HAN CANVIAT



CONFLICTES INTERÈS

- Honoraris com a consultor/ponent: Astrazeneca, Bayer, Boehringer/Lilly, Esteve, Novartis, Pfizer.



Els temps han canviat

Betabloquejants i IECAs, per suposat

EXPERT CONSENSUS DECISION PATHWAY

2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction

A Report of the American College of Cardiology Solution Set Oversight Committee

<https://doi.org/10.1016/j.jacc.2020.11.022>

New York Heart Association (NYHA) functional classification:

- **Class I: No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.**
- **Class II: Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.**
- **Class III: Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.**
- **Class IV: Unable to perform any physical activity without symptoms of HF, or symptoms of HF at rest.**

ACC/AHA Stages of HF:

- **Stage A: At high risk for HF but without structural heart disease or symptoms of HF.**
- **Stage B: Structural heart disease but without signs or symptoms of HF.**
- **Stage C: Structural heart disease with prior or current symptoms of HF.**
- **Stage D: Refractory HF requiring specialized interventions.**

ELS TEMPS HAN CANVIAT

Estimating lifetime benefits of comprehensive disease-modifying pharmacological therapies in patients with heart failure with reduced ejection fraction: a comparative analysis of three randomised controlled trials

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Management of HFrEF

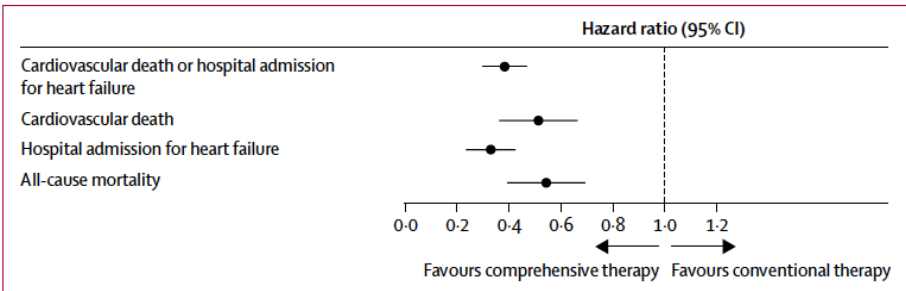
To reduce mortality - for all patients

ACE-I/ARNI

BB

MRA

SGLT2i

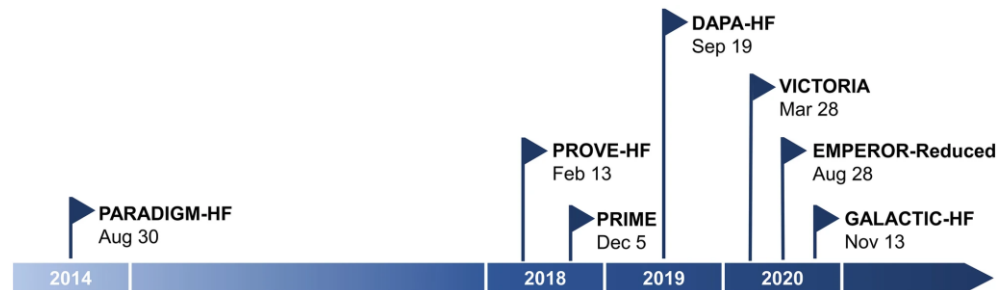


M Vaduganathan. Lancet. 2020

Pharmacological treatments indicated in patients with (NYHA class II–IV) heart failure with reduced ejection fraction (LVEF ≤40%)

Recommendations	Class ^a	Level ^b
An ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death. ^{110–113}	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death. ^{114–120}	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death. ^{121,122}	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death. ^{108,109}	I	A
Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death. ¹⁰⁵	I	B

ELS TEMPS HAN CANVIAT



Angiotensin–Nepriylsin Inhibition versus Enalapril in Heart Failure

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Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

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Vericiguat in Patients with Heart Failure and Reduced Ejection Fraction

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Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure

M. Packer, S.D. Anker, J. Butler, G. Filippatos, S.J. Pocock, P. Carson, J. Januzzi, S. Verma, H. Tsutsui, M. Brueckmann, W. Jamal, K. Kimura, J. Schnee, C. Zeller, D. Cotton, E. Bocchi, M. Böhm, D.-J. Choi, V. Chopra, E. Chuquiere, N. Giannetti, S. Janssens, J. Zhang, J.R. Gonzalez Juanatey, S. Kaul, H.-P. Brunner-La Rocca, B. Merkely, S.J. Nicholls, S. Perrone, I. Pina, P. Ponikowski, N. Sattar, M. Senni, M.-F. Seronde, J. Spinar, I. Squire, S. Taddei, C. Wanner, and F. Zannad, for the EMPEROR-Reduced Trial Investigators*

Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure

J.R. Teerlink, R. Diaz, G.M. Felker, J.J.V. McMurray, M. Metra, S.D. Solomon, K.F. Adams, I. Anand, A. Arias-Mendoza, T. Biering-Sørensen, M. Böhm, D. Bonderman, J.G.F. Cleland, R. Corbalan, M.G. Crespo-Leiro, U. Dahlström, L.E. Echeverría, J.C. Fang, G. Filippatos, C. Fonseca, E. Goncalvesova, A.R. Goudev, J.G. Howlett, D.E. Lanfear, J. Li, M. Lund, P. Macdonald, V. Mareev, S. Momomura, E. O'Meara, A. Parkhomenko, P. Ponikowski, F.J.A. Ramires, P. Serpytis, K. Sliwa, J. Spinar, T.M. Suter, J. Tomcsanyi, H. Vandekerckhove, D. Vinereanu, A.A. Voors, M.B. Yilmaz, F. Zannad, L. Sharpsten, J.C. Legg, C. Varin, N. Honarpour, S.A. Abbasi, F.I. Malik, and C.E. Kurtz, for the GALACTIC-HF Investigators*

