SOCIEDAD ASTURIANA DE CARDIOLOGÍA

Congreso de la
Sociedad Asturiana
de **Cardiología**

4 y 5 de mayo de 2018
Sede **Parador de Cangas de Onís**

MANEJO DEL PACIENTE ESTABLE NYHA II:

¿BUEN O MAL PRONÓSTICO?

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LO USAMOS... PERO COMO DEFINIR ESTABILIDAD?

NICE National Institute for Health and Care Excellence

Adults with stable chronic heart failure
Adults diagnosed with chronic heart failure whose clinical condition has not deteriorated, whose heart medication has not been changed and who have not been admitted to hospital because of heart failure.

[Adapted from Chronic heart failure in adults (NICE guideline CG108)]

European Heart Journal Advance Access published May 20, 2016

European Heart Journal
doi:10.1093/eurheartj/ehw128

ESC GUIDELINES

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

3.2.2. Terminología relativa a la evolución temporal de la insuficiencia cardiaca

En esta guía, el término IC se utiliza para describir el síndrome sintomático, evaluado según la clasificación funcional de la *New York Heart Association* (NYHA) (véase la sección 3.2.3 y la tabla 3.2 del anexo), aunque un paciente puede volverse asintomático por el tratamiento. Asimismo un paciente que nunca ha mostrado los síntomas o signos típicos de IC y tiene la FEVI reducida se describe como un paciente con disfunción sistólica del VI asintomática. De los pacientes que han tenido IC por algún tiempo, se dice normalmente que padecen «IC crónica». Un paciente en tratamiento con síntomas y signos que no han cambiado dur[1 mes]escribe como un paciente «estable». Si la IC estable c[1 mes]iora, se puede describir al paciente como «descompensa[1 mes] puede suceder lenta o repentinamente, suele ser necesario hospitalizar al paciente y es un acontecimiento de considerable importancia pronóstica. La IC de nueva aparición *(de novo)* puede presentarse aguda, por ejemplo, como consecuencia de un infarto agudo de miocardio (IAM), o subaguda, por ejemplo, en pacientes con miocardiopatía dilatada (MCD), que frecuentemente tienen síntomas durante semanas o meses antes de que se confirme el diagnóstico. Aunque los síntomas y signos de IC desaparezcan, la disfunción cardiaca subyacente puede permanecer y los pacientes seguirían en riesgo de «descompensación» recurrente.

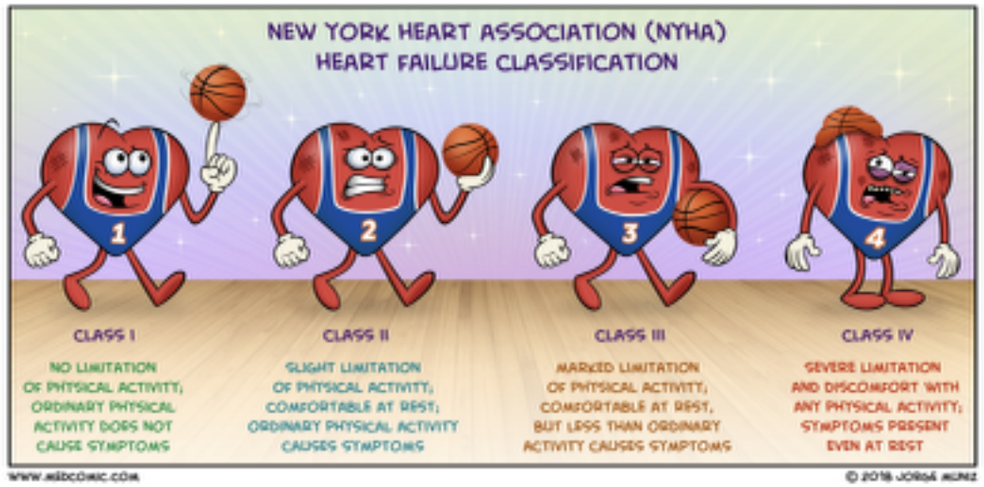
Amma KH. Circulation. 2007 Jun 7;133(23):2254-62

Heart Failure

Prevalence and Prognostic Significance of Heart Failure Stages

Application of the American College of Cardiology/American Heart Association Heart Failure Staging Criteria in the Community

Khawaja Afzal Ammar, MD; Steven J. Jacobsen, MD, PhD; Douglas W. Mahoney, MS; Jan A. Kors, PhD; Margaret M. Redfield, MD; John C. Burnett, Jr, MD; Richard J. Rodeheffer, MD



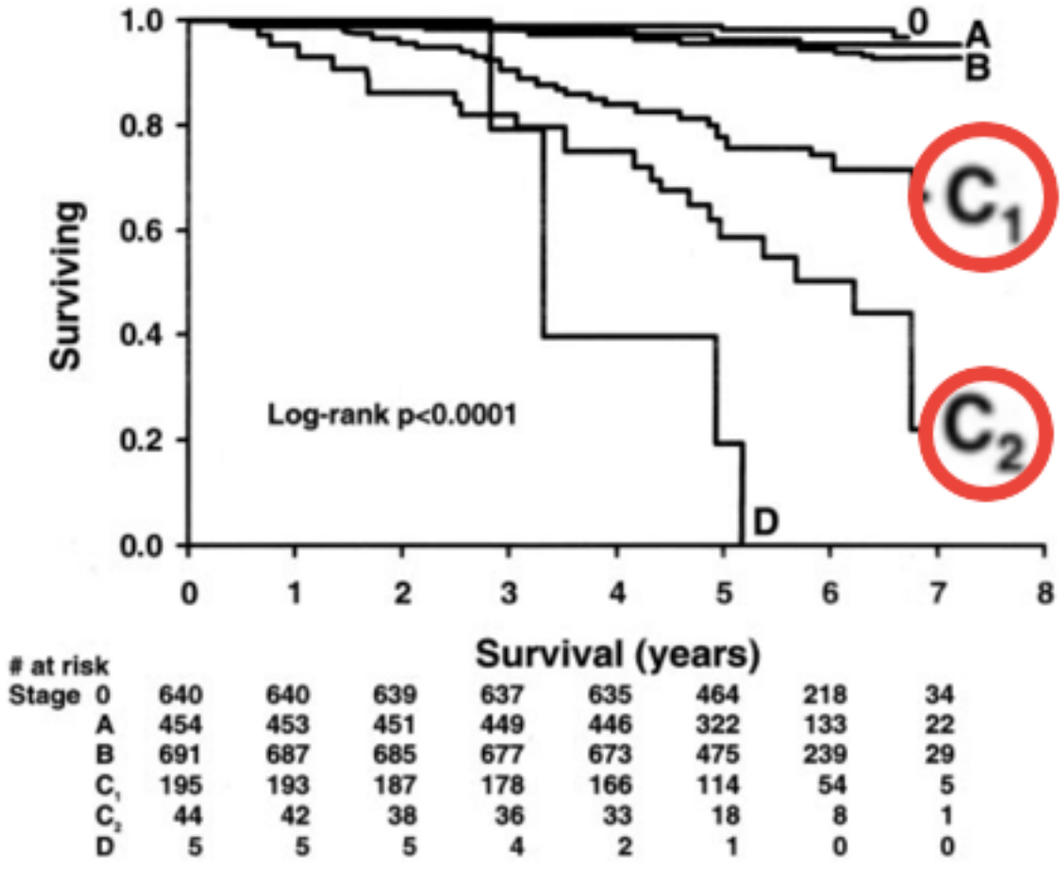
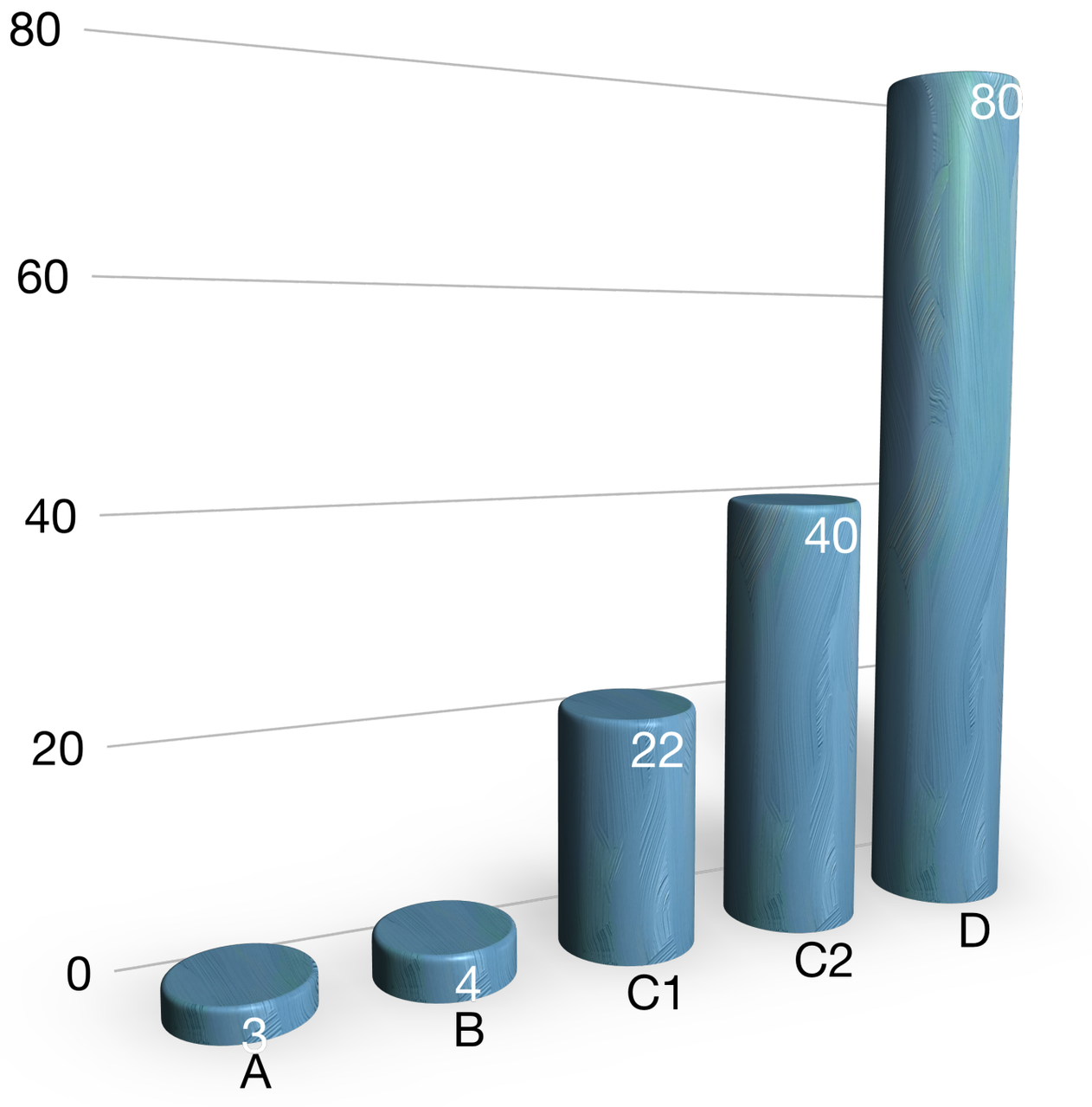


Figure 2. Survival curves according to HF stage.



Amma KH. Circulation. 2007 Jun 7;133(23):2254-62

NUESTROS PROBLEMAS

1. No veo esos pacientes.

2. Mi paciente en clase funcional II = paciente estable = no cambio nada

3. Debería pautar ARNI; pero implica exceso de seguimiento y trabajo

NUESTROS PROBLEMAS

1. No veo esos pacientes.
2. Mi paciente en clase funcional II = paciente estable = no cambio nada
3. Debería pautar ARNI; pero implica exceso de seguimiento y trabajo

NUESTRA PACIENTE ESTABLE (QUE NO VEMOS)

- Mujer 63 años, HTA, DM tipo 2.
- Enero 2017: disnea con las cuestas. Ligeros edemas. Diagnosticada de MCD con coronarias normales. RTG -. FEVI 30%. No AF. proBNP 984 pg/ml
  - Tratamiento:
    - ramipril 5mg/12h
    - carvedilol 12.5/12h
    - metformina/empa 10/850 cada 12h
    - epleronona 25mg/24h
    - furosemida 40mg ajustable

NUESTRA PACIENTE ESTABLE (QUE NO VEMOS)

- Mujer 63 años, HTA, DM tipo 2.
- Enero 2018:
  - ausencia de ingresos
  - se encuentra igual que en la ultima visita
  - ecocardio: sin cambios en la FEVI
  - analítica: proBNP 536pg/ml CA 125: 14mg/dl
  - mismo tratamiento

NUESTRA PACIENTE ESTABLE (QUE NO VEMOS)

GOLD MINUTE

¿Como se encuentra?

“Bastante bien, más o menos como siempre”

NUESTRA PACIENTE ESTABLE (QUE NO VEMOS)

NUESTRA PACIENTE ESTABLE (QUE NO VEMOS)

- **¿Tiene algo de fatiga en su día normal? Hace lo mismo que 12 meses atrás?**

- Me encuentro bien, lo que peor llevo es lo del dúplex de subir y bajar los dos pisos.
- Bueno, y cuando voy a la compra, ahora voy con carro para no fatigarme

¿PACIENTE ESTABLE?

NUESTROS PROBLEMAS

1. No veo esos pacientes. Los tienen todos Raquel y Alberto

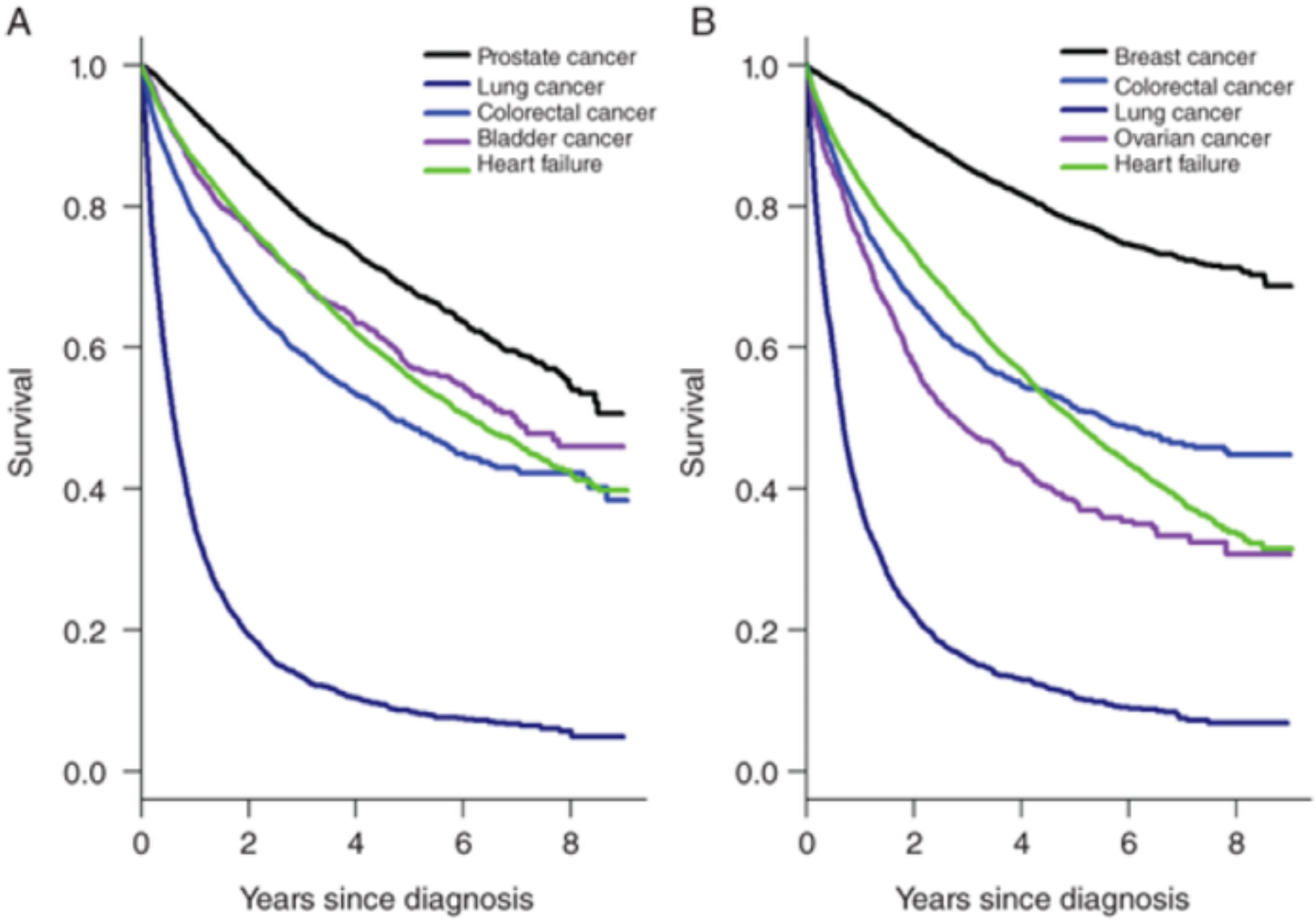
2. Mi paciente en clase funcional II = paciente estable = no cambio nada

