Sesión Bibliográfica

Elena Magaz García

13/9/2019

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Clinical practice update on heart failure 2019: pharmacotherapy, procedures, devices and patient management. An expert consensus meeting report of The Heart Failure Association of the European Society of Cardiology.

- **1. Sacubitrilo/valsartán.**
- **2.Inhibidores del cotransportador de sodio-glucosa tipo 2 (iSGLT2)**
- **3. Quelantes de potasio**
- **4. Rivaroxabán**
- **5. Diureticos.**

1. Sacubitrilo/valsartán

-Uno de los fármacos que más publicaciones ha producido desde la publicación de su pivotal en 2014 .
-Numerosos subestudios del PARADIGM-HF que avalan su uso en diferentes perfiles de pacientes, con beneficio frente a enalapril en todos ellos (ancianos, diabéticos, ingreso previo por IC, etiología de la miocardiopatía, tratamiento previo, etc.).

Evidencia en pacientes hospitalizados: **el beneficio es mayor cuanto antes se inicie el fármaco.**

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2. Sacubitrilo/valsartán

Tanto es así que **este posicionamiento de la ESC defiende que ya existe evidencia, aunque hace falta más, para iniciarlo también en pacientes *naive*** (que nunca han tomado [IECA] o [ARA-II]).

ORIGINAL ARTICLE

Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction

JAMA | Original Investigation

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

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction

S.D. Solomon, J.J.V. McMurray, I.S. Anand, J. Ge, C.S.P. Lam, A.P. Maggioni, F. Martinez, M. Packer, M.A. Pfeffer, B. Pieske, M.M. Redfield, J.L. Rouleau, D.J. van Veldhuisen, F. Zannad, M.R. Zile, A.S. Desai, B. Claggett, P.S. Jhund, S.A. Boytsov, J. Comin-Colet, J. Cleland, H.-D. Düngen, E. Goncalvesova, T. Katova, J.F. Kerr Saraiva, M. Lelonek, B. Merkely, M. Senni, S.J. Shah, J. Zhou, A.R. Rizkala, J. Gong, V.C. Shi, and M.P. Lefkowitz, for the PARAGON-HF Investigators and Committees

DOI: 10.1056/NEJMoa1908655

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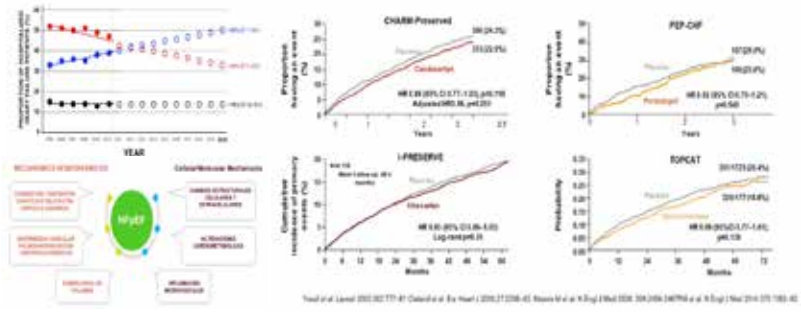
- La epidemiologia de la IC está cambiando, siendo la ICFE preservada más prevalente.
- En 2020, el 65% de los pacientes hospitalizados por IC presentarán una FE ≥ 40%.



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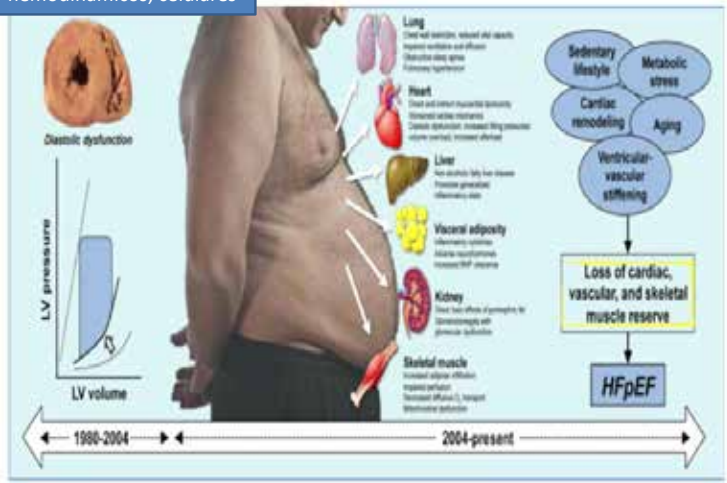
Mecanismos hemodinámicos, celulares



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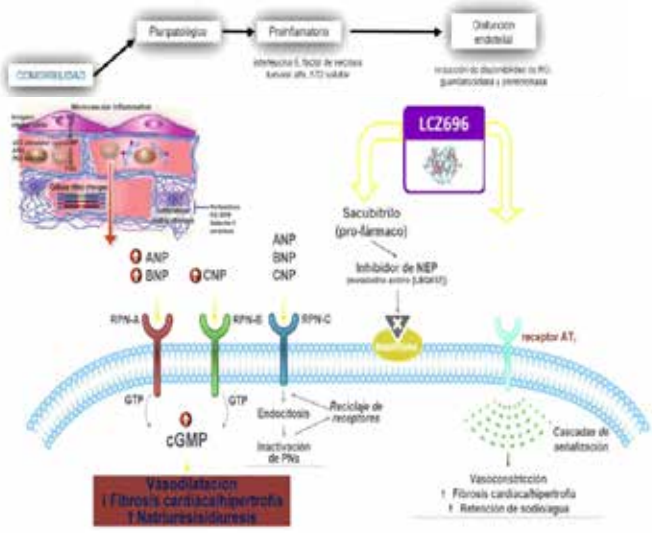