Dębska-Kozłowska, A. *Heart Fail*
DOI: 10.1177/1078242420941111

METHODS

In this double-blind trial, we randomly assigned 8442 patients with class II, III, or IV heart failure and an ejection fraction of 40% or less to receive either LCZ696 (at a dose of 200 mg twice daily) or enalapril (at a dose of 10 mg twice daily), in addition to recommended therapy. The primary outcome was a composite of death from cardiovascular causes or hospitalization for heart failure, but the trial was designed to detect a difference in the rates of death from cardiovascular causes.

METHODS

In this phase 3, placebo-controlled trial, we randomly assigned 4744 patients with New York Heart Association class II, III, or IV heart failure and an ejection fraction of 40% or less to receive either dapagliflozin (at a dose of 10 mg once daily) or placebo, in addition to recommended therapy. The primary outcome was a composite of worsening heart failure (hospitalization or an urgent visit resulting in intravenous therapy for heart failure) or cardiovascular death.

METHODS

In this phase 3, randomized, double-blind, placebo-controlled trial, we assigned 5050 patients with chronic heart failure (New York Heart Association class II, III, or IV) and an ejection fraction of less than 45% to receive vericiguat (target dose, 10 mg once daily) or placebo, in addition to guideline-based medical therapy. The primary outcome was a composite of death from cardiovascular causes or first hospitalization for heart failure.

METHODS

In this double-blind trial, we randomly assigned 3730 patients with class II, III, or IV heart failure and an ejection fraction of 40% or less to receive empagliflozin (10 mg once daily) or placebo, in addition to recommended therapy. The primary outcome was a composite of cardiovascular death or hospitalization for worsening heart failure.

METHODS

We randomly assigned 8256 patients (inpatients and outpatients) with symptomatic chronic heart failure and an ejection fraction of 35% or less to receive omecamtiv mecarbil (using pharmacokinetic-guided doses of 25 mg, 37.5 mg, or 50 mg twice daily) or placebo, in addition to standard heart-failure therapy. The primary outcome was a composite of a first heart-failure event (hospitalization or urgent visit for heart failure) or death from cardiovascular causes.