3. Debería pautar ARNI; pero implica exceso de seguimiento y trabajo

MI PACIENTE ESTABLE

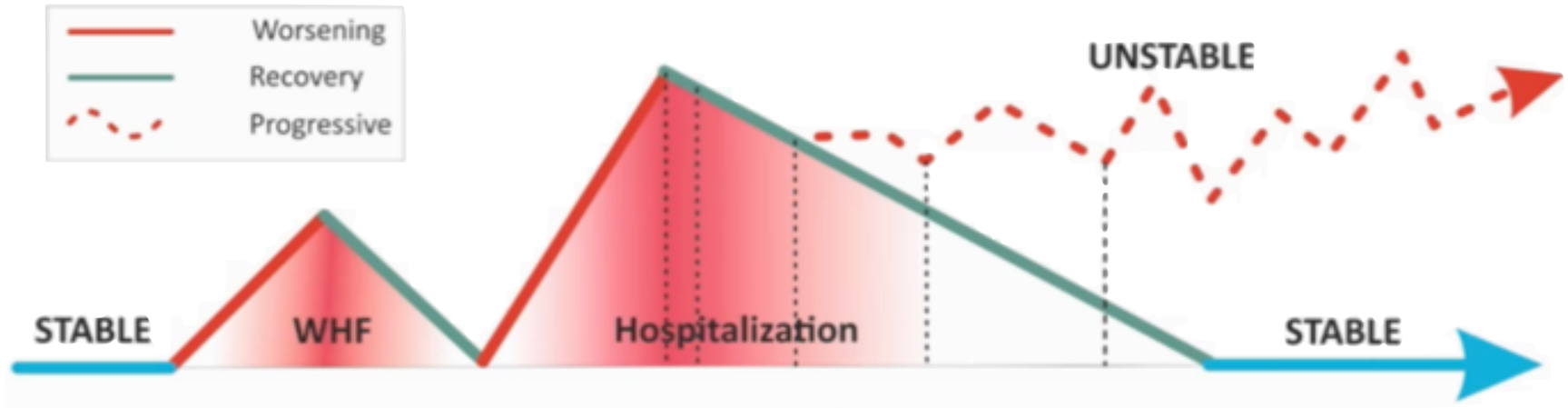
- **Mi paciente está estable con el tratamiento actual**
- **Si está estable, para qué cambiar el tratamiento**
- **Si está en CF I-II, con lo que lleva está bien**
- **Esto es mucho trabajo para 15 minutos**
- **El paciente tiene una IC leve, casi mejor no tocar**

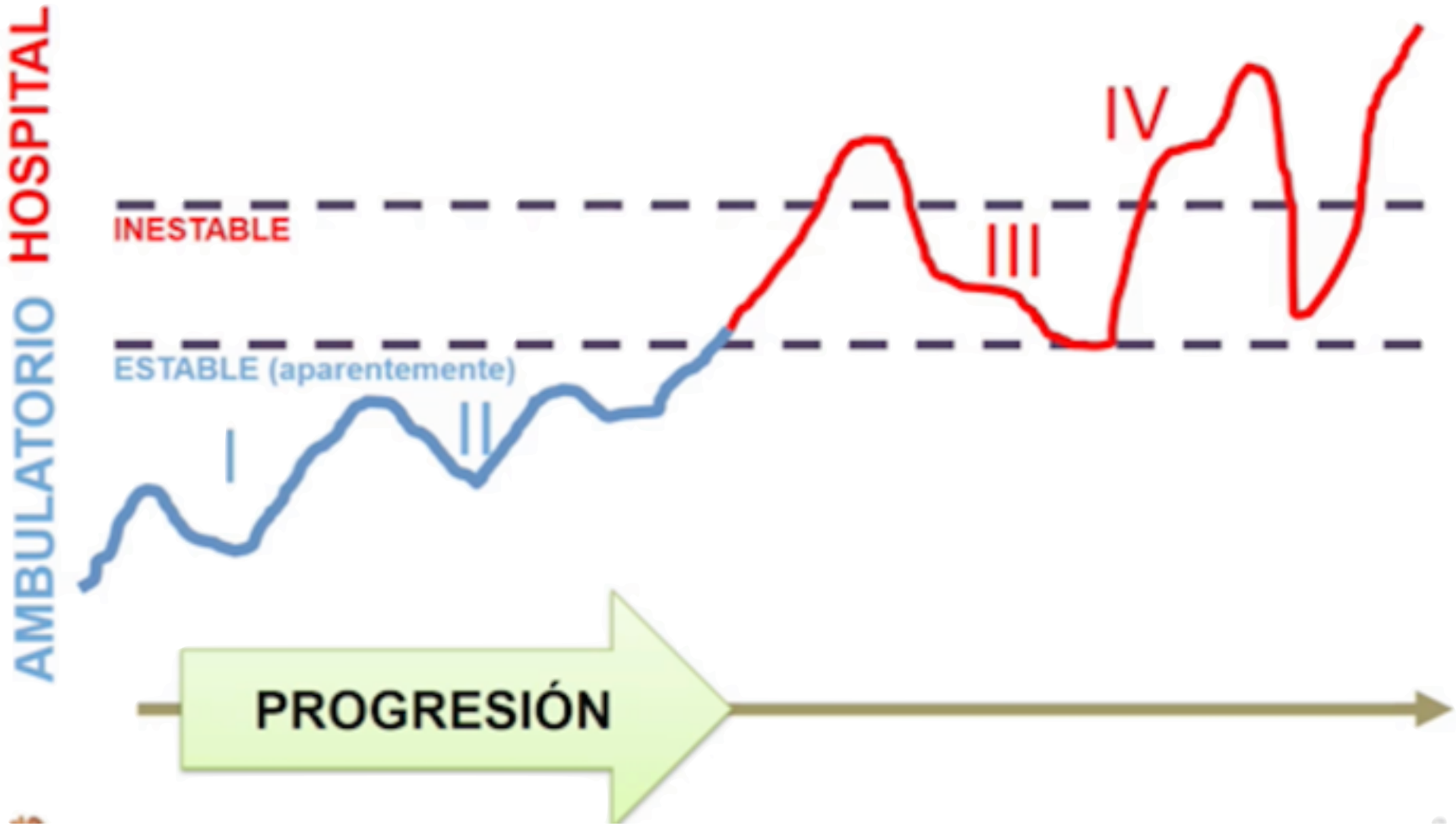
MI PACIENTE ESTABLE



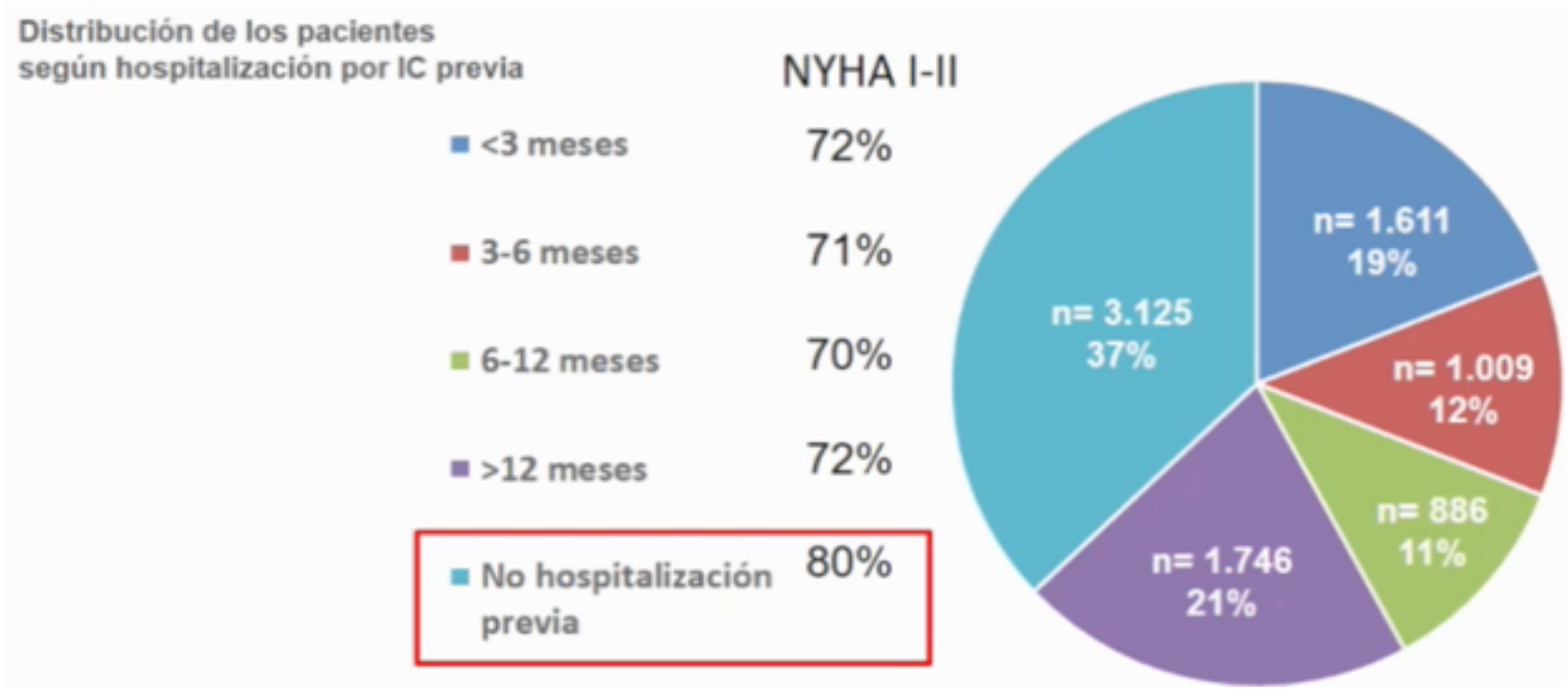
Mamas MA et al. Eur J Heart Fail. 2017; 19(9): 1095-1104.

IC LEVE= “LA GRAN MENTIRA”





IC LEVE= “LA GRAN MENTIRA”



8399p , más de la mitad sin ingreso por IC o hacía más de 1 año

20% evento primario

17% fallece

51% falleció sin evento previo

60% de las muertes = MS

Solomon S. JACC Heart F 2016, 4 (10) 816-822

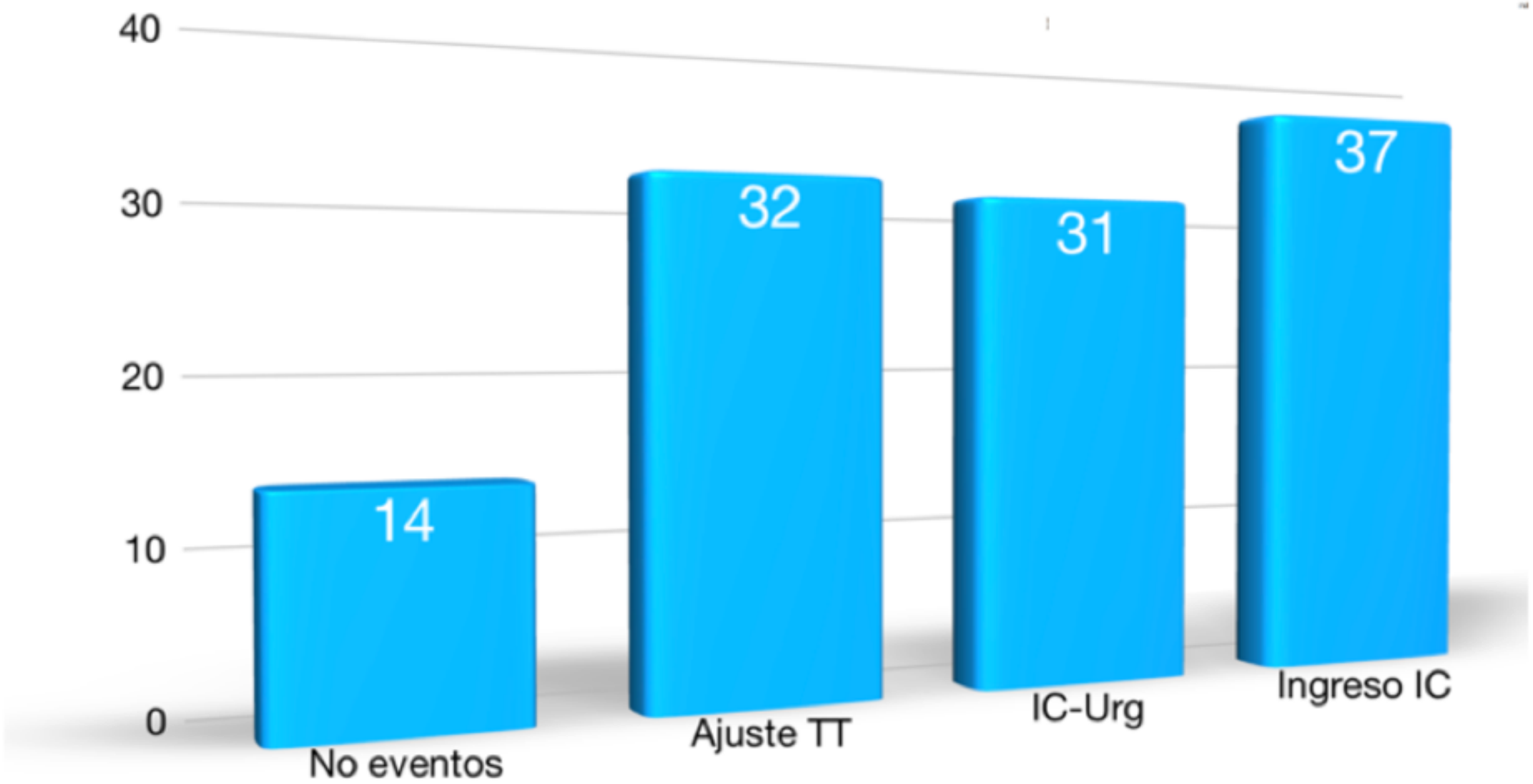
IC LEVE= “LA GRAN MENTIRA”

Heart Failure

Importance of Clinical Worsening of Heart Failure Treated in the Outpatient Setting

Evidence From the Prospective Comparison of ARNI With ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial (PARADIGM-HF)

Naoki Okumura, MD, PhD; Pardeep S. Jhund, MBChB, MSc, PhD; Jianjian Gong, MD; Martin P. Lefkowitz, MD; Adel R. Rizkala, PharmD; Jean L. Rouleau, MD; Victor C. Shi, MD; Karl Swedberg, MD; Michael R. Zile, MD; Scott D. Solomon, MD; Milton Packer, MD; John J.V. McMurray, MD; PARADIGM-HF Investigators and Committees*



Okumura N et al. Circulation. 2016 Jun 7;133(23):2254-62

CLASE II

EXPERT CONSENSUS DECISION PATHWAY

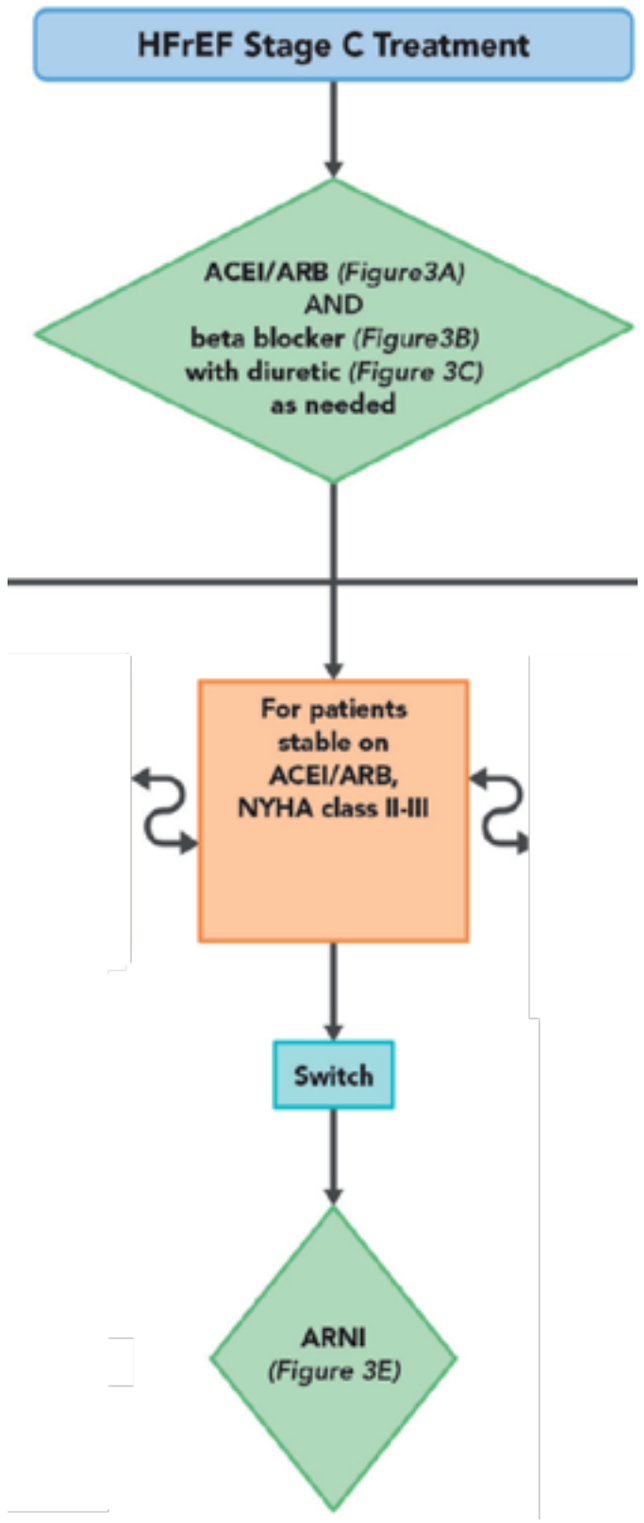
2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction

A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways

Definitions

HFrEF: Clinical diagnosis of HF and LVEF ≤40%.
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.



CLASE II

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- *Class IV:* Unable to perform any physical activity without symptoms of HF, or symptoms of HF at rest.

Symptomatic hypotension was more common with sacubitril/valsartan but was not associated with a worsening of renal function. Angioedema was numerically higher but not statistically significantly different from enalapril in the sacubitril/valsartan group. It should be noted that most patients likely to have angioedema were excluded by the requirement to tolerate enalapril.