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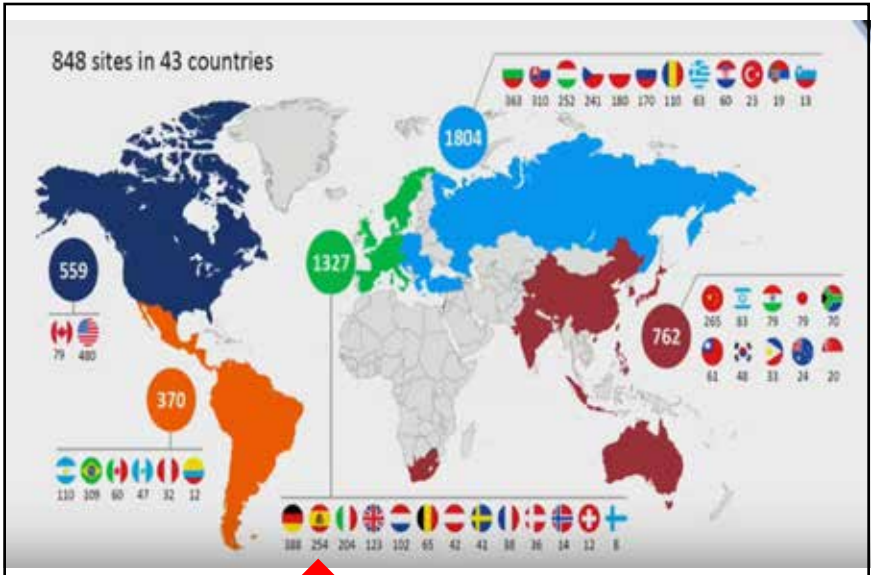

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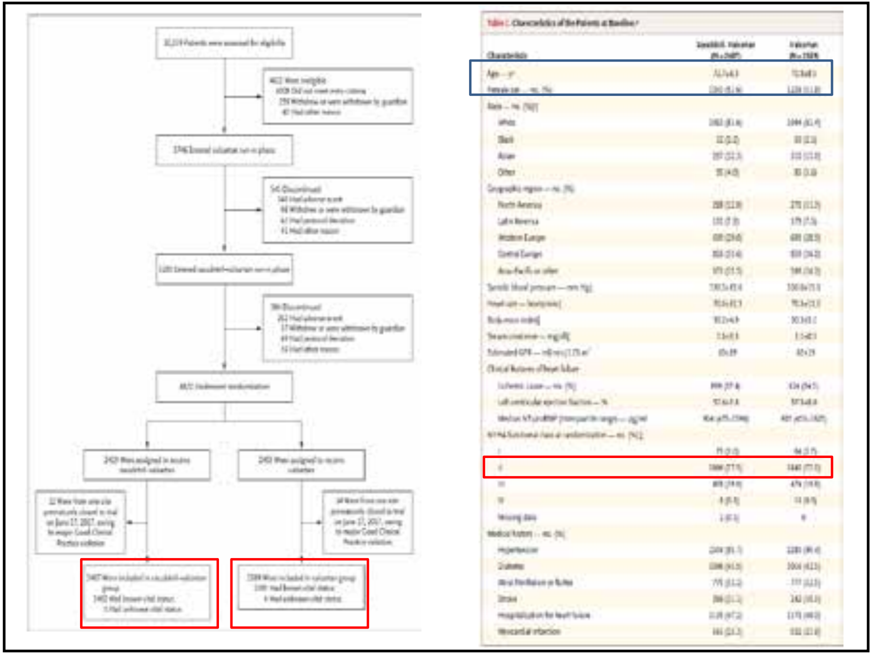
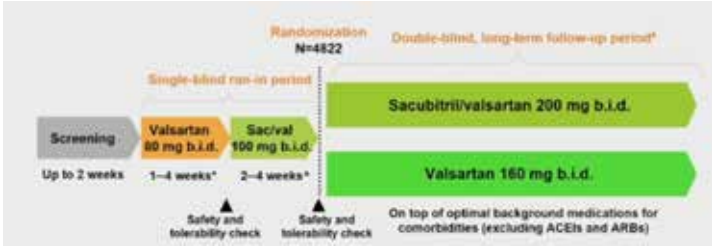


Table 1. (Continued.)

Characteristic	Sacubitril–Valsartan (N = 2407)	Valsartan (N = 2389)
Treatment — no. (%)		
Diuretic agent at randomization	2294 (95.3)	2291 (95.9)
ACE inhibitor or ARB at screening	2074 (86.2)	2065 (86.4)
Mineralocorticoid-receptor antagonist at randomization	592 (24.6)	647 (27.1)
Beta-blocker at randomization	1922 (79.9)	1899 (79.5)



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6. Supplementary Table S1. Detailed Inclusion and Exclusion Criteria

Eligibility Criteria
Inclusion criteria
1. Written informed consent must be obtained before any assessment is performed 2. ≥50 years of age, male or female 3. LVEF ≥45% by echocardiography during the screening epoch, or within 6 months prior to screening visit (any local LVEF measurement made using echocardiography only) 4. Symptom(s) of HF requiring treatment with diuretic(s) for at least 30 days prior to screening visit 5. Current symptom(s) of HF (NYHA functional class II to IV) at screening visit 6. Structural heart disease evidenced by at least 1 of the following echocardiography findings (any local measurement made during the screening epoch or within the 6 months prior to screening visit): a) LA enlargement defined by at least 1 of the following: LA width (diameter) ≥3.8 cm or LA length ≥5.0 cm or LA area ≥20 cm^2 or LA volume ≥55 ml or LA volume index ≥29 ml/m^2 b) LVH defined by septal thickness or posterior wall thickness ≥1.1 cm 7. Patients with at least 1 of the following: a) HF hospitalization (defined as HF listed as the major reason for hospitalization) within 9 months prior to screening visit and NT-proBNP >200 pg/ml for patients not in AF or >600 pg/ml for patients in AF on screening ECG, or b) NT-proBNP >300 pg/ml for patients not in AF or >900 pg/ml for patients in AF on the screening visit ECG