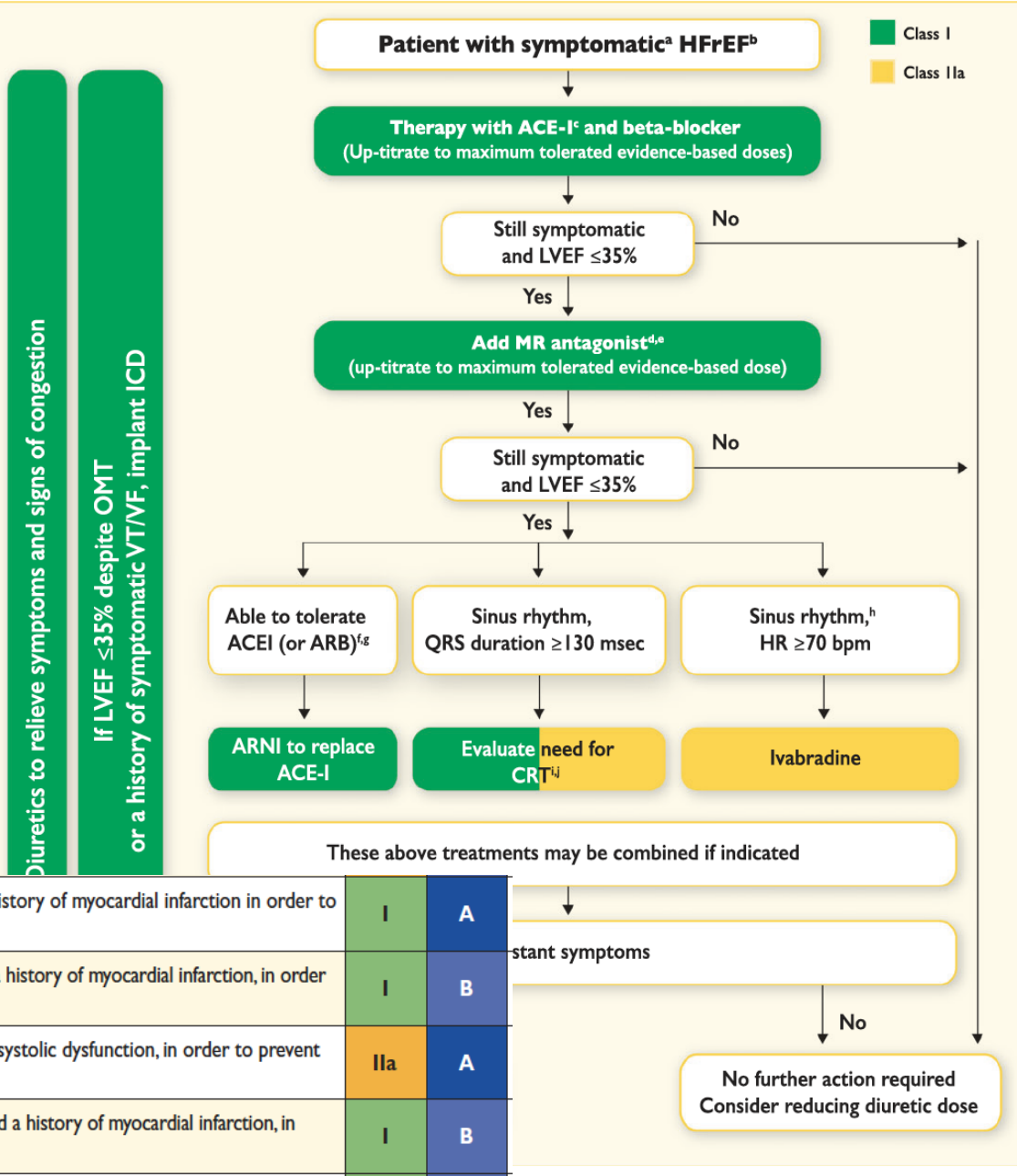
ESC GUIDELINES 2016



European Heart Journal (2016) 37, 2129–2200
doi:10.1093/eurheartj/ehw128

ESC GUIDELINES

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



ACE-I is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction in order to prevent or delay the onset of HF and prolong life.	I	A
ACE-I is recommended in patients with asymptomatic LV systolic dysfunction without a history of myocardial infarction, in order to prevent or delay the onset of HF.	I	B
ACE-I should be considered in patients with stable CAD even if they do not have LV systolic dysfunction, in order to prevent or delay the onset of HF.	IIa	A
Beta-blocker is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction, in order to prevent or delay the onset of HF or prolong life.	I	B

NO EVIDÈNCIA

NO EVIDÈNCIA = NO BENEFICI



NO EVIDÈNCIA ≠ NO BENEFICI



ASSIMPTOMÀTIC, SEGUR?

A Comparison of Patient and Physician-Rated New York Heart Association Class in a Community-Based Heart Failure Clinic

KEVIN M. GOODE, PhD, SAMANTHA NABB, PhD, JOHN G.F. CLELAND, MD, AND ANDREW L. CLARK, MD

J Cardiac Fail 2008;14:379-387

Methods and Results: NYHA class was rated independently by a physician and patient in 1752 patients referred with suspected heart failure. Pa-NYHA and Dr-NYHA varied by 1 class in 37.1% cases and by 2 classes in 12.8% cases.

Table 2. Discordance and Agreement Between Patient and Physician-Rated New York Heart Association in All Patients

		Patient-Rated NYHA					NYHA in Agreement n (%)	Patient-Rated Worse Than Physician-Rated n (%)	Patient-Rated Better Than Physician-Rated n (%)
		I	II	III	IV	Total			
Physician-Rated NYHA	I	385 (22.0%)	96 (5.5%)	31 (1.8%)	21 (1.2%)	533 (30.4%)	385 (72.2%)	148 (27.8%)	—
	II	214 (12.2%)	391 (22.3%)	112 (6.4%)	130 (7.4%)	847 (48.3%)	391 (46.2%)	242 (28.6%)	214 (25.3%)
	III	31 (1.8%)	125 (7.1%)	84 (4.8%)	100 (5.7%)	340 (19.4%)	84 (24.7%)	100 (29.4%)	156 (45.9%)
	IV	1 (0.1%)	9 (0.5%)	5 (0.3%)	17 (1.0%)	32 (1.8%)	17 (53.1%)	—	15 (46.9%)
	Total	631 (36.0%)	621 (35.4%)	232 (13.2%)	268 (15.3%)	1752 (100%)	877 (50.1%)	490 (27.9%)	385 (22.0%)

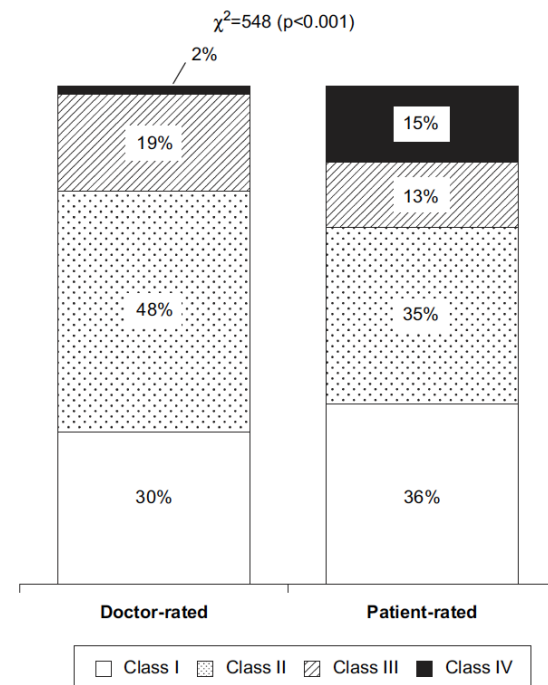
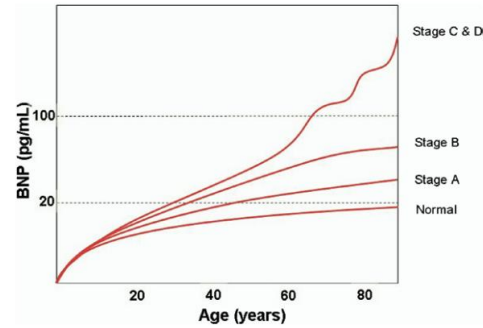


Fig. 1. Differences in distribution of physician-rated and patient-rated NYHA.