The most recent clinical HF guidelines (3) recommend ARNI, ACEI, or ARB to reduce morbidity and mortality in patients with chronic HFrEF and that patients with NYHA class II to III symptoms who can tolerate an ACEI or ARB should transition to an ARNI to further reduce morbidity and mortality (Class I, Level of Evidence: B-R) (1,2). Use of an aldosterone antagonist, although also recommended to improve outcomes, is not considered mandatory prior to changing a patient to ARNI. Guidance for the transition from an ACEI or ARB to ARNI are detailed in Figures 2 and 3 and in Tables 1 to 4.

When making the transition from an ACEI to ARNI, a 36-hour washout period should be strictly observed to avoid angioedema, a delay that is not required when switching from an ARB to ARNI. In a recent study (9), a condensed and conservative approach to initiation of sacubitril/valsartan was explored; the investigators compared titration to a target dose between 3 and 6 weeks. Both approaches were tolerated similarly, but the gradual titration approach maximized attainment

CLASE II

of the target dose of sacubitril/valsartan in patients previously receiving low doses of ACEI/ARB.

Initiation of an ARNI de novo without prior exposure to ACEI or ARB

It is possible that a patient may be identified who meets all criteria for initiation of ARNI, but the patient has not yet been treated with an ACEI or ARB. The committee is aware that clinicians may occasionally consider initiating ARNI in patients who have not previously been treated with ACEI or ARB. To be explicitly clear, no predicate data supports this approach. For well-informed patients who, within a framework of shared-decision making, accept the uncertainty about effectiveness and safety as well as potentially greater out-of-pocket costs, de novo initiation of ARNI with close follow-up and serial assessments (blood pressure, electrolytes, and renal function) might be considered. Any such usage should consider concerns regarding risk of angioedema or hypotension (**Figures 2 and 3, and Tables 1 to 4**).

Ivabradine

Heart rate independently predicts outcomes in HFrEF. Evidence from beta-blocker trials suggests that heart

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ENTRESTO safely and effectively. See full prescribing information for ENTRESTO.

ENTRESTO™ (sacubitril and valsartan) tablets, for oral use
Initial U.S. Approval: 2015

WARNING: FETAL TOXICITY
See full prescribing information for complete boxed warning.
- **When pregnancy is detected, discontinue ENTRESTO as soon as possible. (5.1)**
- **Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus. (5.1)**

----------RECENT MAJOR CHANGES----------

Warnings and Precautions, Angioedema (5.2) 11/2017

----------INDICATIONS AND USAGE----------

ENTRESTO is a combination of sacubitril, a neprilysin inhibitor, and valsartan, an angiotensin II receptor blocker, indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction. (1.1)

ENTRESTO is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other ARB. (1.1)

----------DOSAGE AND ADMINISTRATION----------

- The recommended starting dose of ENTRESTO is 49/51 mg (sacubitril/valsartan) twice-daily. Double the dose of ENTRESTO after 2 to 4 weeks to the target maintenance dose of 97/103 mg (sacubitril/valsartan) twice-daily, as tolerated by the patient. (2.1)
- Reduce the starting dose to 24/26 mg (sacubitril/valsartan) twice-daily for:
  - patients not currently taking an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) or previously taking a low dose of these agents (2.2)
  - patients with severe renal impairment (2.3)
  - patients with moderate hepatic impairment (2.4)

  Double the dose of ENTRESTO every 2 to 4 weeks to the target maintenance dose of 97/103 mg (sacubitril/valsartan) twice-daily, as tolerated by the patient. (2.2, 2.3, 2.4)

----------DOSAGE FORMS AND STRENGTHS----------

- Film-coated tablets (sacubitril/valsartan): 24/26 mg; 49/51 mg; 97/103 mg (3)

----------CONTRAINDICATIONS----------

- Hypersensitivity to any component. (4)
- History of angioedema related to previous ACE inhibitor or ARB therapy. (4)
- Concomitant use with ACE inhibitors. (4, 7.1)
- Concomitant use with aliskiren in patients with diabetes. (4, 7.1)

----------WARNINGS AND PRECAUTIONS----------

- Observe for signs and symptoms of angioedema and hypotension. (5.2, 5.3)
- Monitor renal function and potassium in susceptible patients. (5.4, 5.5)

----------ADVERSE REACTIONS----------

Adverse reactions occurring ≥5% are hypotension, hyperkalemia, cough, dizziness, and renal failure. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Novartis Pharmaceuticals Corporation at 1-888-669-6682 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- Dual blockade of the renin-angiotensin system: Do not use with an ACEi, do not use with aliskiren in patients with diabetes, and avoid use with an ARB. (4, 7.1)
- Potassium-sparing diuretics: May lead to increased serum potassium. (7.2)
- NSAIDs: May lead to increased risk of renal impairment. (7.3)
- Lithium: Increased risk of lithium toxicity. (7.4)

----------USE IN SPECIFIC POPULATIONS----------

- Lactation: Breastfeeding or drug should be discontinued. (8.2)
- Severe Hepatic Impairment: Use not recommended. (2.4, 8.6)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 11/2017

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/207620s008lbl.pdf

TABLE 3 Recommended Starting Dose of Sacubitril/Valsartan

Population	Initial Dose
Moderate- or high-dose ACEI *Equivalent of enalapril ≥10 mg twice daily*	49/51 mg twice daily
Moderate- or high-dose ARB *Equivalent of valsartan ≥80 mg twice daily*	
Low dose ACEI *Equivalent of <10 mg of enalapril twice daily*	24/26 mg twice daily
Low dose ARB *Equivalent of valsartan ≤80 mg twice daily*	
ACEI/ARB naïve*	
Severe renal impairment† (eGFR <30 mL/min/1.73 m²)	
Moderate hepatic impairment (Child-Pugh Class B)	
Elderly (age ≥75 years)	

BENEFICIOS DEL TRATAMIENTO

BCN BIOHF

iCor.cat · IGTP · Germans Trias i Pujol Hospital · Institut Català de la Salut

Variables clínicas

Edad, años*: 62

Sexo *: Hombre / Mujer

Clase funcional de la NYHA *: I-II / III-IV

Na, mmol/L: 137

FGRe, ml/min/1.73m2: 58

Hb, g/dL: 13

FE de VI, %: 30

Duración de la IC en meses: 12

Diabetes mellitus *: Si / No

Nº ingresos por IC en el año previo *: 0

Tratamientos

Diurético de asa, mg/d *

Furosemida: 40

Torasemida: 0

Estatinas *: Si / No

Betabloqueantes *: Si / No

IECA o ARA 2 *: Si / No

ARM *: Si / No

ARNi *: No

TRC *: Si / No

DAI *: Si / No

Biomarcadores

hs-cTnT, ng/L (pg/mL)

ST2, ng/mL

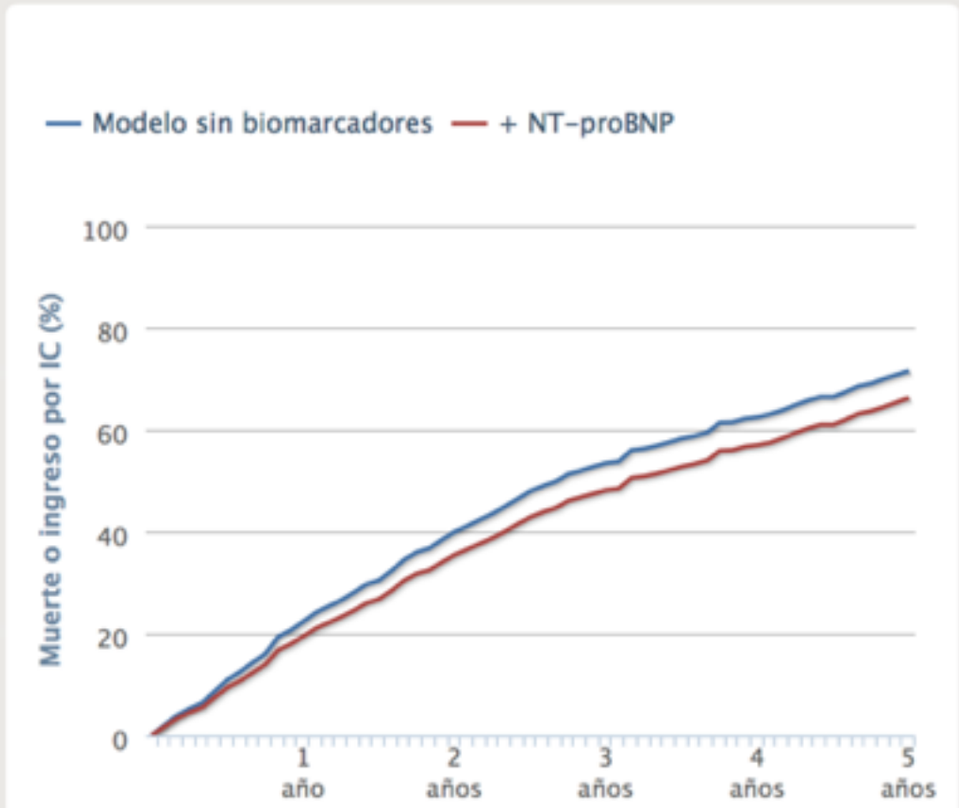
NT-proBNP, ng/L (pg/mL): 589

Cálculo riesgo de muerte

Cálculo riesgo de ingreso por IC

Cálculo riesgo de muerte o ingreso por IC

Muerte o ingreso por IC	Riesgo a 1 año	Riesgo a 2 años	Riesgo a 3 años	Riesgo a 4 años	Riesgo a 5 años
Modelo sin biomarcadores	22.3%	39.9%	53.4%	62.4%	71.5%
+ NT-proBNP	19.4%	35.4%	48.1%	56.9%	66.2%



Expectativa de vida	años
Modelo sin biomarcadores	5.8
+ NT-proBNP	6.3

BENEFICIOS DEL TRATAMIENTO

BCN BIOHF

iCor.cat · IGTP · Germans Trias i Pujol Hospital · Institut Català de la Salut

Variables clínicas

Edad, años*: 62

Sexo *: Hombre / Mujer

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Furosemida: 40

Torasemida: 0

Estatinas *: Si / No

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hs-cTnT, ng/L (pg/mL)

ST2, ng/mL

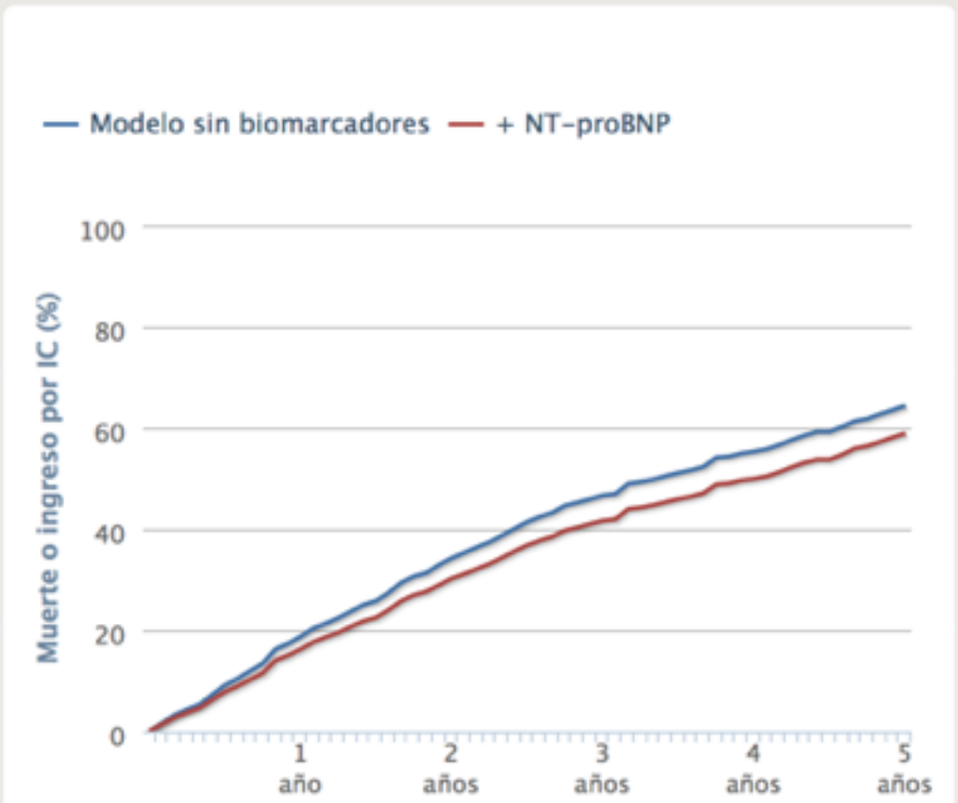
NT-proBNP, ng/L (pg/mL): 589

Cálculo riesgo de muerte

Cálculo riesgo de ingreso por IC

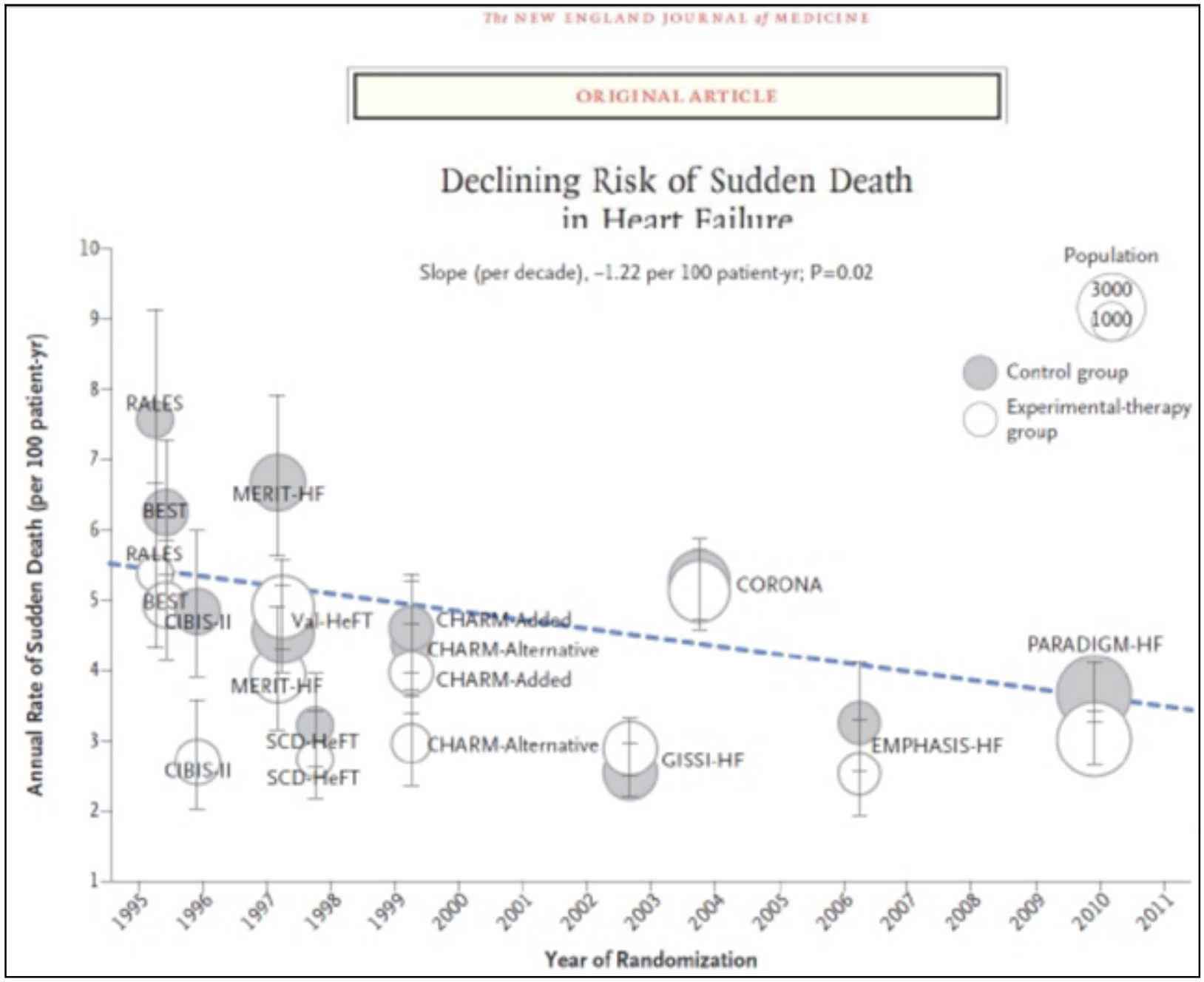
Cálculo riesgo de muerte o ingreso por IC

Muerte o ingreso por IC	Riesgo a 1 año	Riesgo a 2 años	Riesgo a 3 años	Riesgo a 4 años	Riesgo a 5 años
Modelo sin biomarcadores	18.7%	34.2%	46.6%	55.3%	64.4%
+ NT-proBNP	16.2%	30.2%	41.6%	49.9%	58.9%



Expectativa de vida	años
Modelo sin biomarcadores	6.7
+ NT-proBNP	7.3

MUERTE SUBITA



- 40,195 patients HFrEF from 12 clinical trials over 19 years
- Annual rate of SCD declined by 44%
- from 6.5% in the earliesttrial (RALES, 1998) to 3.3% in the most recent (PARADIGM-HF, 2014), P =0.02.

The contemporary cumulative incidence of SCD ~1% by 3 months , <2% by 6 months on ACEI, ARB, BB, MRA , 1.7% on sacubitril and valsartan.