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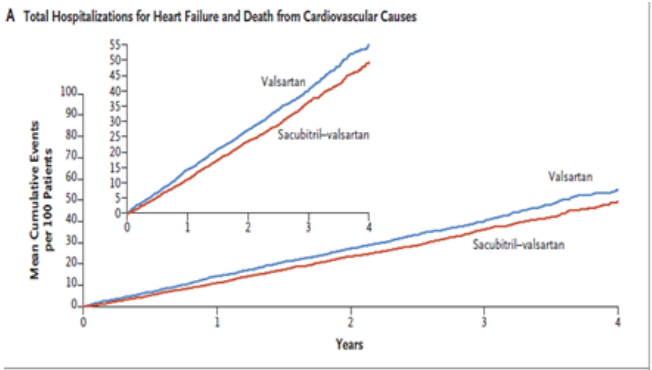
Table 2. Primary and Secondary Outcomes.*

Outcome	Sacubitril–Valsartan (N = 2407)	Valsartan (N = 2389)	Ratio or Difference (95% CI)
Primary composite outcome and components			
Total hospitalizations for heart failure and death from cardiovascular causes†			RR, 0.87 (0.75–1.01)
Total no. of events	894	1009	
Rate per 100 patient-yr	12.8	14.6	
Total no. of hospitalizations for heart failure	690	797	RR, 0.85 (0.72–1.00)
Death from cardiovascular causes — no. (%)	204 (8.5)	212 (8.9)	HR, 0.95 (0.79–1.16)
Secondary outcomes			
Change in NYHA class from baseline to 8 mo — no./total no. (%)			OR, 1.45 (1.13–1.86)
Improved	347/2316 (15.0)	289/2302 (12.6)	
Unchanged	1767/2316 (76.3)	1792/2302 (77.8)	
Worsened	202/2316 (8.7)	221/2302 (9.6)	
Change in KCCQ clinical summary score at 8 mo‡	−1.6±0.4	−2.6±0.4	Difference, 1.0 (0.0–2.1)
Renal composite outcome — no. (%)§	33 (1.4)	64 (2.7)	HR, 0.50 (0.33–0.77)
Death from any cause — no. (%)	342 (14.2)	349 (14.6)	HR, 0.97 (0.84–1.13)



VALSARTÁN (n= 2389)
1009 events, 14.6 per 100 pt- years

SACUBITRILO/VALSARTÁN (n= 2407)
894 events, 12.8 per 100 pt- years

Rate ratio 0,87 (95% CI 0.75, 1 01)
P=0,059

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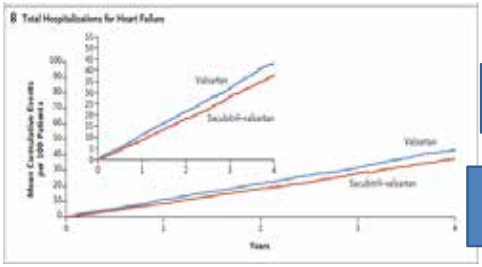
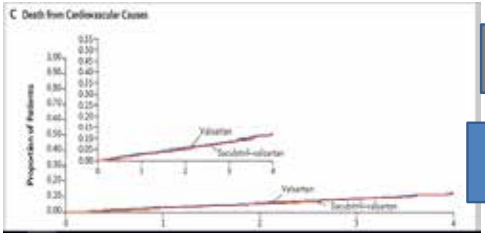


Rate ratio 0,85 (95% CI 0.72, 1,00)
P=0,056

VALSARTÁN 797 events
SACUBITRILO/VALSARTÁN 690 events



Hazard ratio 0,95 (95% CI 0.79, 1,16)
P=0,62

VALSARTÁN 212 events
SACUBITRILO/VALSARTÁN 204 events

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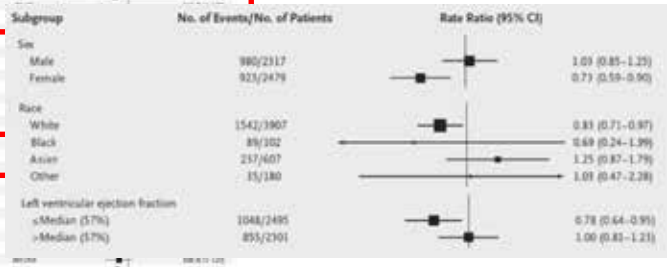

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Table 3. Adverse Events during Randomized Treatment.

Event	Sacubitril–Valsartan (N=2407)	Valsartan (N=2389)	P Value
Hypotension with systolic blood pressure <100 mm Hg — no. (%)	380 (15.8)	257 (10.8)	<0.001
Elevated serum creatinine — no. (%)			
≥2.0 mg/dl	261 (10.8)	328 (13.7)	0.002
≥2.5 mg/dl	97 (4.0)	109 (4.6)	0.36
≥3.0 mg/dl	38 (1.6)	40 (1.7)	0.79
Elevated serum potassium — no./total no. (%)			
>5.5 mmol/liter	316/2386 (13.2)	361/2367 (15.3)	0.048
>6.0 mmol/liter	75/2386 (3.1)	101/2367 (4.3)	0.04
Angioedema — no. (%)	14 (0.6)	4 (0.2)	0.02
Liver-related adverse event — no. (%)	151 (6.3)	178 (7.5)	0.11

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Conclusiones

- En pacientes con HFpEF, SAC/VAL vs valsartán: **↓del 13%** en el resultado primario, **sin alcanzar la significación estadística**, que fue impulsado principalmente por una reducción en primeras y recurrentes hospitalizaciones por IC.
- **Síntomas, calidad de vida y función renal** mejora con sacubitril/valsartán .
- SAC/VAL es **seguro** en HFpEF.
- Mayor beneficio en **mujeres y FEVI< 57%** .
- Probablemente el uso de valsartán como comparador, atenua los resultados beneficiosos de SAC/VAL

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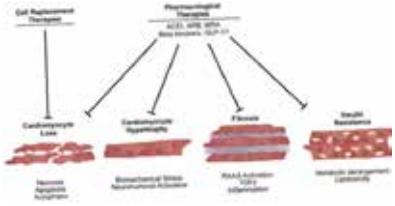
JAMA | Original Investigation

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; Beana 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. Published online September 2, 2019.doi:10.1001/jama.2019.12821