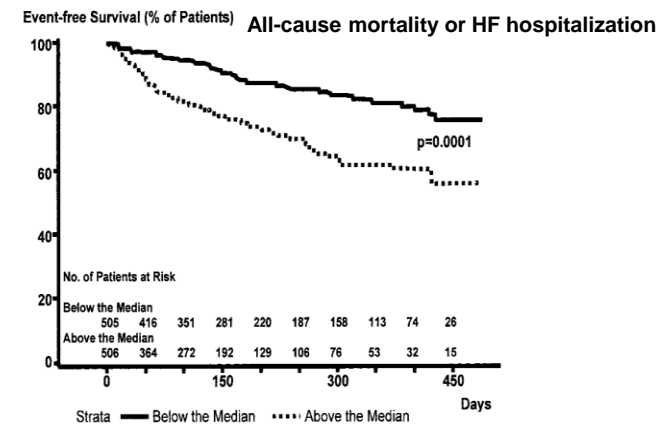
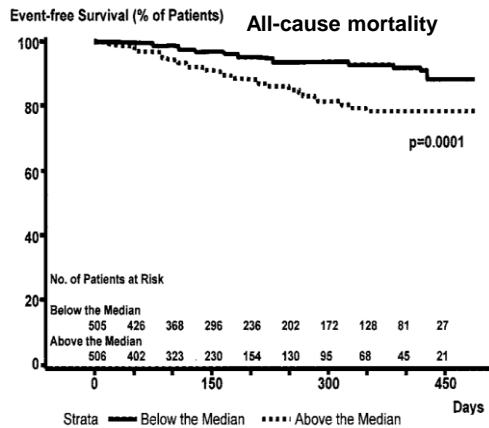
AFECTACIÓ SUBCLÍNICA: BIOMARCADORS

Prognostic Implications of Changes in N-Terminal Pro-B-Type Natriuretic Peptide in Patients With Heart Failure

Zile, RZ. et al. J Am Coll Cardiol 2016;68:2425–36



Daniels, LB. et al. J Am Coll Cardiol 2007;50:2357–68



Hartmann, F. et al. Circulation. 2004;110:1780-1786.

FIGURE 1 Effects on Risk of Primary Endpoint if NT-proBNP Achieved or Did Not Achieve a Value of <1,000 pg/ml 1 Month After Randomization

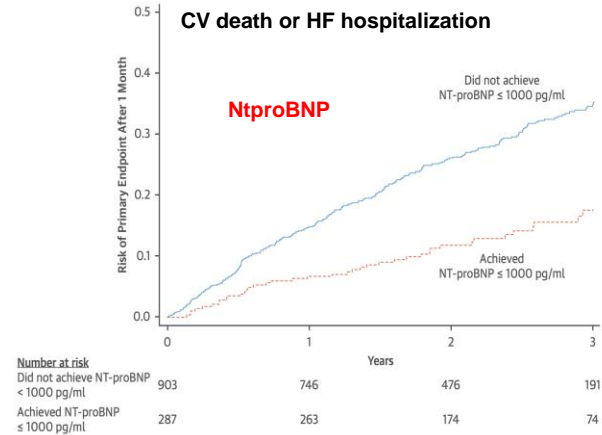


TABLE 1 Change in NT-proBNP From Baseline (V2/V2a) to 1 Month After Randomization (V7)

Change in NT-proBNP at 1 Month	All Patients (N = 1,942)	Sacubitril/Valsartan (n = 971)	Enalapril (n = 971)	Between Treatment		
				Odds Ratio	95% CI	p Value
Among patients with NT-proBNP (of any value) at baseline						
Any reduction	1,262 (65.0)	729 (75.1)	533 (54.9)	2.48	2.04–3.00	<0.001
Reduction >10%	1,106 (57.0)	667 (68.7)	439 (45.2)	2.66	2.21–3.20	<0.001
Reduction >20%	910 (46.9)	562 (57.9)	348 (35.8)	2.46	2.05–2.95	<0.001
Reduction >30%	709 (36.5)	461 (47.5)	248 (25.5)	2.64	2.18–3.19	<0.001
Reduction >40%	523 (26.9)	358 (36.9)	165 (17.0)	2.85	2.31–3.53	<0.001
Reduction >50%	357 (18.4)	256 (26.4)	101 (10.4)	3.08	2.40–3.96	<0.001
Change ≤10%	293 (15.1)	114 (11.7)	179 (18.4)	0.59	0.46–0.76	<0.001
Increase 10%–50%	315 (16.2)	120 (12.4)	195 (20.1)	0.56	0.44–0.72	<0.001
Increase >50%	228 (11.7)	70 (7.2)	158 (16.3)	0.40	0.30–0.54	<0.001
Among patients with NT-proBNP >1,000 mg/dl at baseline						
NT-proBNP ≤1,000 pg/ml	288 (23.9)	187 (30.6)	101 (17.0)	2.15	1.63–2.83	<0.001
NT-proBNP ≤750 pg/ml	154 (12.8)	108 (17.6)	46 (7.7)	2.55	1.77–3.68	<0.001
NT-proBNP ≤500 pg/ml	67 (5.6)	52 (8.5)	15 (2.5)	3.58	1.99–6.44	<0.001