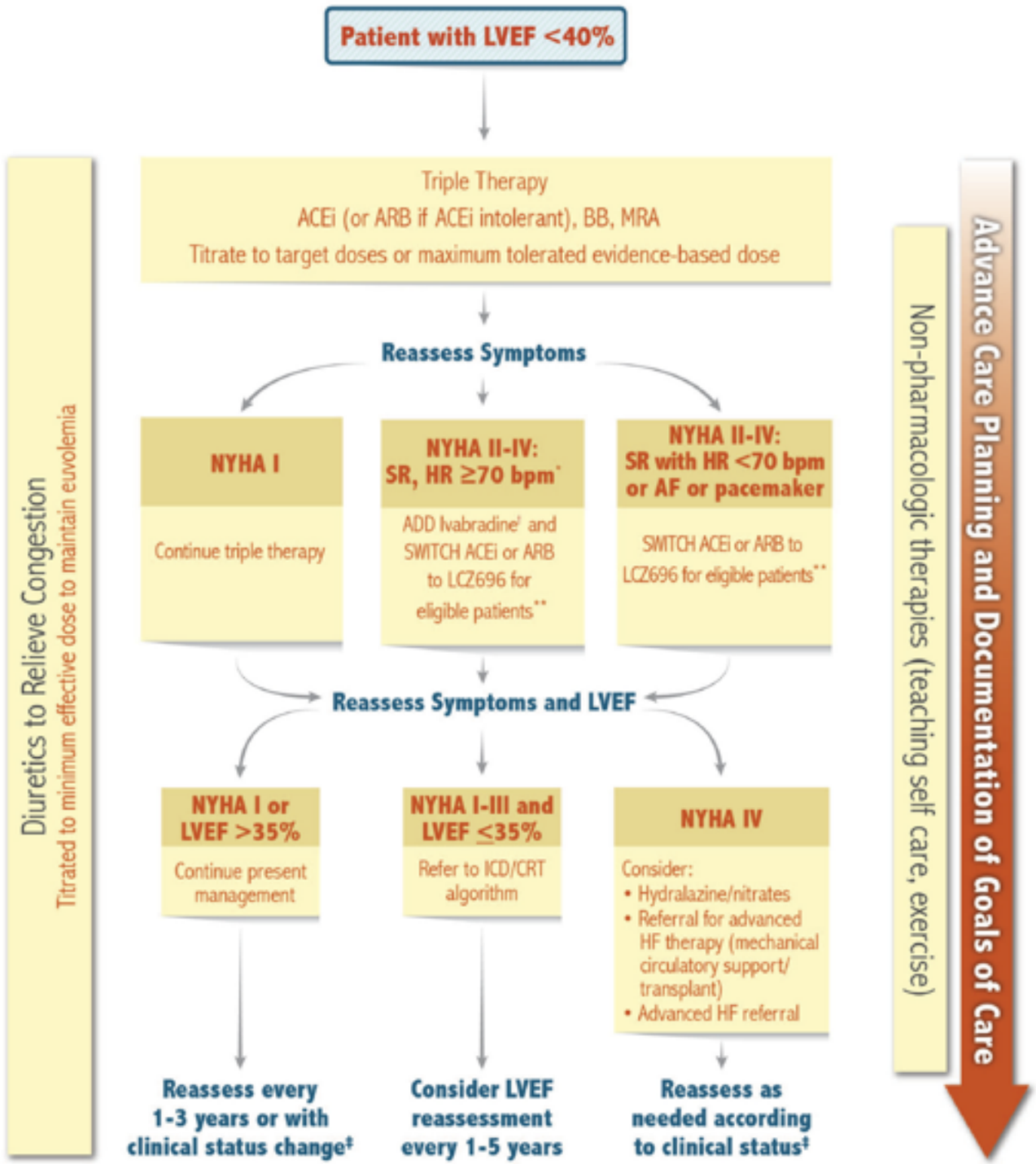
Primary prevention with ICD may be difficult to demonstrate

CLASE II / ESPERO A TITULAR

Titular o no titular

Canadian Cardiovascular Society
Leadership. Knowledge. Community.

Therapeutic Approach to Patients with Heart Failure and Reduced Ejection Fraction



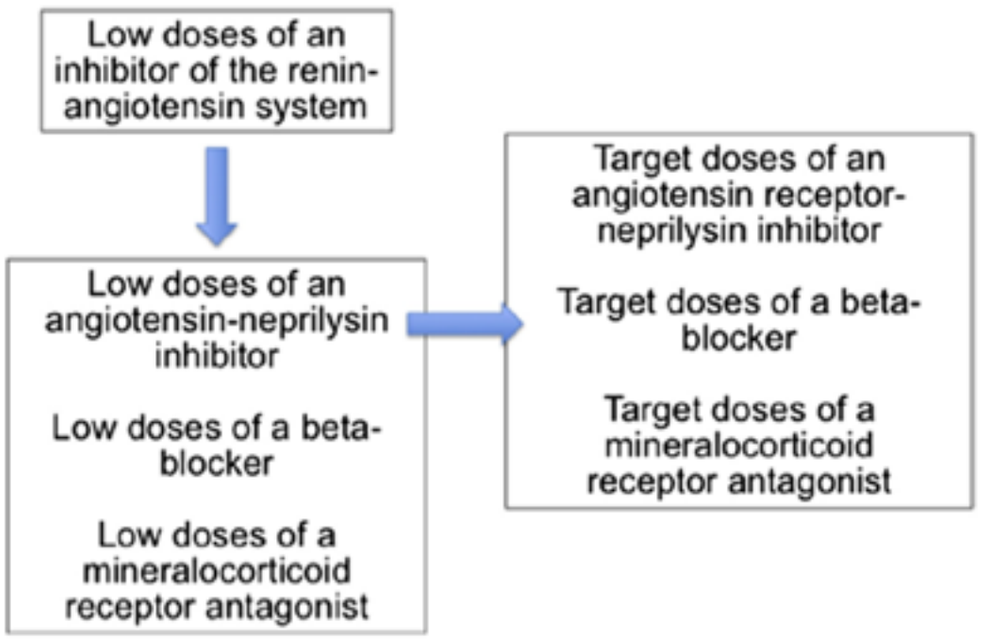
Howlett, Jonathan G. et al. Canadian Journal of Cardiology , Volume 32 , Issue 3 , 296 - 310

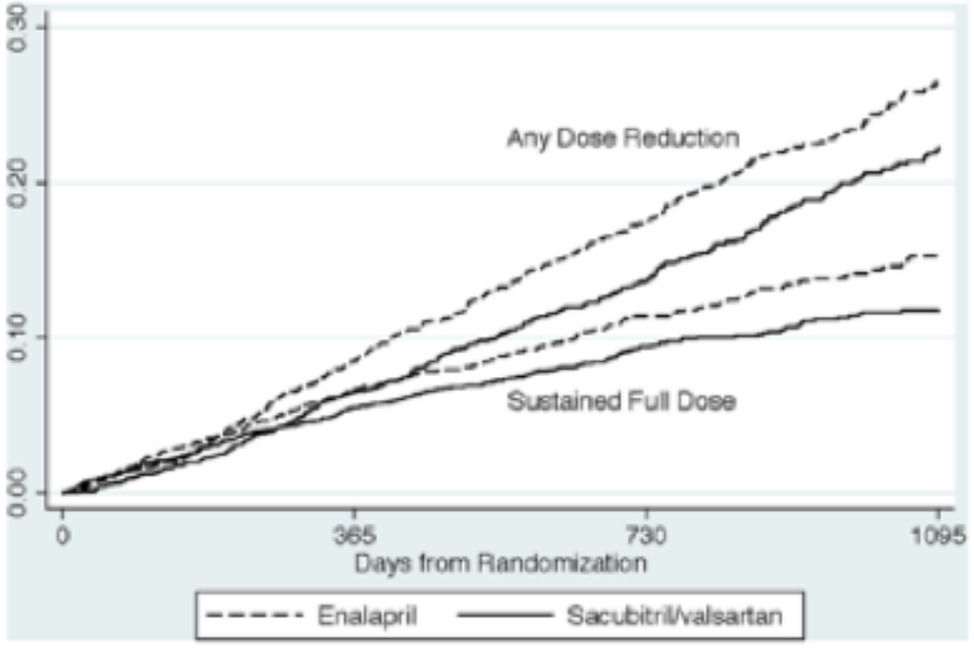
CLASE II / ESPERO A TITULAR

Titular o no titular

antagonists to target doses (34-36). Now that the PARADIGM-HF trial has demonst need to inhibit neprilysin, we should do so early possible and not delay until we have achiev doses of a conventional inhibitor of the renin-angiotensin system. Differences in outcome are apparent within 30 days of initiation of neprilysin inhibition (29). A decision to prescribe target doses of an ACE inhibitor or angiotensin receptor blocker before initiating treatment with a neprilysin inhibitor ignores the fact that the early addition of neprilysin inhibition is accompanied by greater benefits on cardiovascular death (especially sudden death) and fewer discontinuations due to renal insufficiency and hyperkalemia.

FIGURE 4 Approach: Low-Dose ACE Inhibitor Then Angiotensin-Neprilysin Inhibitor Plus Neurohormone Modulators





Parker M. Love of Angiotensin-Converting Enzyme Inhibitors in the Time of Cholera. JACC Heart Fail. VOL. 4, NO. 5, 2016

CLASE II / ESPERO A TITULAR

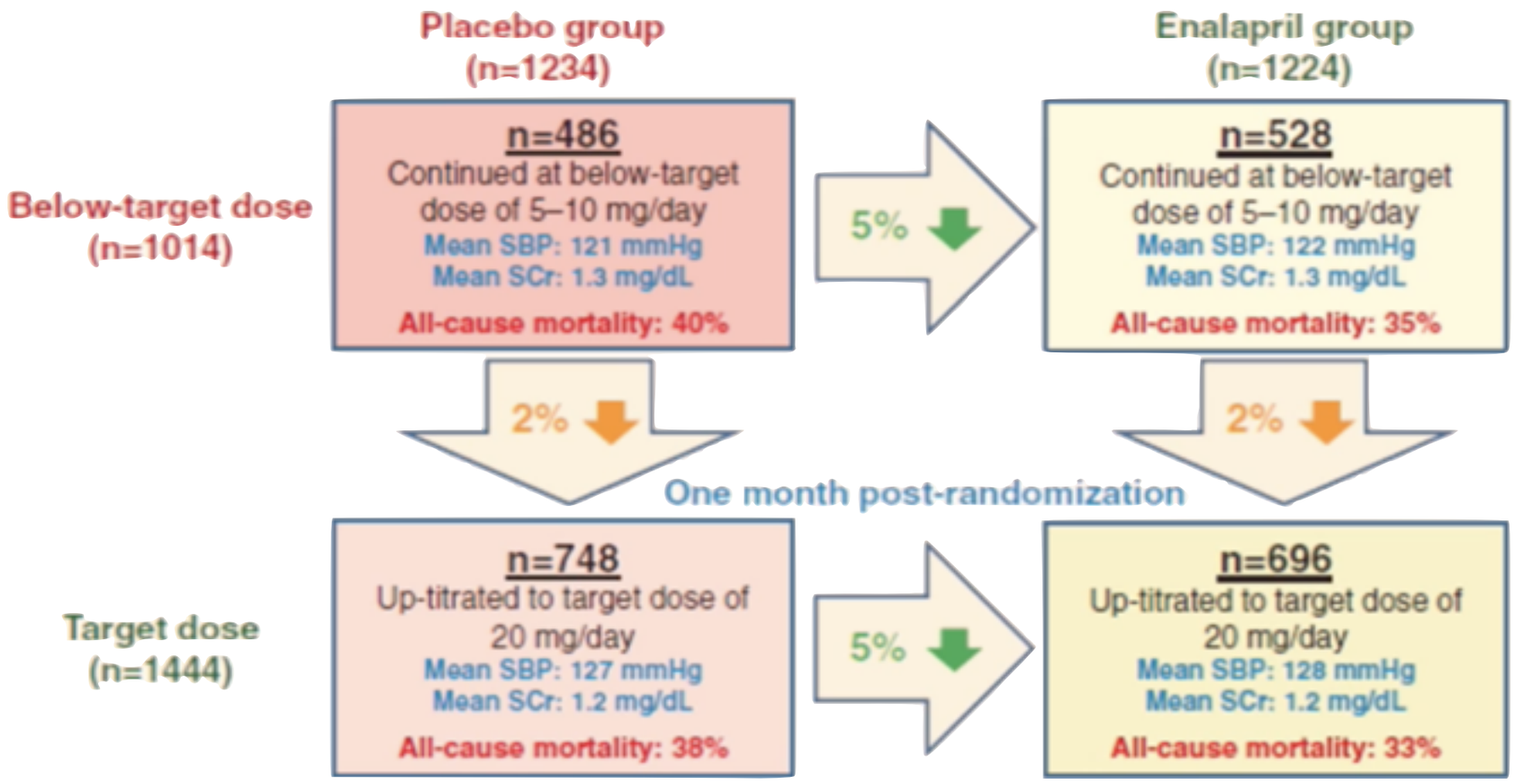
Titular o no titular

European Journal of Heart Failure (2018) 20, 359–369
doi:10.1002/ejhf.937

RESEARCH ARTICLE

Similar clinical benefits from below-target and target dose enalapril in patients with heart failure in the SOLVD Treatment trial

Phillip H. Lam[1,2†], Daniel J. Dooley[1,2†], Gregg C. Fonarow[3], Javed Butler[4], Deepak L. Bhatt[5], Gerasimos S. Filippatos[6], Prakash Deedwania[7], Daniel E. Forman[8], Michel White[9], Ross D. Fletcher[1,10], Cherinne Arundel[1,11], Marc R. Blackman[1,10,11], Chris Adamopoulos[12], Ioannis E. Kanonidis[13], Inmaculada B. Aban[14], Kanan Patel[15], Wilbert S. Aronow[16], Richard M. Allman[17], Stefan D. Anker[18,19], Bertram Pitt[20], and Ali Ahmed[1,11,14*]



Lam PH, et al. Eur J Heart Fail. 2018 Feb;20

CLASE II / ESPERO A TITULAR

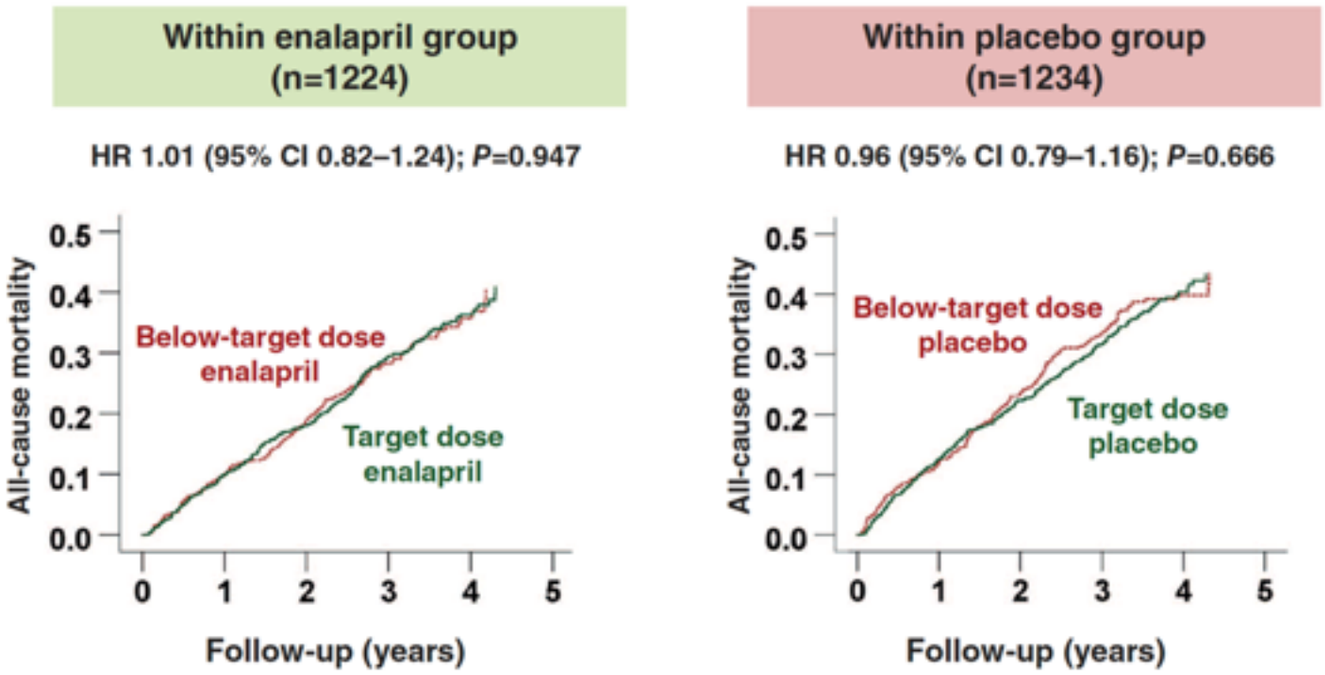
Titular o no titular

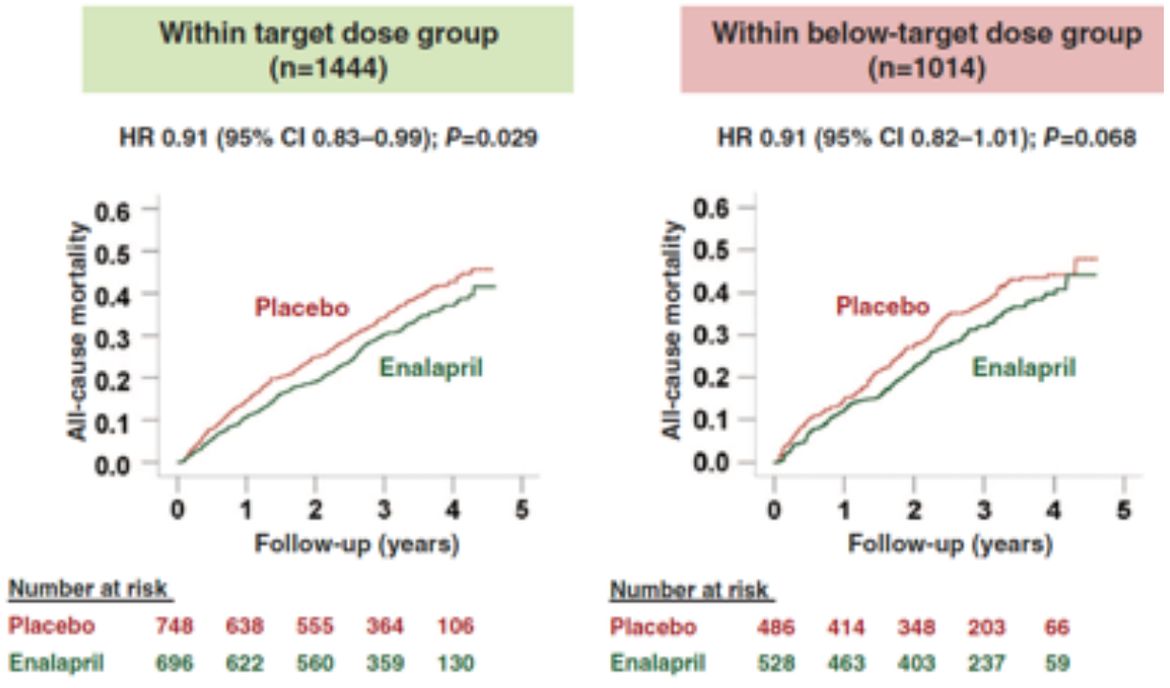
European Journal of Heart Failure (2018) 20, 359–369
doi:10.1002/ejhf.937