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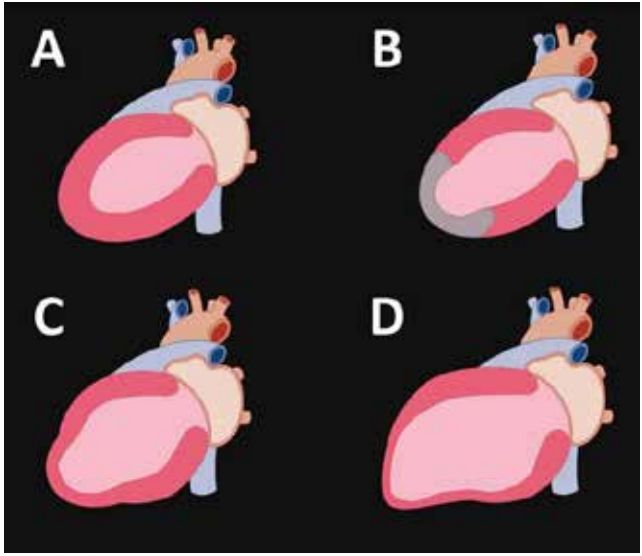

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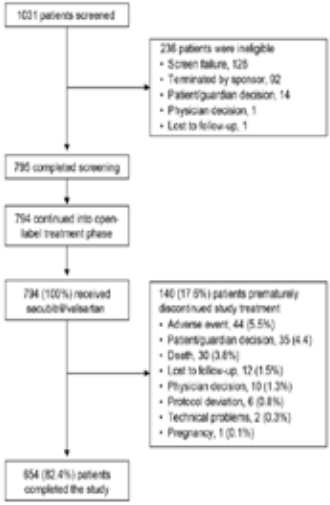
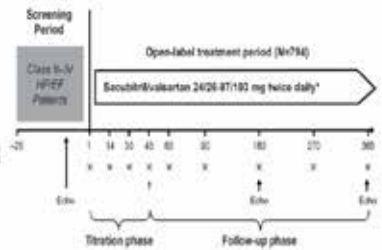
eFigure 2: Study flow diagram and patient disposition.



eFigure 1: Study procedures during PROVE-HF. Patients were included in the remodeling analyses if their echocardiograms were performed within ± 7 days of the 6 and 12 month follow up visit.



X = Vital status/events (CV death, HF hospitalization, worsening HF), physical examination, blood samples for safety chemistry and biomarkers, urine sampling, HF symptom assessment, KCCQ-23.

* Standard HF therapy was continued throughout the study with the exception of ACEI, ARB; †At Day 45, KCCQ-23 was not administered.

CV denotes cardiovascular; HF denotes heart failure; KCCQ-23 denotes Kansas City Cardiomyopathy Questionnaire-23.

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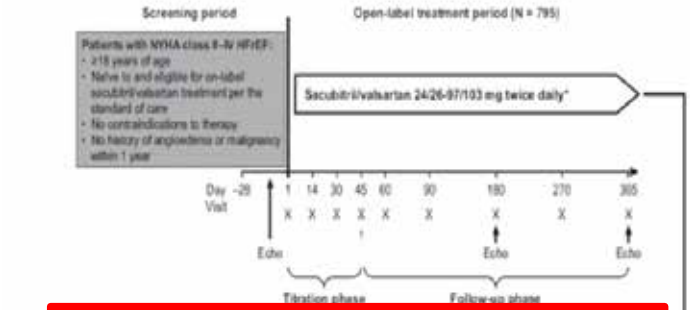

Key endpoints		
Primary	**Secondary**	**Exploratory**
• Changes in NT-proBNP concentrations and cardiac remodeling from baseline to 1 year	• Changes in concentrations of NT-proBNP and remodeling from baseline to 6 months • Changes in patient-reported outcomes using the KCCQ-23 from baseline to 1 year	• Changes in biomarker concentrations relative to the number of CV events within 12 months

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eTable 1: Patient eligibility criteria for PROVE-HF.

Key Inclusion Criteria	Key Exclusion Criteria
• Aged ≥18 years • Patients with HFrEF who are candidates for on-label sacubitril/valsartan treatment per the standard of care • NYHA functional class II, III, or IV • LVEF ≤40% within the preceding 6 months according to any local measurement, and no subsequent documentation of EF >40% o For EF measurements expressed as ranges, the average of the range endpoint values should be <40% • Stable dose of loop diuretic for the 2 weeks preceding study start	• History of hypersensitivity/allergy or suspected contraindication to any study-drug component or to drugs of similar chemical classes, including ACEIs, angiotensin receptor blockers, or neprilysin inhibitors • Any angioedema history (drug related or otherwise) • Concomitant use of ACEI therapy, nesiritide, aliskiren, or drugs that may affect absorption of the study medication • Current or previous treatment with sacubitril/valsartan • Inadequate washout of other investigational drugs before study initiation • Enrollment in another clinical trial within 30 days of screening • Potassium >5.2 mEq/L at screening • History of malignancy within 1 year • Pregnancy, lactation, or use of any method of contraception that is not highly effective • Implantation of CRT/D within 6 months of screening visit • Prior heart transplant or left ventricular assist device or intent to implant either