LA IMPORTÀNCIA DEL REMODELAT

Table 2 Absolute Effect of Drug/Device on Change in EF Compared With Placebo

Intervention (Ref. #)	No. of Studies (n [Range])	ΔEF (95% CI)†	Mean Follow-Up Weeks [Range]
Amiodarone (17,68,69)	3 (942 [30-674])	3.8 (-1.7 to 9.2)	60.7 [26-104]
Amlodipine (70)	1 (362)	1.9 (1.8 to 2.0)	12
Bisoprolol (41)	1 (28)	12.0 (4.4 to 19.6)	52
Bucindolol (19,71-73)	4 (2,915 [19-2,708])	4.2 (3.7 to 4.7)	22 [12-52]
CRT (74-77)	4 (1,052)	2.7 (1.9 to 3.5)	21 [6-26]
Candesartan (78)	1 (305)	4.0 (0.5 to 7.5)	26
Captopril (79-84)	6 (543 [40-204])	3.3 (0.3 to 6.4)	36.7 [12-52]
Carvedilol (23,24,49,85-104)	22 (2,780 [15-415])	6.9 (5.8 to 8.0)	30 [13-52]
Digoxin (84,105-109)	6 (624 [13-196])	2.7 (1.2 to 4.1)	48.3 [12-208]
Enalapril (20,42,110-113)	6 (431 [12-301])	3.7 (1.5 to 5.9)	24 [4-52]
Enalapril-Prev (21)*	1 (108)	2.0 (-0.8 to 4.8)	52
Enoximone (114-119)	6 (203 [12-114])	3.4 (0.5 to 6.3)	8.7 [4-16]
Etanercept (120)	1 (47)	4.4 (3.7 to 5.1)	13
Felodipine (43,121,122)	3 (532 [20-260])	4.0 (1.2 to 6.7)	30 [12-52]
Flosequinan (123,124)	2 (210 [17-193])	-3.0 (-3.6 to -2.4)	10 [8-12]
Hydralazine-ISDN (16,22)	2 (1,137 [459-678])	2.9 (0.8 to 5.0)	39 [26-52]
Ibopamine (125)	1 (18)	0.0 (-4.9 to 4.9)	5
Metoprolol CR (39,40,126,127)	4 (587 [41-426])	4.5 (1.8 to 7.1)	25.5 [24-26]
Mibefradil (44)	1 (117)	0.5 (-2.8 to 3.8)	26
Milrinone (109)	1 (108)	2.2 (1.5 to 2.9)	53
Moxonidine (128)	1 (85)	4.0 (-0.5 to 8.5)	19
Prazosin (16,129-131)	4 (523 [22-456])	2.5 (0.6 to 4.4)	28.3 [9-52]
Spironolactone (132-134)	3 (185 [37-106])	3.0 (1.9 to 4.1)	25.7 [8-52]
Tolvaptan (45)	1 (240)	0.8 (-0.3 to 1.9)	54
Valsartan (38)	1 (5,010)	1.3 (0.7 to 1.9)	78

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LA IMPORTÀNCIA DEL REMODELAT

Association of Change in N-Terminal Pro-B-Type Natriuretic Peptide Following Initiation of Sacubitril-Valsartan Treatment With Cardiac Structure and Function in Patients With Heart Failure With Reduced Ejection Fraction

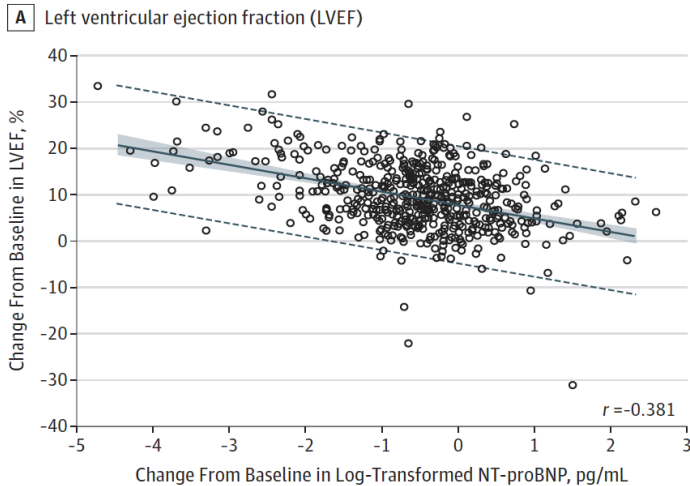
James L. Januzzi Jr, MD; Margaret F. Prescott, PhD; Javed Butler, MD, MPH, MBA; G. Michael Felker, MD, MHS; Alan S. Maisel, MD; Kevin McCague, MA; Alexander Camacho, PhD; Ileana L. Piña, MD, MPH; Ricardo A. Rocha, MD; Amil M. Shah, MD, MPH; Kristin M. Williamson, PharmD; Scott D. Solomon, MD; for the PROVE-HF Investigators