RESEARCH ARTICLE

Similar clinical benefits from below-target and target dose enalapril in patients with heart failure in the SOLVD Treatment trial

Phillip H. Lam[1,2†], Daniel J. Dooley[1,2†], Gregg C. Fonarow[3], Javed Butler[4], Deepak L. Bhatt[5], Gerasimos S. Filippatos[6], Prakash Deedwania[7], Daniel E. Forman[8], Michel White[9], Ross D. Fletcher[1,10], Cherinne Arundel[1,11], Marc R. Blackman[1,10,11], Chris Adamopoulos[12], Ioannis E. Kanonidis[13], Inmaculada B. Aban[14], Kanan Patel[15], Wilbert S. Aronow[16], Richard M. Allman[17], Stefan D. Anker[18,19], Bertram Pitt[20], and Ali Ahmed[1,11,14*]





Lam PH, et al. Eur J Heart Fail. 2018 Feb;20

CLASE II / ESPERO AL INGRESO

Esperar al ingreso

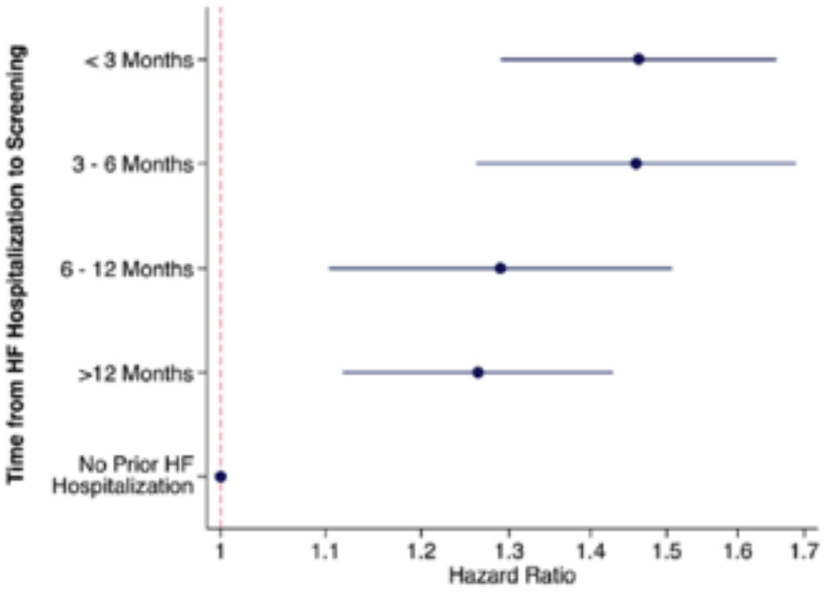
JACC: HEART FAILURE VOL. 4, NO. 10, 2016
ISSN 2213-1779
http://dx.doi.org/10.1016/j.jchf.2016.05.002

Efficacy of Sacubitril/Valsartan Relative to a Prior Decompensation

The PARADIGM-HF Trial

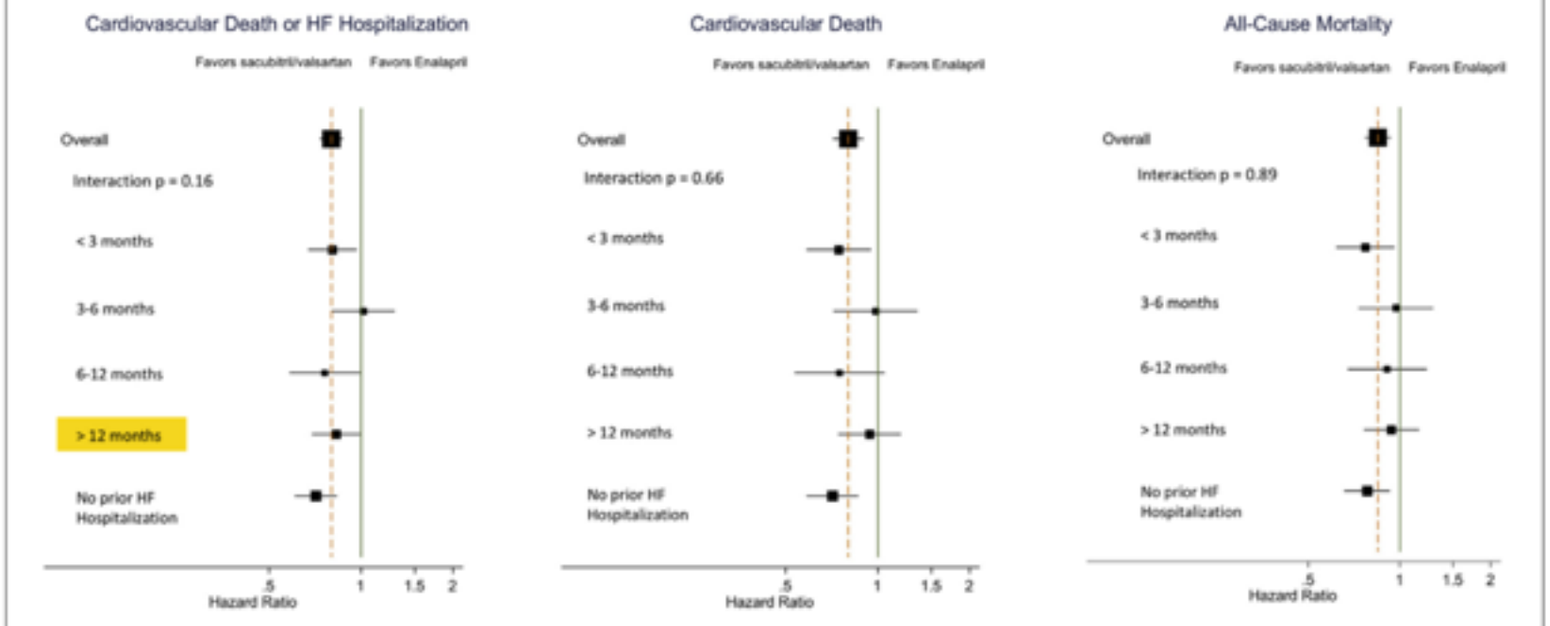
Scott D. Solomon, MD,[a] Brian Claggett, PhD,[a] Milton Packer, MD,[b] Akshay Desai, MD,[a] Michael R. Zile, MD,[c] Karl Swedberg, MD,[d] Jean Rouleau, MD,[e] Victor Shi, MD,[f] Martin Lefkowitz, MD,[f] John J.V. McMurray, MD[g]

FIGURE 1 Hazard Ratio for Primary Endpoint



Hazard ratio for primary endpoint (cardiovascular death or HF hospitalization) based on the presence of and time from a HF hospitalization prior to screening, adjusted for baseline characteristics which significantly differed across groups. HF = heart failure.

FIGURE 2 Treatment Effect of Sacubitril/Valsartan Therapy



Forest plot shows treatment effects of sacubitril/valsartan (hazard ratio with 95% confidence interval) based on the presence of and time from a heart failure hospitalization prior to screening on the outcomes of cardiovascular death or heart failure hospitalization **(left)**, cardiovascular death **(middle)**, and all-cause mortality **(right)**.

Solomon S. JACC Heart F 2016, 4 (10) 816-822

CLASE II / BNP SI O SI

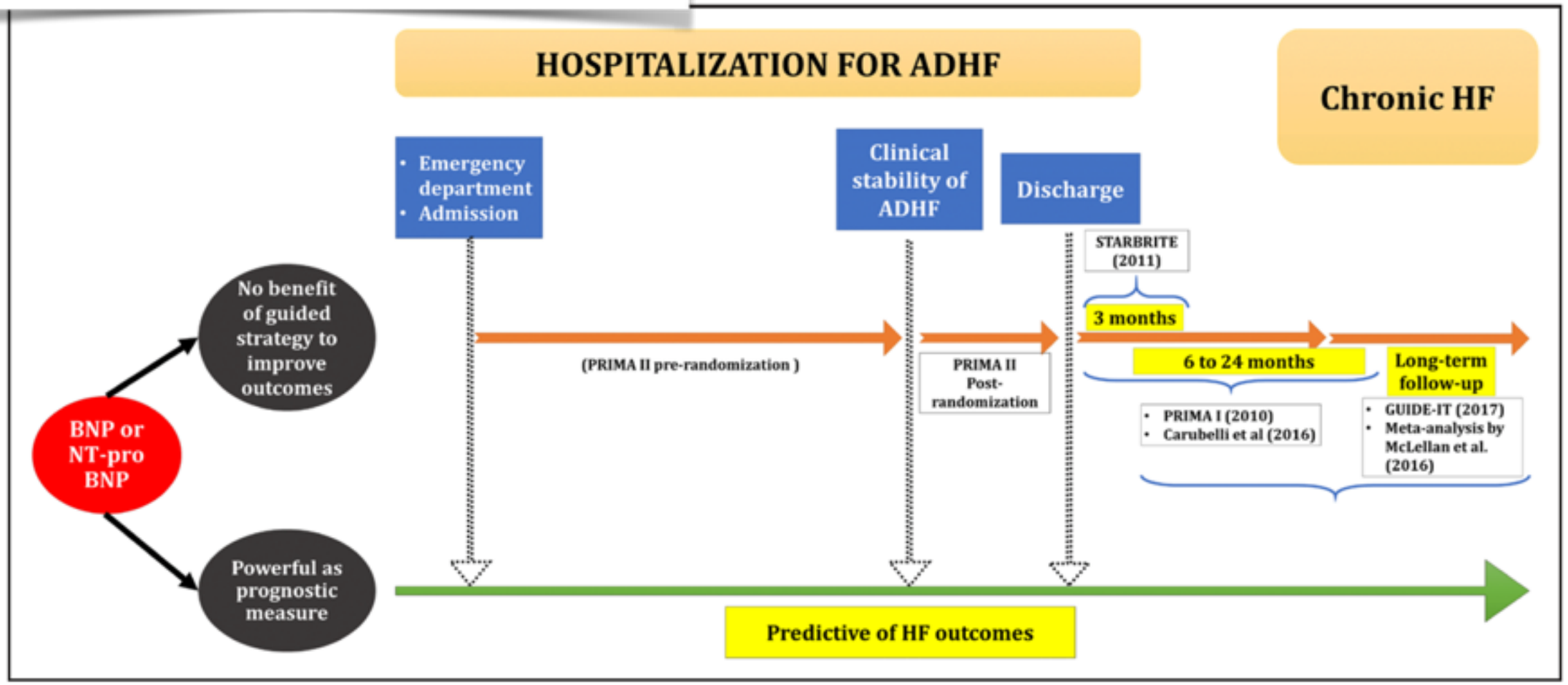
No tengo BNP

Circulation

ORIGINAL RESEARCH ARTICLE

NT-proBNP (N-Terminal pro-B-Type Natriuretic Peptide)-Guided Therapy in Acute Decompensated Heart Failure

PRIMA II Randomized Controlled Trial (Can NT-ProBNP-Guided Therapy During Hospital Admission for Acute Decompensated Heart Failure Reduce Mortality and Readmissions?)



Ni el tratamiento guiado (PRIMA II, 2018) ni la monitorización intrahospitalaria (REDHOT-II, 2009); veremos que pasa con NICE que aleatoriza monitorización con NT-proBNP tras el alta en IC con FE preservada

Stienen S. Circulation. 2018;137:1671–1683

CLASE II / MEJORIA SINTOMÁTICA

MEJORA CF II

Research

JAMA Cardiology | Original Investigation

Effects of Sacubitril/Valsartan on Physical and Social Activity Limitations in Patients With Heart Failure

A Secondary Analysis of the PARADIGM-HF Trial

Alvin Chandra, MD; Eldrin F. Lewis, MD; Brian L. Claggett, PhD; Akshay S. Desai, MD, MPH; Milton Packer, MD; Michael R. Zile, MD; Karl Swedberg, MD, PhD; Jean L. Rouleau, MD; Victor C. Shi, MD; Martin P. Lefkowitz, MD; Tzvetana Katova, MD, PhD; John J. V. McMurray, MD; Scott D. Solomon, MD

Figure 1. Change Score Differences Between Enalapril and Sacubitril/Valsartan at 8-Month Follow-up, Adjusted for Respective Baseline Mean Score

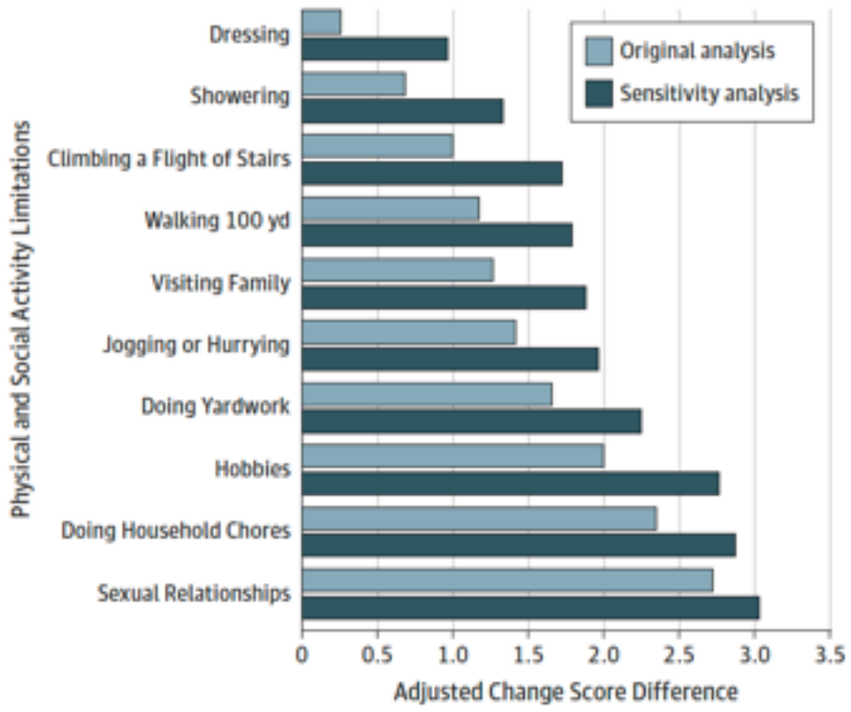


Table 1. Baseline Characteristics Stratified by Quartiles of Mean Combined Scores of All Physical and Social Activities Among Patients With Baseline KCCQ Data[a]

Characteristic	Quartile 1 (n = 1983)	Quartile 2 (n = 1988)	Quartile 3 (n = 1811)	Quartile 4 (n = 1836)	*P* Value for Trend
Scores of combined physical and social activities, mean (SD) [range]	41.5 (12.6) [14.3-57.5]	68.6 (5.8) [57.5-77.5]	84.6 (3.7) [77.5-90]	96.5 (3.0) [90-100]	NA
Baseline age, mean (SD), y	65.4 (11.2)	65.0 (11.0)	63.7 (10.9)	62.5 (11.3)	<.001
Female sex	594 (30.0)	408 (20.5)	350 (19.3)	279 (15.2)	<.001
Race/ethnicity					
White	1594 (80.4)	1550 (78.0)	1227 (67.8)	1097 (59.7)	<.001
Black	106 (5.3)	91 (4.6)	92 (5.1)	112 (6.1)	
Asian	139 (7.0)	182 (9.2)	286 (15.8)	384 (20.9)	
Other	144 (7.3)	165 (8.3)	206 (11.4)	243 (13.2)	
Region					
North America	175 (8.8)	163 (8.2)	122 (6.7)	140 (7.6)	.01
Latin America	225 (11.3)	258 (13.0)	330 (18.2)	431 (23.5)	
Western Europe and other[b]	527 (26.6)	507 (25.5)	500 (27.6)	479 (26.1)	
Central Europe	926 (46.7)	883 (44.4)	579 (32.0)	412 (22.4)	
Asia Pacific	130 (6.6)	177 (8.9)	280 (15.5)	374 (20.4)	
Baseline medical history					
Hypertension	1543 (77.8)	1484 (74.6)	1265 (69.9)	1193 (65.0)	<.001
Diabetes	802 (40.4)	681 (34.3)	621 (34.3)	543 (29.6)	<.001
Atrial fibrillation	918 (46.3)	805 (40.5)	641 (35.4)	547 (29.8)	<.001
Hospitalization for heart failure	1351 (68.1)	1292 (65.0)	1117 (61.7)	1051 (57.2)	<.001
Myocardial infarction	932 (47.0)	945 (47.5)	784 (43.3)	709 (38.6)	<.001
Stroke	218 (11.0)	200 (10.1)	132 (7.3)	113 (6.2)	<.001
BMI, mean (SD)	29.5 (6.1)	28.7 (5.6)	28.1 (5.2)	27.4 (4.9)	<.001
NYHA functional class III or IV	958 (48.3)	561 (28.2)	304 (16.8)	151 (8.2)	<.001
KCCQ overall summary score, mean (SD)	47.6 (13.2)	69.7 (8.6)	83.1 (6.7)	93.5 (5.4)	<.001
Left ventricle ejection fraction, mean (SD), %	30.0 (6.1)	29.8 (6.3)	29.6 (6.3)	29.1 (6.1)	<.001
BNP, median (IQR), pg/mL	268 (158-499)	250 (158-462)	242 (152-428)	238 (144-434)	<.001
NT-proBNP, median (IQR), pg/mL	1813 (945-3676)	1641 (930-3364)	1505 (856-2923)	1409 (827-2862)	<.001
Randomized to sacubitril/valsartan	962 (48.5)	958 (48.2)	900 (49.7)	976 (53.2)	.003