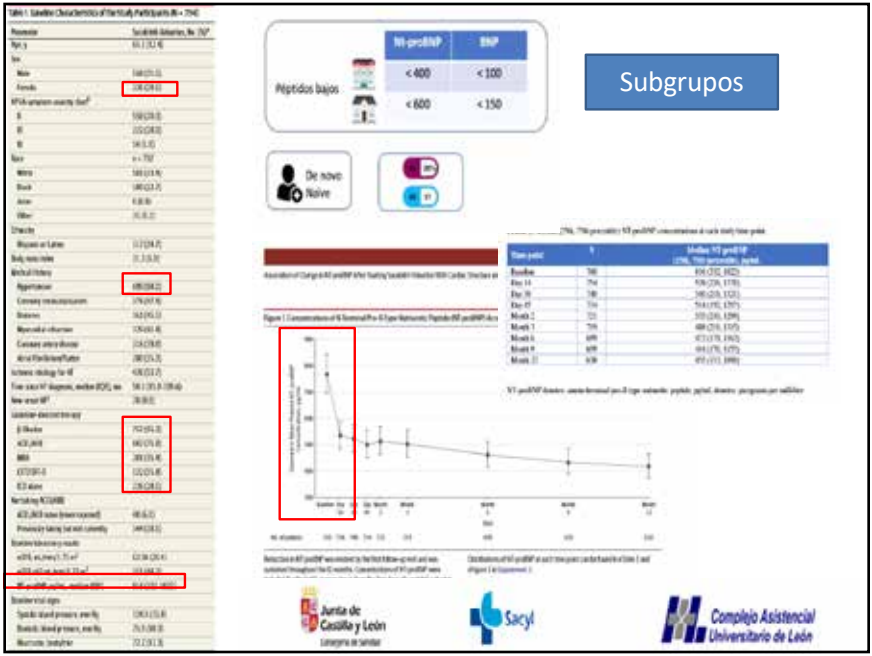
Péptidos bajos
NT-proBNP
BNP
< 400
< 100
< 600
< 150
Subgrupos
De novo
Naïve
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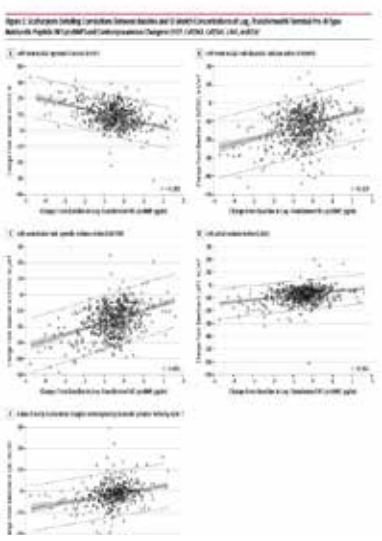
Table 2. Change in Cardiac Remodeling Measurements From Baseline to 6 and 12 Months After Initiation of Sacubitril Valsartan in All Study Participants[a]

	All Patients				
	Baseline Value, Median (25th to 75th Percentile)	6-mo Value, Median (25th to 75th Percentile)	LS Mean Change From Baseline at 6 mo (95% CI)	12-mo Value, Median (25th to 75th Percentile)	LS Mean Change From Baseline at 12 mo (95% CI)
LVEF, %	n = 757	n = 716		n = 648	
	28.2 (24.5 to 32.7)	34.1 (29.0 to 39.65)	5.2 (4.8 to 5.6)	37.8 (32.3 to 45.2)	9.4 (8.8 to 9.9)
LVEDVI, mL/m^2	n = 756	n = 716		n = 648	
	86.91 (76.17 to 100.43)	79.50 (69.34 to 91.57)	−6.65 (−7.11 to −6.19)	74.15 (63.46 to 86.30)	−12.25 (−12.92 to −11.58)
LVESVI, mL/m^2	n = 756	n = 716		n = 648	
	61.68 (51.95 to 75.00)	52.25 (42.34 to 65.25)	−8.67 (−9.18 to −8.15)	45.46 (34.84 to 57.56)	−15.29 (−16.03 to −14.55)
LAVI, mL/m^2	n = 747	n = 696		n = 639	
	37.76 (31.63 to 46.09)	32.80 (27.62 to 40.13)	−4.36 (−4.73 to −3.99)	29.31 (24.40 to 35.85)	−7.57 (−7.98 to −7.15)
E/e'	n = 642	n = 604		n = 552	
	11.70 (8.80 to 16.00)	10.50 (7.70 to 14.70)	−1.23 (−1.63 to −0.83)	10.20 (7.70 to 14.30)	−1.30 (−1.74 to −0.86)

Abbreviations: E/e', ratio of early transmitral Doppler velocity/early diastolic annular velocity; LAVI, left atrial volume index; LS, least square; LVEF, left ventricular ejection fraction; LVEDVI, left ventricular end-diastolic volume index; LVESVI, left ventricular end-systolic volume index.

[a] All comparisons were significant at $P < .001$.



1-log-unit decrease NT-proBNP

4.9% in LVEF at each time point
(Z = 36.26, P < .001)

Parameter	N	Pearson r (95% CI)	P value
NT-proBNP (pg/mL) / LVEF (%)	651	-0.226 (-0.298, -0.152)	<.0001
NT-proBNP (pg/mL) / LVEDVi (mL/m²)	650	0.164 (0.088, 0.238)	<.0001
NT-proBNP (pg/mL) / LVESVi (mL/m²)	650	0.233 (0.159, 0.305)	<.0001
NT-proBNP (pg/mL) / LAVi (mL/m²)	625	0.190 (0.113, 0.264)	<.0001
NT-proBNP (pg/mL) / E/E'	495	0.208 (0.124, 0.292)	<.0001

3/4 mejora la función ventricular un 5%
1/4 mejora la función ventricular un 13%

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Table 3. Change in Cardiac Remodeling Measurements From Baseline to 6 and 12 Months After Initiation of Sacubitril-Valsartan Among Patients With New-Onset HF or Not Taking ACEI or ARB at Baseline