JAMA. 2019 Sep 17;322(11):1085-1095



N=794

Guideline-directed therapy	
β-Blocker	757 (95.3)
ACEI/ARB	602 (75.8)
MRA	281 (35.4)
CRT/CRT-D	122 (15.4)
ICD alone	226 (28.5)
Not taking ACEI/ARB	
ACEI/ARB naive (never exposed)	48 (6.0)
Previously taking but not currently	144 (18.1)



All Patients			
	Baseline Value, Median (25th to 75th Percentile)	LS Mean Change From Baseline at 6 mo (95% CI)	LS Mean Change From Baseline at 12 mo (95% CI)
LVEF, %	n = 757		
	28.2 (24.5 to 32.7)	5.2 (4.8 to 5.6)	9.4 (8.8 to 9.9)

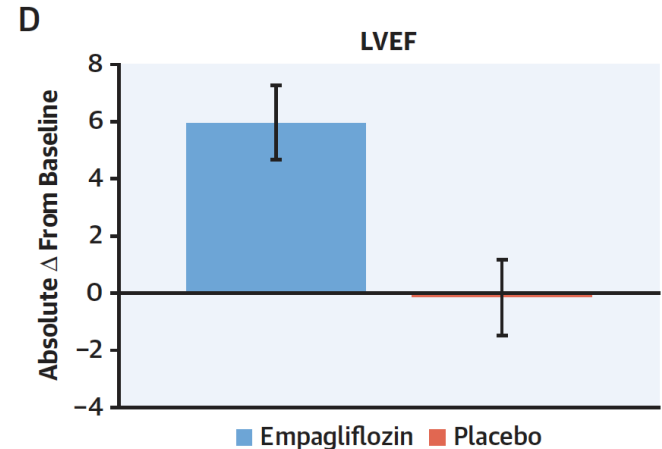
Randomized Trial of Empagliflozin in Nondiabetic Patients With Heart Failure and Reduced Ejection Fraction



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J Am Coll Cardiol 2021;77:243–55

	All	Empagliflozin	Placebo
Total	84 (100)	42 (100)	42 (100)
Medications			
Statin	63 (75)	33 (79)	30 (71)
ACE inhibitor/ARB (alone)	35 (42)	16 (38)	19 (45)
ARNi	36 (43)	21 (50)	15 (36)
B-blockers	74 (88)	36 (86)	38 (90)
Loop diuretics	46 (55)	22 (52)	24 (57)
Thiazide diuretics	5 (6)	3 (7)	2 (5)
Mineralocorticoid antagonists	28 (33)	13 (31)	15 (36)

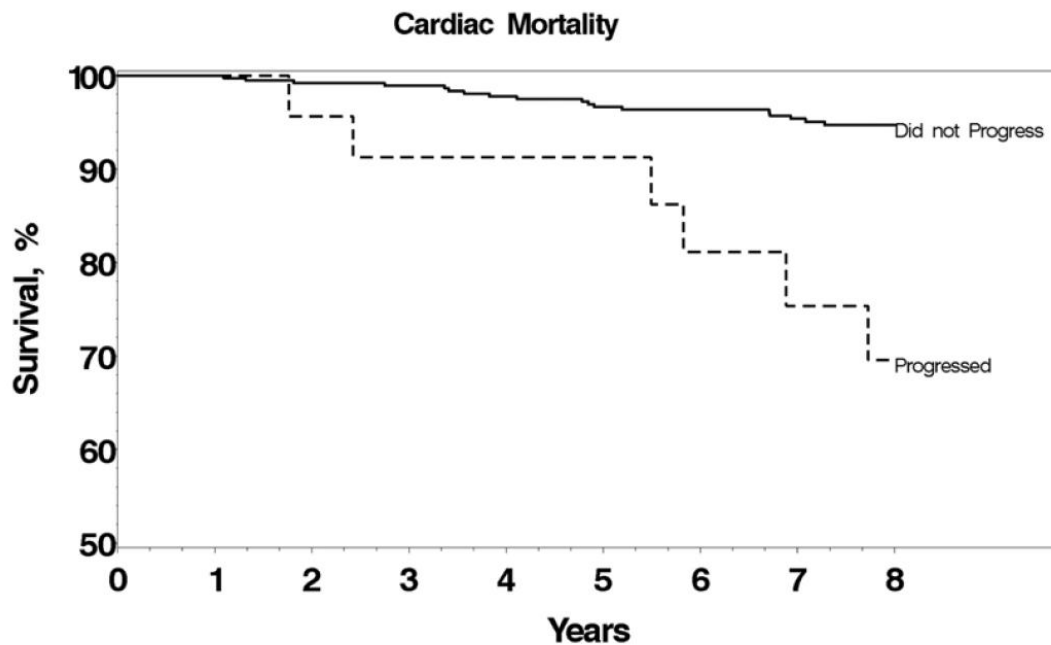


ESTADI B... FINS QUAN?