Alvin Chandra A et al.*AMA Cardiol.* Published online April 04, 2018

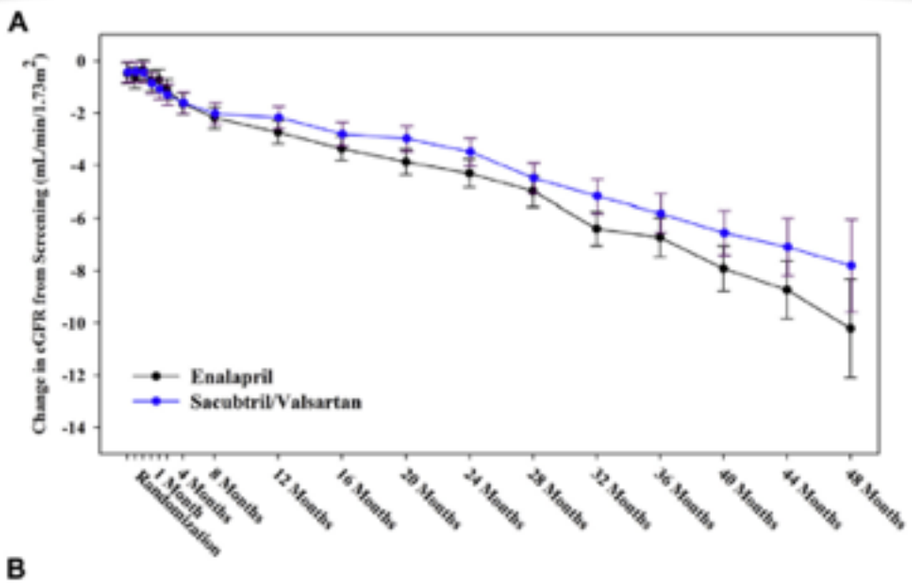
CLASE II / NEFROPROTECCION

CARDIORENAL

JACC: HEART FAILURE VOL. ■, NO. ■, 2018

Renal Effects and Associated Outcomes During Angiotensin-Neprilysin Inhibition in Heart Failure

Kevin Damman, MD, PhD,[a] Mauro Gori, MD,[b,c] Brian Claggett, PhD,[b] Pardeep S. Jhund, MB, PhD,[d] Michele Senni, MD,[c] Martin P. Lefkowitz, MD,[e] Margaret F. Prescott, PhD,[e] Victor C. Shi, MD,[e] Jean L. Rouleau, MD,[f] Karl Swedberg, MD, PhD,[g,h] Michael R. Zile, MD,[i] Milton Packer, MD,[j] Akshay S. Desai, MD, MPH,[b] Scott D. Solomon, MD,[b] John J.V. McMurray, MD[d]



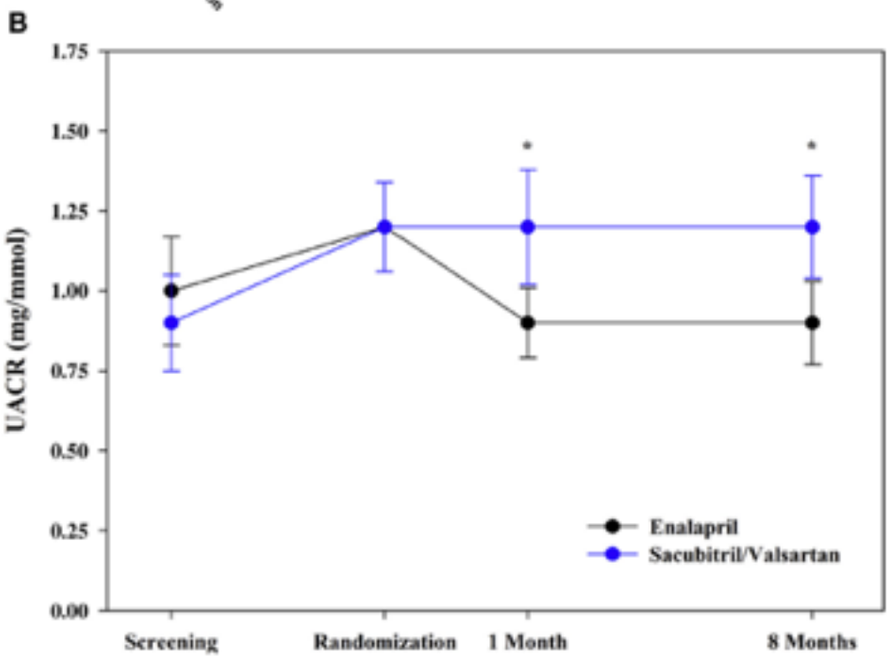


TABLE 1 Baseline Characteristics According to CKD and Albuminuria Status at Screening

	No CKD (eGFR ≥60 ml/min/1.73 m²)	CKD (eGFR <60 ml/min/1.73 m²)	p Value	No Albuminuria (UACR <3.5 mg/mmol)	Albuminuria* (UACR ≥3.5 mg/mmol)	p Value
n (%)	5,654 (67)	2,745 (33)		1,431 (76)	441 (24)	
Age (yrs)	61 ± 11	70 ± 9	<0.001	67 ± 10	68 ± 10	0.040
Males (%)	79.4	75.7	<0.001	80.1	83.9	0.074
Ethnicity (%)			<0.001			0.099
White	62.6	73.1		95.5	93.4	
Black	6.2	2.8		2.8	4.3	
Asian	20.0	13.7		0.1	0.7	
Other	11.2	10.4		1.6	1.6	
SBP (mm Hg)	128 ± 17	129 ± 17	0.027	122 ± 15	127 ± 16	<0.001
DBP (mm Hg)	78 ± 10	76 ± 11	<0.001	73 ± 10	75 ± 11	0.008
Heart rate (beats/min)	73 ± 12	71 ± 12	<0.001	71 ± 12	73 ± 12	0.010
Weight (kg)	81 ± 20	80 ± 18	0.12	87 ± 18	90 ± 20	0.006
Creatinine (mg/dl)†	0.97 (0.85-1.09)	1.37 (1.26-1.54)	<0.001	1.07 (0.93-1.28)	1.14 (0.95-1.41)	<0.001
eGFR (ml/min/1.73 m²)	81 ± 14	49 ± 8	<0.001	68 ± 18	65 ± 19	0.007
UACR (mg/mmol)	1.0 (0.5-3.2)	1.6 (0.5-5.1)	<0.001	0.8 (0.35-2.0)	7.55 (2.55-21.8)	<0.001
Ischemic etiology (%)	57	66	<0.001	64	66	0.28
LVEF (%)	29 ± 6	30 ± 6	0.077	30 ± 6	30 ± 6	0.73
BNP (pmol/l)‡	58 (33-108)	80 (45-154)	<0.001	60 (35-109)	97 (49-177)	<0.001
NT-proBNP (pmol/l)§	90 (53-163)	143 (82-256)	<0.001	99 (58-177)	146 (78-271)	<0.001
NYHA functional class I/II/III/IV	4.9/72.0/22.4/0.7	4.1/67.7/27.5/0.7	<0.001	3/73/23/1	1/71/27/1	0.056
KCCQ	78 (61-90)	74 (57-87)	<0.001	76 (61-89)	75 (54-87)	0.026
Medical history (%)						
Hypertension	67	78	<0.001	75	86	<0.001
Diabetes	32	39	<0.001	34	55	<0.001
Atrial fibrillation	33	44	<0.001	46	55	0.002
Prior HF hospitalization	63	63	0.97	59	63	0.097
Myocardial Infarction	40	50	<0.001	49	49	0.81
Stroke	7	11	<0.001	10	12	0.19

Damman K et al *JACC HF 2018; 65*

CLASE II / NEFROPROTECCION

CARDIORENAL

Articles

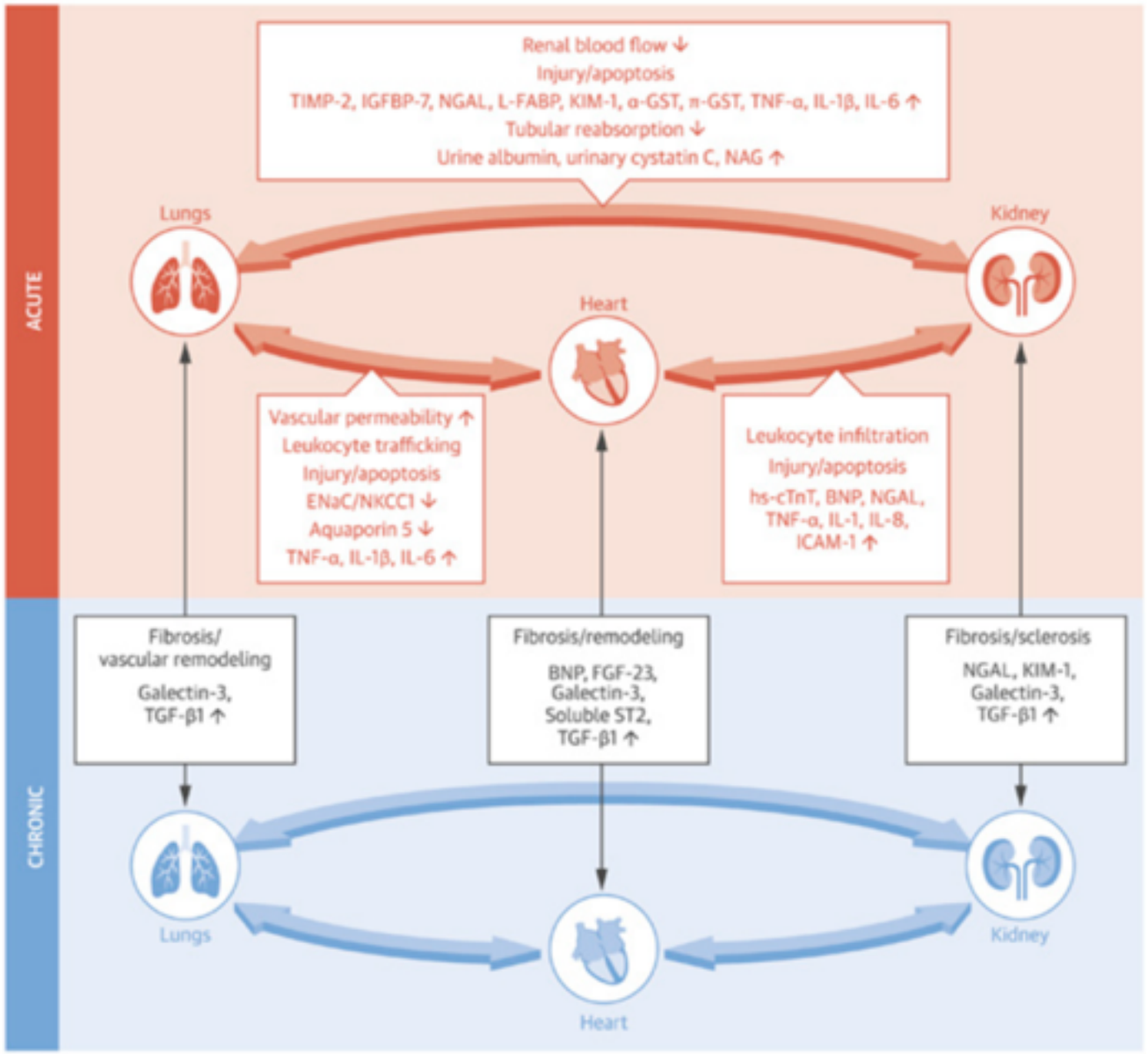
Effect of neprilysin inhibition on renal function in patients with type 2 diabetes and chronic heart failure who are receiving target doses of inhibitors of the renin-angiotensin system: a secondary analysis of the PARADIGM-HF trial

Milton Packer, Brian Claggett, Martin P Lefkowitz, John J V McMurray, Jean L Rouleau, Scott D Solomon, Michael R Zile

	Patients without diabetes		Patients with diabetes		p value*
	Enalapril (n=2335)	Sacubitril/valsartan (n=2280)	Enalapril (n=1877)	Sacubitril/valsartan (n=1907)	
Age (years)	63·8 (11·9)	63·2 (12·1)	63·8 (10·4)	64·4 (10·7)	0·009
Sex					
Female	537 (23%)	486 (21%)	416 (22%)	393 (21%)	0·26
Male	1798 (77%)	1794 (79%)	1461 (78%)	1514 (79%)	–
BMI (kg/m²)	27·4 (5·3)	27·3 (5·1)	29·1 (5·7)	29·1 (5·8)	<0·0001
NYHA functional class					
1	121 (5%)	111 (5%)	88 (5%)	69 (4%)	<0·0001
2	1631 (70%)	1682 (74%)	1290 (69%)	1316 (69%)	–
3	559 (24%)	468 (21%)	490 (26%)	501 (26%)	–
4	18 (1%)	14 (1%)	9 (<1%)	19 (1%)	–
Data missing	6 (<1%)	5 (<1%)	0	2 (<1%)	–
Previous hospital admission for heart failure	1432 (61%)	1363 (60%)	1235 (66%)	1244 (65%)	<0·0001
Systolic blood pressure (mm Hg)	120 (15)	121 (15)	122 (16)	123 (15)	<0·0001
Heart rate (bpm)	71 (12)	71 (12)	74 (12)	73 (12)	<0·0001
Ischaemic cardiomyopathy	1318 (56%)	1263 (55%)	1212 (65%)	1243 (65%)	<0·0001
Left ventricular ejection fraction (%)	29·6 (6·3)	29·5 (6·1)	29·2 (6·3)	29·7 (6·2)	0·13
NTproBNP (pg/mL)	1651 (918-3248)	1592 (874-3092)	1546 (838-3331)	1671 (908-3308)	0·21
BNP (pg/mL)	248 (154-464)	249 (152-468)	254 (153-465)	260 (157-478)	0·43
Serum creatinine (mg/dL)	1·11 (0·29)	1·11 (0·29)	1·13 (0·31)	1·14 (0·30)	<0·0001
History of hypertension	1523 (65%)	1490 (65%)	1448 (77%)	1479 (78%)	<0·0001
History of myocardial infarction	935 (40%)	915 (40%)	881 (47%)	903 (47%)	<0·0001
History of atrial fibrillation	859 (37%)	823 (36%)	715 (38%)	694 (36%)	0·58
Treatments at randomisation					
β blocker	2173 (93%)	2131 (93%)	1739 (93%)	1768 (93%)	0·71
Digoxin	685 (29%)	661 (29%)	631 (34%)	562 (29%)	0·004
Mineralocorticoid receptor antagonist	1334 (57%)	1239 (54%)	1066 (57%)	1032 (54%)	0·09

Data are mean (SD), number (%), or median (IQR). Some percentages do not add up to 100 because of rounding. NYHA=New York Heart Association. NTproBNP=N-terminal pro-BNP. BNP=B-type natriuretic peptide. *For differences between patients with and those without diabetes.

Table 1: **Demographics and baseline characteristics**

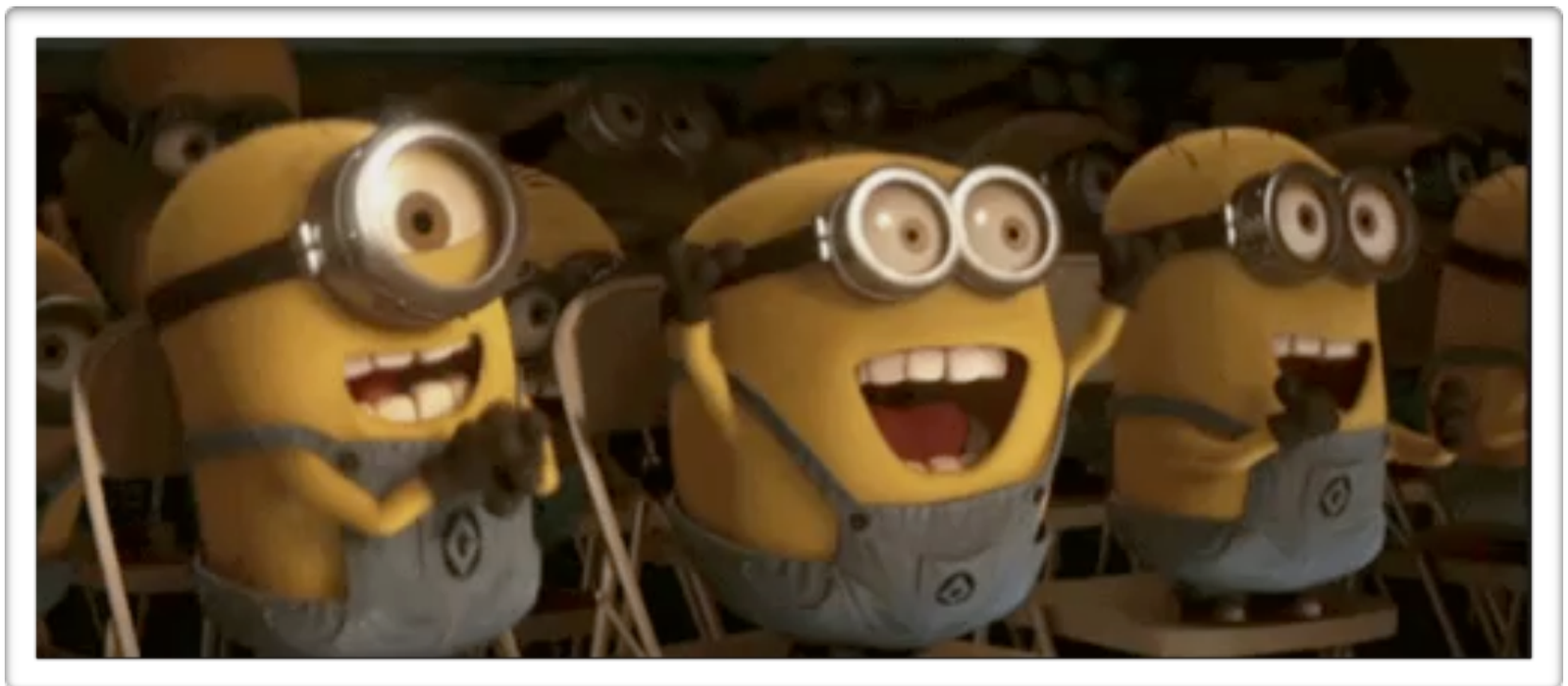


Husain-Syed F et al. *JACC 2015; 65*

NUESTROS PROBLEMAS

1. No veo esos pacientes. Los tienen todos Raquel y Alberto
2. Mi paciente en clase funcional II = paciente estable = no cambio nada
3. Debería pautar ARNI; pero implica exceso de seguimiento y trabajo

EL SISTEMA NO ME DEJA



Quien quiere hacer algo encuentra un medio; quien no quiere hacer nada, encuentra una excusa.