New-Onset HF or ACEI/ARB Naive	Baseline Value, Median (25th to 75th Percentile)	6-mo Value, Median (25th to 75th Percentile)	LS Mean Change From Baseline at 6 mo (95% CI)	P Value	12-mo Value, Median (25th to 75th Percentile)	LS Mean Change From Baseline at 12 mo (95% CI)	P Value
LVEF, %	n = 138	n = 102			n = 98		
Yes	28.4 (25.2 to 33.0)	35.7 (30.7 to 42.1)	6.9 (5.7 to 8.0)	<.001	43.5 (35.4 to 50.5)	12.8 (11.05 to 14.5)	<.001
No	28.1 (24.3 to 32.6)	33.8 (28.7 to 39.1)	4.9 (4.5 to 5.3)	<.001	37.0 (33.8 to 44.4)	8.8 (8.3 to 9.3)	<.001
LVEDVI, No., mL/m^2	n = 138	n = 102			n = 98		
Yes	85.97 (70.13 to 95.47)	74.59 (62.70 to 85.90)	−7.25 (−8.50 to −5.97)	<.001	67.66 (57.77 to 79.39)	−13.81 (−15.78 to −11.83)	<.001
No	82.43 (76.89 to 101.38)	80.38 (70.46 to 93.89)	−6.56 (−7.85 to −6.07)	<.001	75.12 (64.11 to 86.81)	−13.02 (−12.71 to −11.29)	<.001
LVESVI, No., mL/m^2	n = 138	n = 102			n = 98		
Yes	59.28 (49.64 to 71.29)	46.29 (36.44 to 58.94)	−10.01 (−11.45 to −8.58)	<.001	37.69 (28.97 to 51.16)	−17.88 (−20.07 to −15.68)	<.001
No	61.82 (52.70 to 75.91)	52.94 (43.28 to 66.42)	−8.46 (−9.81 to −7.90)	<.001	46.70 (36.47 to 58.1)	−14.06 (−15.64 to −14.09)	<.001
LAVI, No. mL/m^2	n = 131	n = 101			n = 98		
Yes	36.86 (31.53 to 45.02)	32.14 (25.24 to 38.78)	−4.83 (−5.84 to −3.83)	<.001	28.13 (21.32 to 35.57)	−8.44 (−9.73 to −7.15)	<.001
No	32.90 (31.63 to 46.25)	32.94 (27.90 to 40.65)	−4.28 (−4.68 to −3.88)	<.001	29.43 (25.04 to 35.90)	−7.42 (−7.85 to −6.99)	<.001
E/e', No.	n = 84	n = 88			n = 85		
Yes	11.85 (8.35 to 16.60)	9.70 (7.00 to 14.25)	−1.86 (−3.01 to −0.70)	.002	9.00 (6.80 to 12.70)	−2.60 (−3.83 to −1.37)	<.001
No	11.60 (8.80 to 16.00)	10.60 (7.80 to 14.80)	−1.13 (−1.54 to −0.72)	<.001	10.30 (7.80 to 14.40)	−1.10 (−1.57 to −0.63)	<.001

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; index; LS, least square; LVESVI, left ventricular end-diastolic volume index;

Table 4: Changes in Cardiac Remodeling Measurements From Baseline to 6 and 12 Months After Initiation of Sacubitril/Valsartan Among Patients With NT-proBNP Concentrations Below PARADIGM-HF Inclusion Criteria

NT-proBNP <820 pg/mL if Not Hospitalized or <400 pg/mL if Hospitalized or BNP <150 pg/mL if Not Hospitalized or <100 pg/mL if Hospitalized[a]	Baseline Value, Median (25th to 75th Percentile)	6-mo Value, Median (25th to 75th Percentile)	LS Mean Change From Baseline at 6 mo (95% CI)	*P* Value	12-mo Value, Median (25th to 75th Percentile)	LS Mean Change From Baseline at 12 mo (95% CI)	*P* Value
TVI, %	n = 227	n = 227			n = 256		
Yes	30.8 (25.9 to 34.1)	35.5 (30.7 to 41.1)	5.1 (4.5 to 5.8)	<.001	40.1 (34.9 to 46.3)	9.4 (8.6 to 10.2)	<.001
No	26.8 (23.3 to 31.9)	33.3 (27.2 to 38.6)	5.1 (4.9 to 5.9)	<.001	36.5 (30.3 to 44.1)	9.4 (8.7 to 10.2)	<.001
LVESVI, mL/m^2	n = 372	n = 323			n = 256		
Yes	31.01 (22.27 to 40.10)	24.85 (16.80 to 34.05)	−6.32 (−7.02 to −5.62)	<.001	19.01 (11.43 to 29.54)	−11.32 (−12.24 to −10.40)	<.001
No	31.21 (19.46 to 106.26)	24.37 (12.33 to 98.50)	−6.90 (−7.42 to −6.37)	<.001	17.75 (10.43 to 91.23)	−12.85 (−13.82 to −11.88)	<.001
LVEDVI, mL/m^2	n = 372	n = 323			n = 256		
Yes	56.38 (48.4) to 65.00)	47.83 (39.08 to 56.79)	−8.51 (−9.86 to −7.15)	<.001	40.66 (32.17 to 50.94)	−14.15 (−15.15 to −13.15)	<.001
No	66.22 (54.64 to 80.73)	55.73 (44.32 to 72.05)	−9.09 (−9.75 to −8.38)	<.001	48.91 (36.25 to 63.61)	−16.86 (−17.14 to −15.91)	<.001
LAVI, mL/m^2	n = 354	n = 263			n = 250		
Yes	32.85 (28.06 to 38.57)	28.94 (24.96 to 33.32)	−4.06 (−4.53 to −3.65)	<.001	26.00 (22.88 to 30.57)	−7.04 (−7.54 to −6.58)	<.001
No	41.76 (34.72 to 48.68)	36.39 (29.46 to 43.62)	−4.54 (−5.00 to −3.90)	<.001	32.53 (26.74 to 38.83)	−7.88 (−8.41 to −7.20)	<.001
E/e′	n = 344	n = 334			n = 325		
Yes	9.00 (7.20 to 13.25)	8.50 (6.80 to 12.60)	−0.40 (−0.80 to 0.00)	.10	8.20 (7.00 to 12.40)	−0.91 (−1.41 to −0.42)	<.001
No	12.00 (9.80 to 18.00)	11.60 (8.40 to 16.00)	−1.16 (−2.25 to −1.13)	<.001	11.00 (8.30 to 15.80)	−1.41 (−2.06 to −0.73)	<.001

Abbreviations: E/e′, ratio of early transmitral Doppler velocity/early diastolic annular velocity; LAVI, left atrial volume index; LS, least square; LVEDVI, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESVI, left ventricular end-systolic volume index; NT-proBNP, N-terminal pro-B-type natriuretic peptide; No, not in the subgroup; Yes, in the subgroup.