Progression of Preclinical Heart Failure

A Description of Stage A and B Heart Failure in a Community Population
 KA Young. Circ Cardiovasc Qual Outcomes. 2021;14:e007216

B



Did not Progress
 Progressed

99.2 (365)
 95.7 (22)

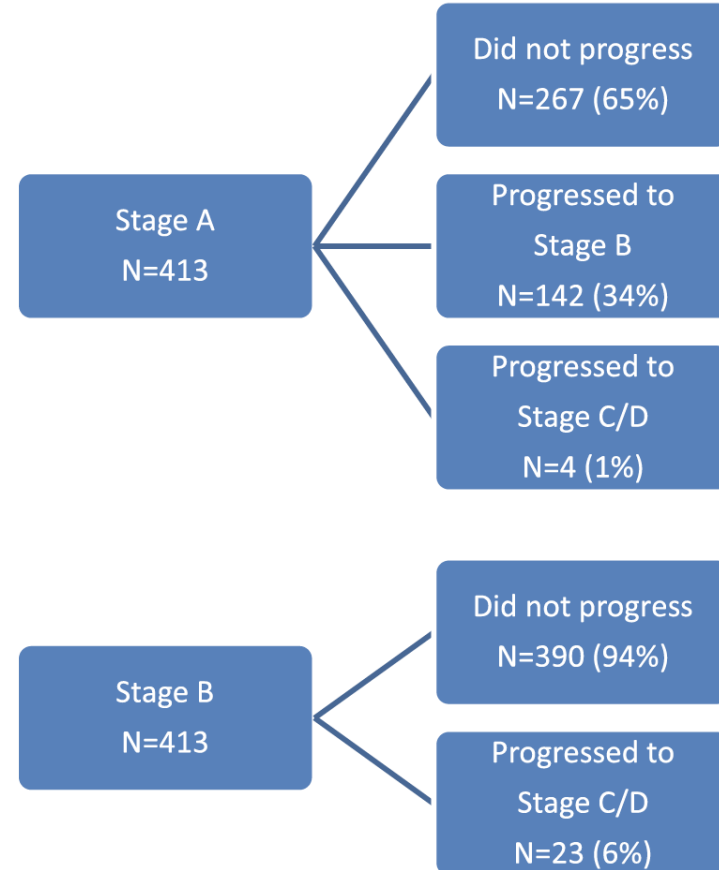
97.8 (347)
 91.3 (20)

96.4 (318)
 81.2 (16)

94.7 (207)
 69.6 (10)

Visit 1
 (1997-2000)

Visit 2
 (2001-2004)



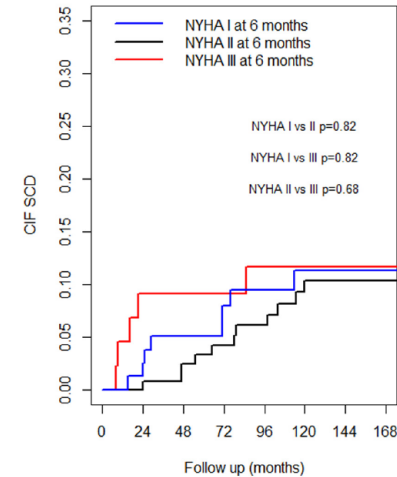
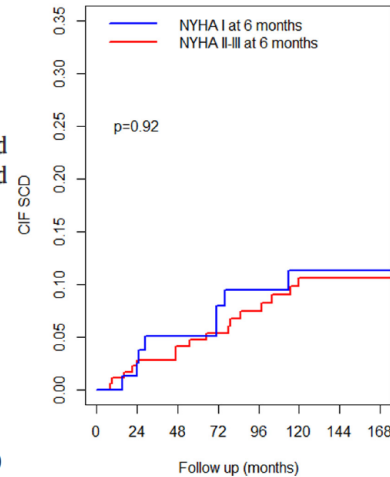
I LES ARÍTMIES?

Risk of sudden cardiac death in New York Heart Association class I patients with dilated cardiomyopathy: A competing risk analysis

Davide Stolfo, MD^{a,b,*}, Stefano Albani, MD^a, Gianluigi Savarese, MD^b, Giulia Barbati, PhD^{a,c}, Federica Ramani^a, Marta Gigli, MD^a, Federico Biondi, MD^a, Matteo Dal Ferro, MD^a, Massimo Zecchin, MD^a, Marco Merlo, MD^a, Gianfranco Sinagra, MD^a

Int J Cardiol. 2020 May 15;307:75-81

Methods: A total of 272 DCM patients with EF \leq 35% and NYHA class I-III after \geq 3 months of guideline-directed medical therapy were included. The risk of SCD and SCD/malignant ventricular arrhythmias (MVA) was assessed in NYHA I vs. NYHA II and NYHA III groups by competing risk analysis.