LA IMPORTANCIA DE AP

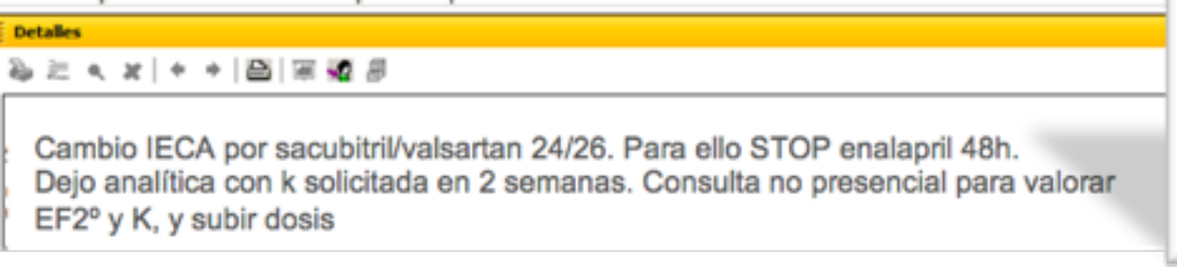
TAS>100

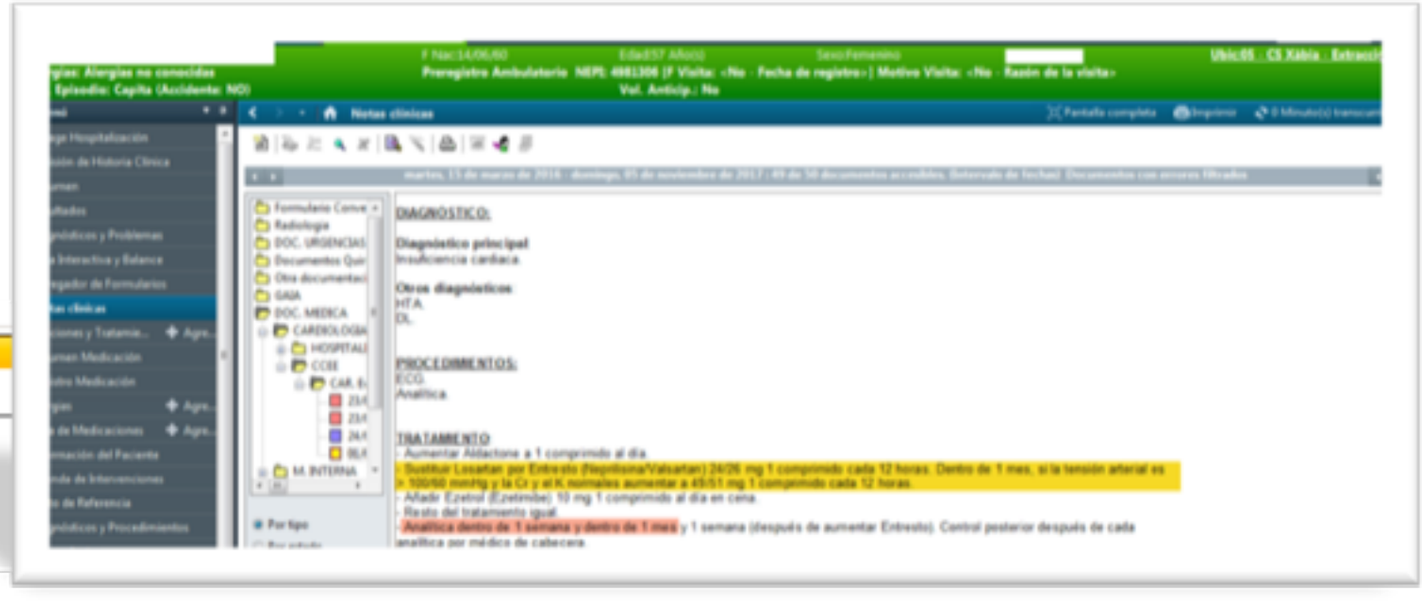
K < 5.4mmol/l

FG>30ml/min/1.73m2

No uso concomitante de IECA

Lunes 16	Martes 17	Mierc 18	Jueves 19	Viernes 20	Sábado 21	Domingo 22
			CAR	AP		
			ARA II	ARNI		
			IECA	→		ARNI





LA IMPORTANCIA DE AP

GENERALITAT VALENCIANA
CONSELLERIA DE SANITAT UNIVERSAL I SALUT PÚBLICA
Direcció General de Farmàcia i Productes Sanitaris

GENERALITAT VALENCIANA
CONSELLERIA DE SANITAT
Registre General
Data 24 FEB. 2017
EIXIDA 9313

NOTA INFORMATIVA DE 20 DE FEBRERO DE 2017 DE LA DIRECCIÓN GENERAL DE FARMACIA Y PRODUCTOS SANITARIOS SOBRE LOS CRITERIOS Y PROCEDIMIENTOS DE UTILIZACIÓN DE SACUBITRILO/VALSARTAN (ENTRESTO®, NEPARVIS®) EN EL ÁMBITO DEL SISTEMA PÚBLICO DE SALUD EN LA COMUNITAT VALENCIANA

CAMBIO DE MENTALIDAD

Manejo individual → **Manejo multidisciplinario**

C.- PROCEDIMIENTO DE PRESCRIPCIÓN EN INICIO Y CONTINUACIÓN DE TRATAMIENTO CON SACUBITRILO/VALSARTAN Y SEGUIMIENTO DEL PACIENTE

1.- Inicio de tratamiento:

Se recomienda que la indicación del inicio del tratamiento s especialistas expertos y expertas en insuficiencia cardiaca, adscritos/as a unidades de insuficiencia cardiaca de los centros de l la Conselleria de Sanidad Universal y Salud Pública.

La prescripción se realizará en el sistema de información corpora el módulo de prescripción asistida MPRE-GAIA. Una vez incorporad información, el facultativo o la facultativa responsable deberá formulario que refleja los criterios clínicos establecidos en este doc Cabe informar que se está procediendo a la informatización de los a en la presente nota.

2.- Seguimiento:

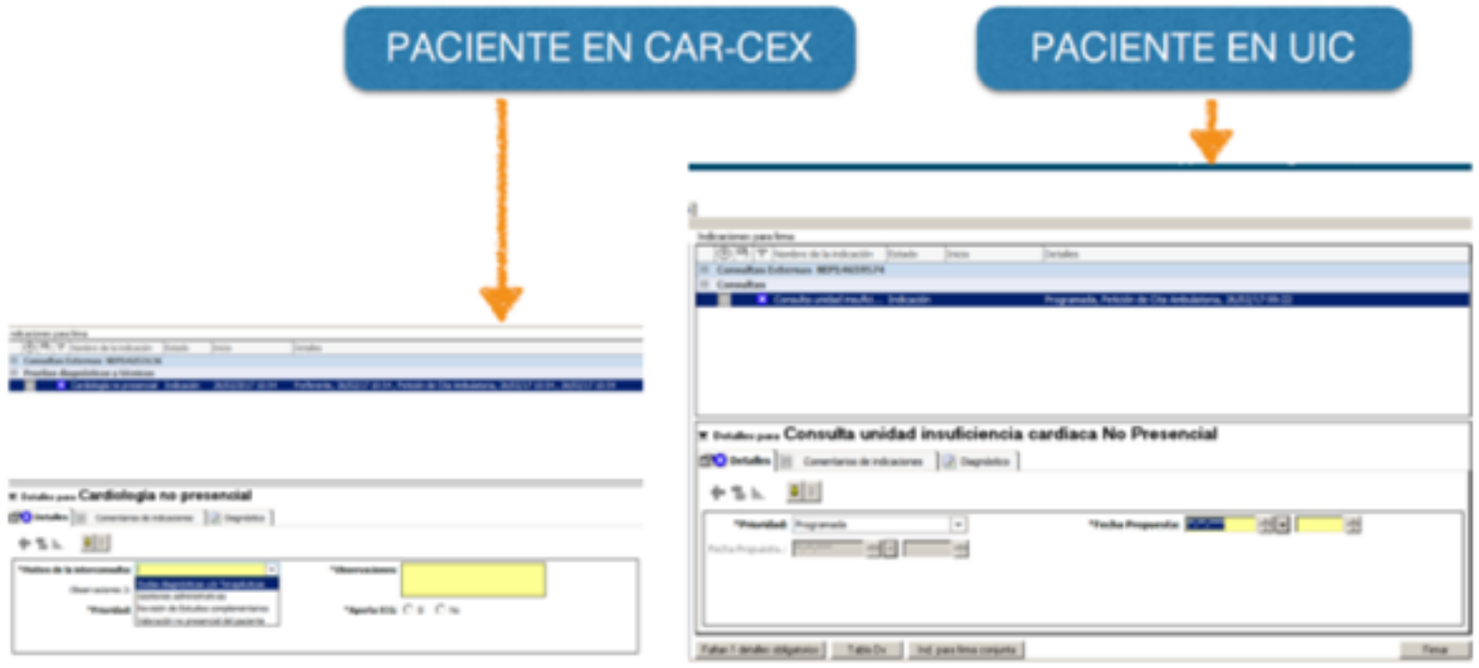
Se recomienda el seguimiento estrecho y especializado una vez iniciado el tratamiento, durante la fase de titulación de dosis y hasta que conseguir la estabilidad clínica y posológica.

De acuerdo con los procedimientos y protocolos de seguimiento establecidos en cada departamento, las continuaciones de tratamientos establecidos podrán ser realizadas por facultativos y facultativas especialistas con experiencia en el manejo de la insuficiencia cardiaca, incluyendo especialistas en medicina familiar y comunitaria.

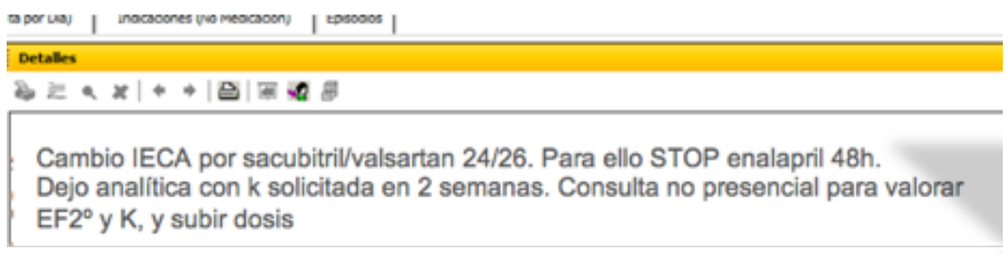
En las continuaciones de tratamiento, tanto si se modifica la dosis como si no varía, se debe comprobar:

LA IMPORTANCIA DE AP

- Dudas remisión
- Titulación fármacos
- Descompensaciones leves



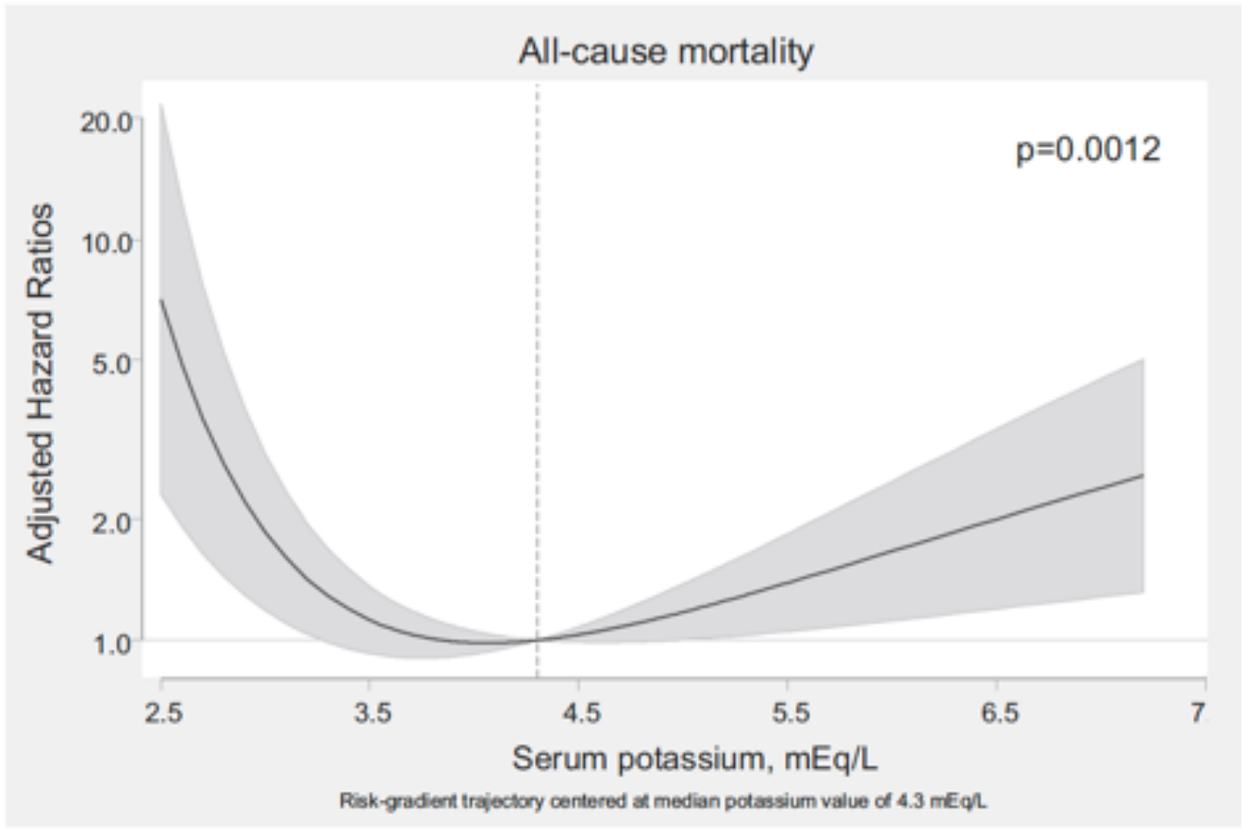
LA IMPORTANCIA DE AP



Circulation

ORIGINAL RESEARCH ARTICLE

Long-Term Potassium Monitoring and Dynamics in Heart Failure and Risk of Mortality



Nuñez J et al. Circulation. 2018;137:1320–1330

LA IMPORTANCIA DE AP

ORIGINAL ARTICLE

Incidence, Predictors, and Outcomes Associated With Hypotensive Episodes Among Heart Failure Patients Receiving Sacubitril/Valsartan or Enalapril

The PARADIGM-HF Trial (Prospective Comparison of Angiotensin Receptor Neprilysin Inhibitor With Angiotensin-Converting Enzyme Inhibitor to Determine Impact on Global Mortality and Morbidity in Heart Failure)

Orly Vardeny, Brian Claggett, Jessica Kachadourian, Scott M. Pearson, Akshay S. Desai, Milton Packer, Jean Rouleau, Michael R. Zile, Karl Swedberg, Martin Lefkowitz, Victor Shi, John J.V. McMurray, Scott D. Solomon

DOI https://doi.org/10.1161/CIRCHEARTFAILURE.117.004745
Circulation: Heart Failure. 2018;11:e004745
Originally published April 11, 2018

Conclusions: Hypotension was more common with sacubitril/valsartan relative to enalapril in PARADIGM-HF but did not differentially affect permanent discontinuations. Patients with hypotension during run-in derived similar benefit from sacubitril/valsartan compared with enalapril as those who did not experience hypotension.