Dosis bajas de S/V

Association of Change in NT-proBNP After Starting Sacubitril-Valsartan With Cardiac Structure and Function in HFrEF — Original Investigation Research

Table 1. Change in Cardiac Remodeling Measurements From Baseline to 6 and 12 Months After Initiation of Sacubitril-Valsartan Among Patients Not Achieving Target Dose of Sacubitril-Valsartan by 12 Months

Unable to Achieve Target Dose of Sacubitril-Valsartan[a]	Baseline Value, Median (25th to 75th Percentile)	6-mo Value, Median (25th to 75th Percentile)	LS Mean Change From Baseline at 6 mo (95% CI)	P Value	12-mo Value, Median (25th to 75th Percentile)	LS Mean Change From Baseline at 12 mo (95% CI)	P Value
LAVI	n = 264	n = 234			n = 203		
Yes	27.9 (24.3 to 32.2)	34.1 (28.7 to 43.0)	5.5 (4.9 to 6.1)	<.001	37.5 (31.8 to 44.8)	9.0 (8.4 to 10.3)	<.001
No	28.4 (24.7 to 33.3)	34.2 (29.3 to 39.5)	5.0 (4.6 to 5.5)	<.001	37.8 (32.3 to 45.3)	9.4 (8.7 to 10.0)	<.001
LVESVI, mL/m^2	n = 263	n = 234			n = 203		
Yes	106.43 (74.93 to 181.35)	78.45 (57.76 to 94.71)	−6.25 (−7.00 to −5.43)	<.001	74.62 (62.71 to 86.44)	−10.90 (−12.21 to −9.72)	<.001
No	87.45 (76.68 to 99.82)	79.75 (70.30 to 92.39)	−6.86 (−7.43 to −6.29)	<.001	73.62 (63.50 to 86.29)	−10.83 (−12.64 to −12.03)	<.001
LVEDVI, mL/m^2	n = 263	n = 234			n = 203		
Yes	63.62 (52.13 to 75.95)	52.71 (42.97 to 67.30)	52.71 (43.57 to 67.30)	<.001	46.25 (34.88 to 58.54)	−14.32 (−15.67 to −12.97)	<.001
No	61.69 (51.92 to 74.57)	52.18 (42.53 to 64.81)	52.18 (42.51 to 64.81)	<.001	45.3 (35.20 to 56.95)	−15.72 (−16.60 to −14.84)	<.001
LAVI, mL/m^2	n = 263	n = 231			n = 202		
Yes	37.35 (31.65 to 46.12)	32.43 (27.20 to 40.65)	−4.27 (−5.05 to −3.49)	<.001	29.33 (24.99 to 35.81)	−7.23 (−7.97 to −6.50)	<.001
No	37.82 (31.49 to 46.08)	32.94 (27.60 to 39.74)	−4.41 (−4.79 to −4.03)	<.001	29.33 (24.31 to 35.98)	−7.26 (−8.20 to −7.25)	<.001
E/e'	n = 217	n = 192			n = 164		
Yes	11.50 (8.30 to 16.00)	10.55 (7.80 to 14.30)	−0.94 (−1.71 to −0.16)	.07	10.10 (7.70 to 15.12)	−0.46 (−1.33 to 0.40)	.29
No	11.70 (9.50 to 16.00)	10.35 (7.60 to 14.85)	−1.37 (−1.64 to −0.90)	<.001	10.25 (7.65 to 14.00)	−1.45 (−2.15 to −1.14)	<.001

Abbreviations: E/e', ratio of early transmitral Doppler velocity to early diastolic annular velocity; LAVI, left atrial volume index; LS, least square; LVESVI, left ventricular end-systolic volume index; LVEF, left ventricular ejection fraction; LVEDVI, left ventricular end-systolic volume index; No, not within subgroup; Yes, in the subgroup.

eTable 5: Adverse events of interest during the 12 months of PROVE-HF.

Event	N = 794; n, (%)
Hypotension (systolic blood pressure <90 mm mercury)	140 (17.6)
Dizziness	133 (16.8)
Hyperkalemia (potassium > 5.3 milliequivalents/liter)	105 (13.2)
Worsening kidney function*	98 (12.3)
Angioedema	
No treatment or antihistamines only without hospitalization	2 (0.3)
Use of catecholamines or glucocorticoids without hospitalization	0
Hospitalization without airway compromise	0
Airway compromise	0

*Worsening (decrease) in estimated glomerular filtration rate of ≥ 35% from baseline, or an increase in creatinine of ≥ 0.5 mg/dL from baseline and a worsening (decrease) in estimated glomerular filtration rate of ≥ 25% from baseline at a given visit.

CONCLUSIONES

- S/V en pacientes con **ICrFEVI ↓cifras de NT-pro-BNP** y se asocia de manera significativa con el remodelado inverso del VI.
- **La mejoría de la FEVI a 12 meses es de 9.4%** en el global de la muestra.
- El grado de remodelado explica como S/V reduce morbilidad y mortalidad en pacientes con ICrFEVI
- Reducción del **NT-proBNP** en las dos primeras semanas.
- Mejora de la FEVI en pacientes naive del **12.8%**
- Mantiene respuesta en pacientes con **péptidos bajos y dosis baja/media** de s/v

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2. Inhibidores del cotransportador de sodio-glucosa tipo 2 (iSGLT2)

el riesgo de desarrollar IC y ↓ los ingresos por esta causa en pacientes diabéticos.

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- Futuro: esperanzador
- Resultados de estudios en marcha
  - -en pacientes con IC (tanto preservada como reducida)
  - -en pacientes sin diabetes.