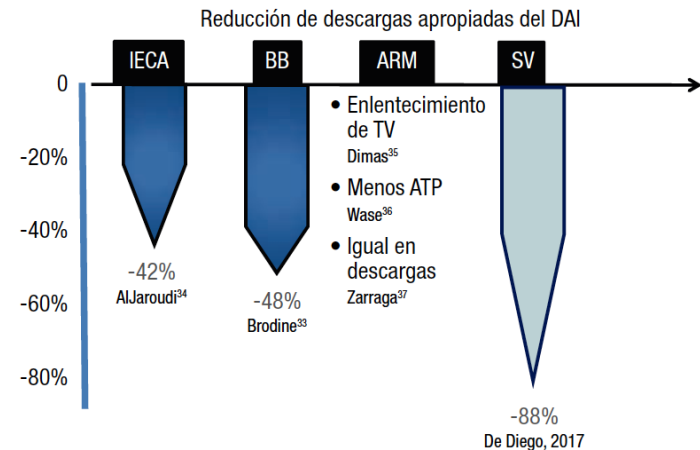
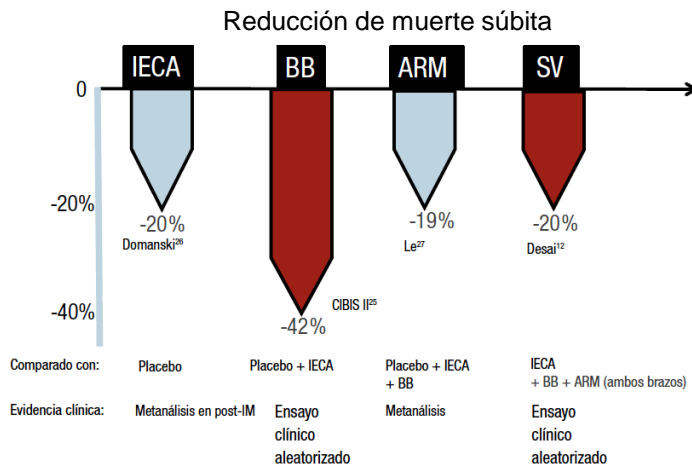


Controversias para una nueva era en el tratamiento de la insuficiencia cardiaca

Paciente «estable» con insuficiencia cardiaca: el momento oportuno

Carlos de Diego^a y Julio Núñez^{b,*}

Rev Esp Cardiol Supl. 2019;18(B):11-16



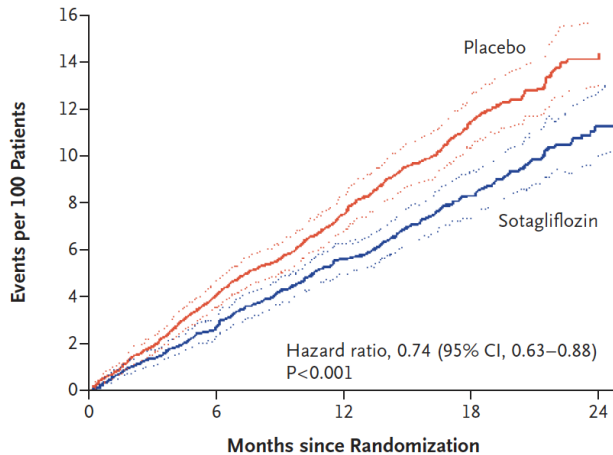
EVIDÈNCIA INDIRECTE

Sotagliflozin in Patients with Diabetes and Chronic Kidney Disease

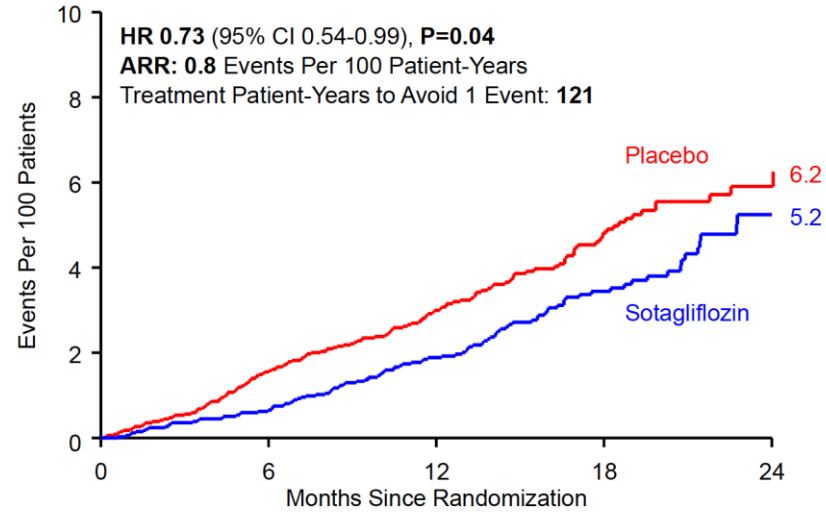
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 for the SCORED Investigators*

DM2 + MRC

N Engl J Med 2021;384:129-39



SCORED Total CV Death, HHF, and Urgent HF Visit in 6738 Patients with no History of HF (EF ≥ 50%)



Bhatt DL. ACC 2021, virtual.

History of heart failure — no. (%)‡	1640 (31.0)	1643 (31.0)
Ejection fraction of <40%	505 (9.5)	528 (10.0)
Ejection fraction of 40 to <50%	290 (5.5)	291 (5.5)
Ejection fraction of ≥50%	843 (15.9)	824 (15.6)
Any RAAS inhibitor — no. (%)¶	4705 (88.9)	4660 (88.1)
ACE inhibitor	2009 (38.0)	2039 (38.5)
Angiotensin-receptor blocker	2619 (49.5)	2562 (48.4)
Angiotensin receptor–neprilysin inhibitor	66 (1.2)	65 (1.2)
Mineralocorticoid-receptor antagonist	810 (15.3)	776 (14.7)
Beta-blocker — no. (%)	3310 (62.5)	3306 (62.5)

QUÈ FARIEU VOSALTRES?

Home 32 anys
"CF-I"
proBNP 882pg/mL
Estudi familiar MCDNI



Betabloquejants i IECAs,
per suposat

Els temps han canviat



III Jornades d'actualització en Insuficiència cardíaca



GRÀCIES PER L'ATENCIÓ