Vardeny O et al. Circ HF. 2018;11:321–327

European Journal of Heart Failure (2018) **20**, 491–500
doi:10.1002/ejhf.1054

RESEARCH ARTICLE

Impact of systolic blood pressure on the safety and tolerability of initiating and up-titrating sacubitril/valsartan in patients with heart failure and reduced ejection fraction: insights from the TITRATION study

Michele Senni[1]*, John J.V. McMurray[2], Rolf Wachter[3], Hugh F. McIntyre[4], Inder S. Anand[5], Vincenzo Duino[1], Arnab Sarkar[6], Victor Shi[7], and Alan Charney[7]

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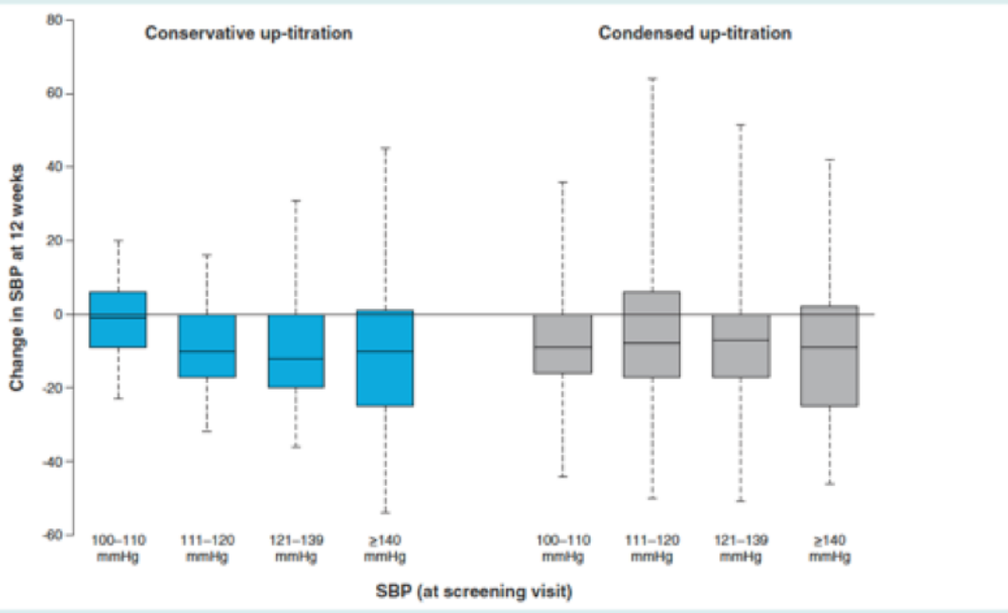
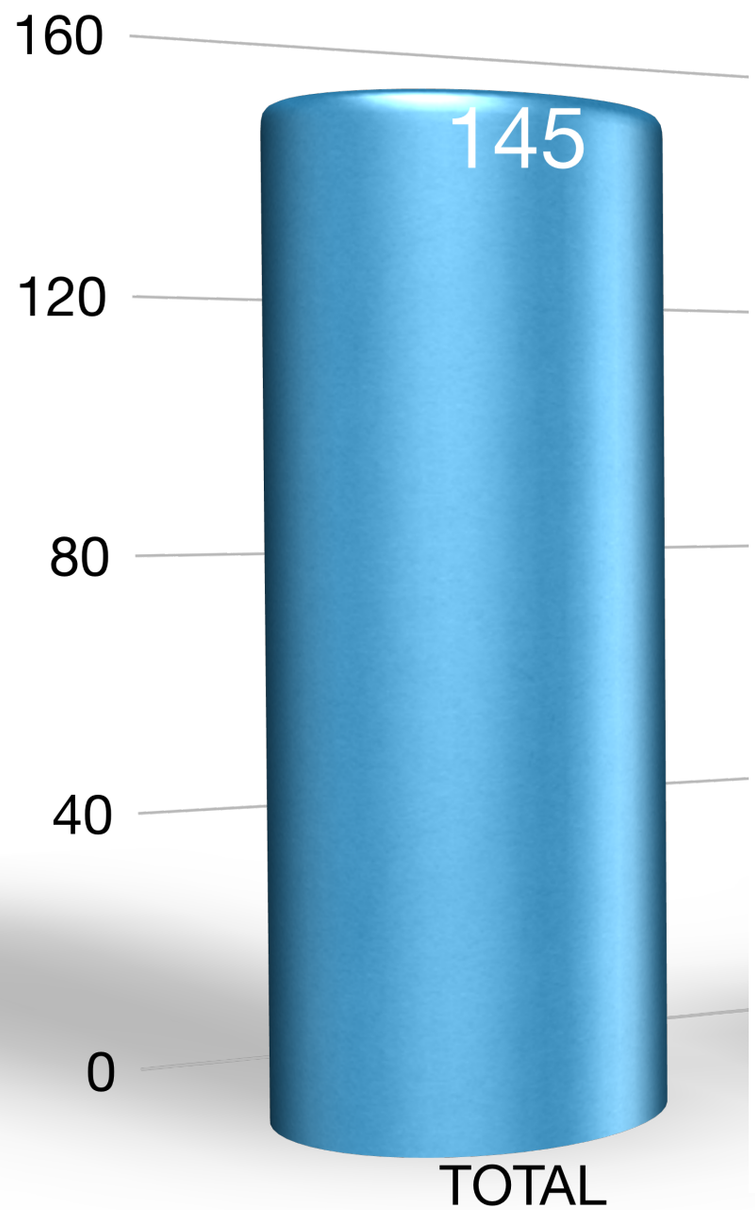
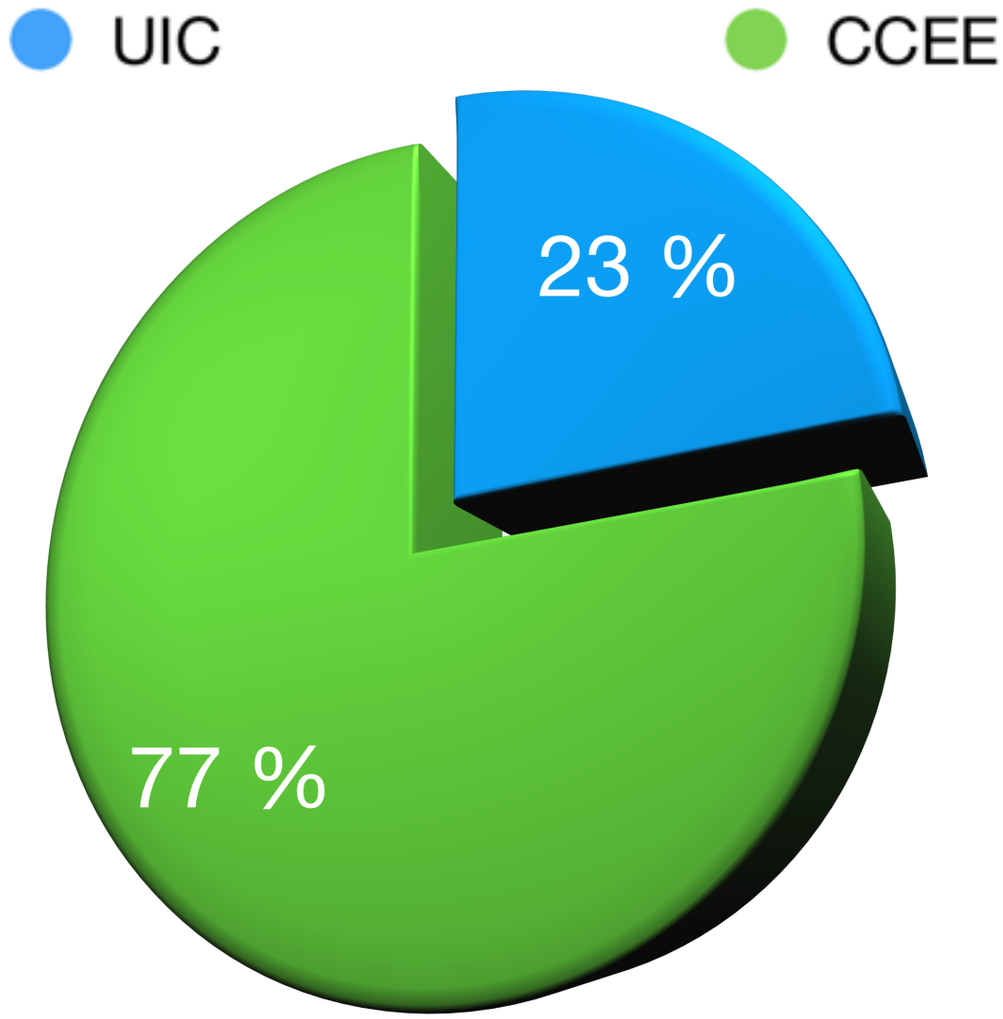


Figure 2 Changes in systolic blood pressure (SBP) at 12 weeks according to SBP categories at screening in patients receiving sacubitril/valsartan according to conservative and condensed up-titration regimens.

Senni M et al. Eur HF. 2018;42:205–211

RESULTADOS





HIPOTA	9
HIPERK	2
IR	1
OTROS	5

GESTOR DOCUMENTAL

TELEFONO: 620599700 (L-V 09-15H)

REFERENTES

NO PRESENCIAL

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julia.seller@marinasalud.es
ainoha.larumbe@marinasalud.es

RESULTADOS DE TODOS

IASIST NOW PART OF IMS HEALTH | HOSPITAL DE DENIA | CARDIOLOGÍA | Todos los módulos | Actual: May 16 - Oct 17 | Norma (Nivel 3 (APR32 ... | Anterior: May 15 - May 16 | Soporte...

IAmetrics Hospital | Todas las dimensiones | Todos los centros | CARDIOLOGÍA

Filtros generales | Rango de edad: Desactivado | Líneas asistenciales: Desactivado | TOP 20

Procesos evaluados en TOP20

(•) Corazón ( ) Digestivo ( ) Mujer ( ) Nervioso ( ) Respiratorio ( ) Riñon ( ) Musculoesquelético

Insuficiencia Cardíaca Congestiva	Actual	Benchmark	Dif		Peer	Dif		Anterior	Dif	
Número de casos	172							151		
Índice de Mortalidad Ajustado por Riesgo	0,5	0,4	40,5%	▲	1,0	-47,1%	▼	1,2	-55,0%	▼
Índice de Readmisiones Ajustado por Riesgo	0,8	0,6	39,3%	▲	1,1	-25,6%	▼	1,1	-27,6%	▼
Índice de Estancias Ajustado por Riesgo	0,6	0,7	-24,7%	▼	1,0	-43,6%	▼	0,6	-7,7%	–

Fuente datos: IASIST Denia

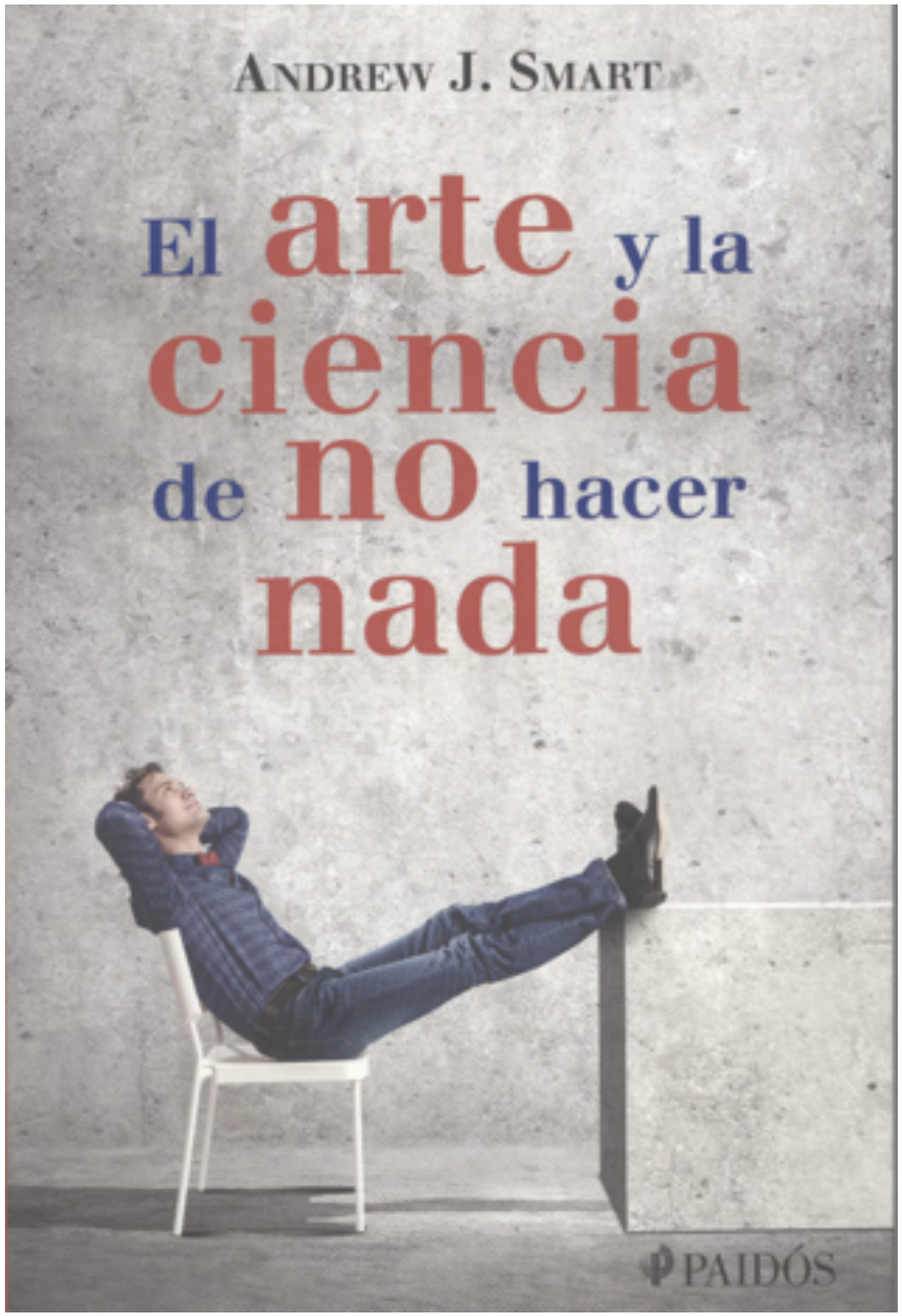
CONCLUSIONES

“IC ESTABLE”

BUEN PRONÓSTICO


R.I.P
MURIÓ SIN
SINTOMAS


Min de
oro
OMEGA



Titular o no titular

BNP o no BNP

Ingreso o no ingreso

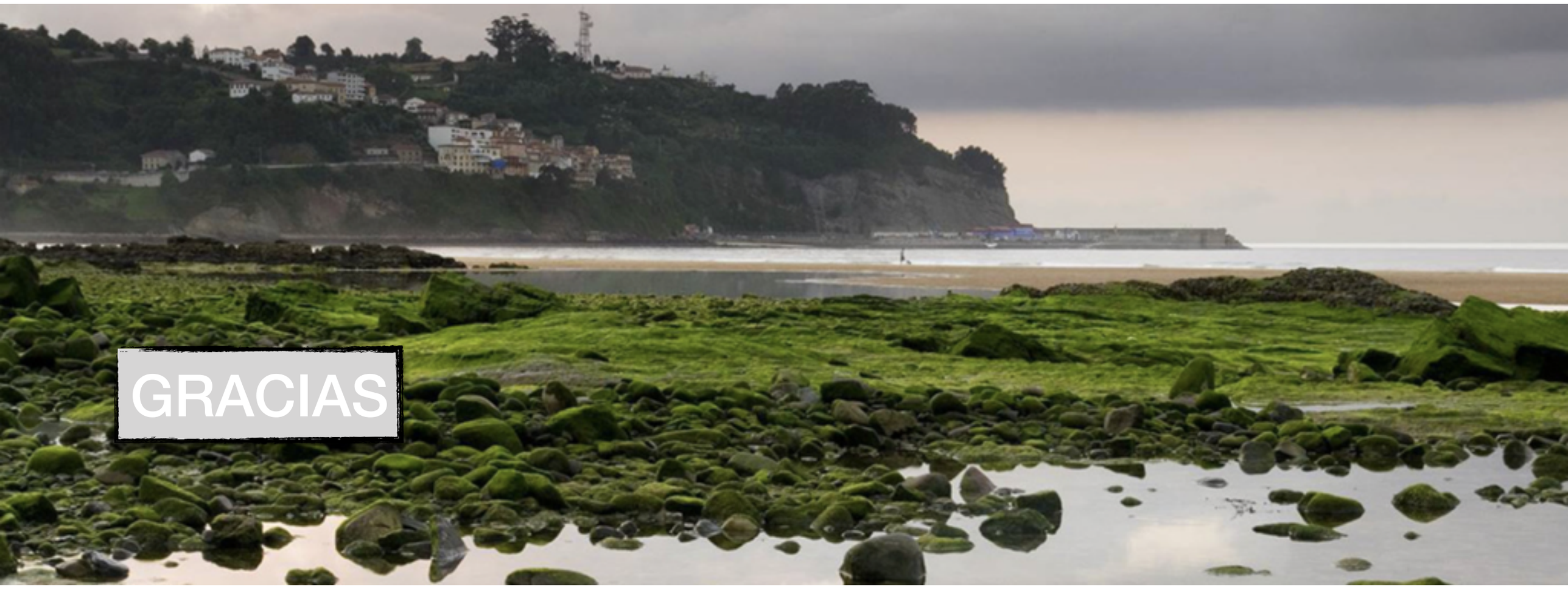
Mejoría sintomas

Valor = (C+H) x A

C= CONOCE ARNI.

H= HABILIDAD PARA DETECTAR QUIEN SE BENEFICIA

A= CAMBIA IECA/ARA II


GRACIAS

os autores del trabajo resaltan que uno de los principales problemas de validez del PARADIGM-HF es la FEVI tan baja (≤ 35%) y las dosis de IECA/ARA-2 empleadas. Reflejan que siguiendo estos estrictos criterios, el 80% de sus pacientes se excluyeron en el proceso de selección, por lo que **realizaron un segundo proceso de selección, con pacientes con una FEVI ≤ 40% y empleo de IECA/ARA-2 a la mitad de la dosis, de tal manera que ampliaron el número de pacientes elegibles para sacubitrilo-valsartán hasta un 40%, en lugar de solo el 24% de la selección principal.**

altas concentraciones de BNP o NT−proBNP (BNP ≥ 150 pg/ml
o NT−proBNP ≥ 600 pg/ml sin ingresos por IC en el .ltimo a.o y BNP ≥ 100 pg/ml o NTproBNP
≥ 400 pg/ml con ingreso previo en el .ltimo a.o

ESC HEART FAILURE
ESC Heart Failure 2018; **5**: 337–343
Published online 18 January 2018 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.12251

ORIGINAL RESEARCH ARTICLE

Eligibility of sacubitril–valsartan in a real-world heart failure population: a community-based single-centre study

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