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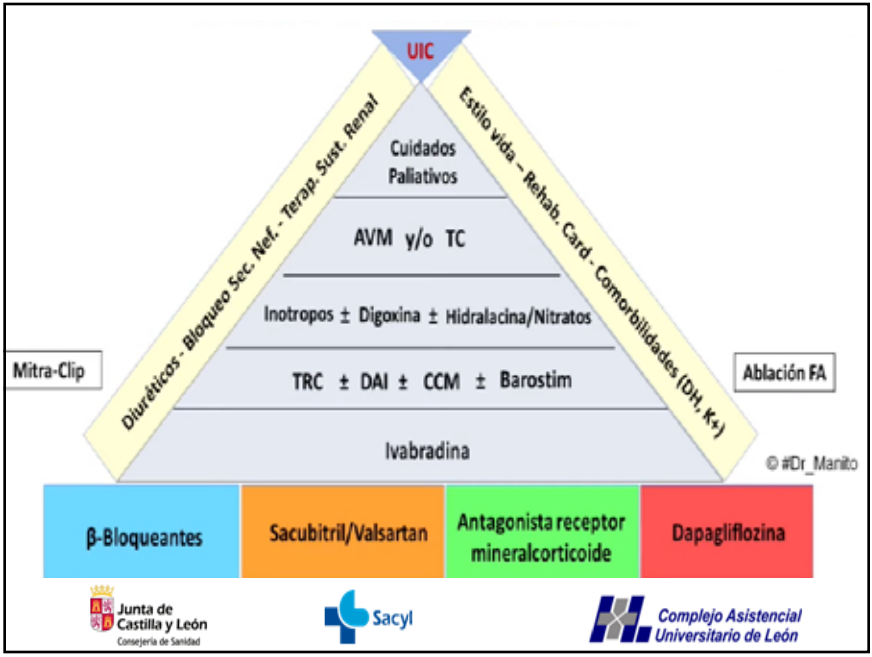
UIC
Diuréticos - Bloqueo Sec. Nef. - Terap. Sust. Renal
Estilo vida – Rehab. Card. - Comorbilidades (DH, K+)
Cuidados Paliativos
AVM y/o TC
Inotropos ± Digoxina ± Hidralacina/Nitratos
TRC ± DAI ± CCM ± Barostim
Ivabradina
Mitra-Clip
Ablación FA
© #Dr_Manito
β-Bloqueantes
Sacubitril/Valsartan
Antagonista receptor mineralcorticoide
Dapagliflozina
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3. Quelantes de potasio

Diversos trabajos avalan el uso de los quelantes de potasio para el manejo de la hiperpotasemia en pacientes con IC, independientemente de la existencia de enfermedad renal crónica, como soporte para la titulación de fármacos que tienen beneficio pronóstico.

Patiromer → beneficios potenciales en los pacientes con IC (menor riesgo de edema y congestión).

→ en España, acaba de ser aprobado, y se espera que en los próximos meses esté disponible para su uso en práctica clínica.

Manejo de los pacientes con IC para optimizar la titulación a dosis máximas toleradas

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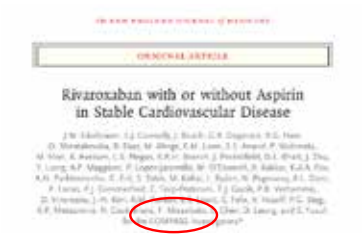
4. Rivaroxabán

La recomendación actual es que rivaroxabán 2,5 mg cada 12 horas puede considerarse para reducir el riesgo de ictus y muerte cardiovascular en pacientes ambulatorios con cardiopatía isquémica e IC con FEVI > 30% y clase funcional I-II de la New York Heart Association (NYHA) añadido a AAS.



ORIGINAL ARTICLE

Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease

N Engl J Med 2017; 377:1319-1330

ORIGINAL ARTICLE

Rivaroxaban in Patients with Heart Failure, Sinus Rhythm, and Coronary Disease

N Engl J Med 2018;379:1332-42.

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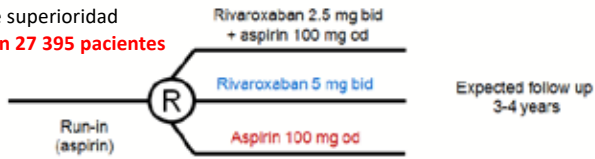
Cardiovascular Outcomes for People Using Anticoagulation Strategies **(COMPASS)** trial

La hipótesis de que rivaroxabán en combinación con aspirina o administrado sólo es más eficaz que aspirina sola en la prevención de recurrencia de eventos cardiovasculares, con seguridad aceptable, en pacientes con enfermedad vascular aterosclerótica estable.

Ensayo de superioridad
Fase 3 **con 27 395 pacientes**



El objetivo primario era la aparición de infarto de miocardio, ictus o muerte cardiovascular

Pantoprazol comparado con placebo reduce los sangrados GI

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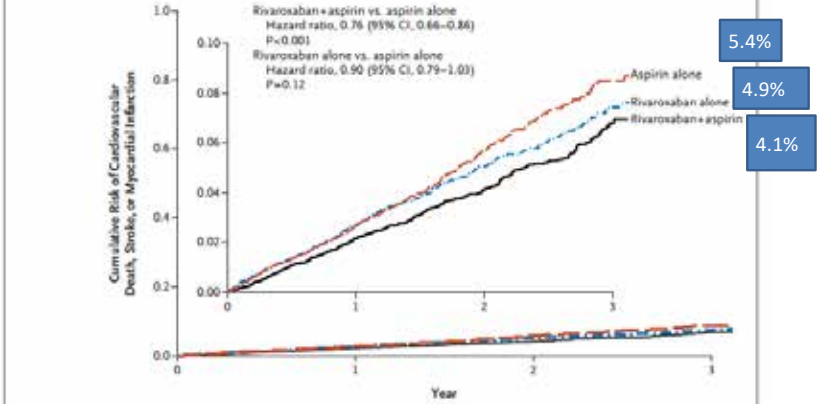
Table 1. Baseline Characteristics of the Participants.*

Characteristic	Rivaroxaban plus Aspirin (N=9152)	Rivaroxaban Alone (N=9117)	Aspirin Alone (N=9126)
Age — yr	68.3±7.9	68.2±7.9	68.2±8.0
Female sex — no. (%)	2059 (22.5)	1972 (21.6)	1989 (21.8)
Body-mass index†	28.3±4.8	28.3±4.6	28.4±4.7
Blood pressure — mm Hg			
Systolic	136±17	136±18	136±18
Diastolic	77±10	78±10	78±10
Cholesterol — mmol/liter	4.2±1.1	4.2±1.1	4.2±1.1
Tobacco use — no. (%)	1944 (21.2)	1951 (21.4)	1972 (21.6)
Hypertension — no. (%)	6907 (75.5)	6848 (75.1)	6877 (75.4)
Diabetes — no. (%)	3448 (37.7)	3419 (37.5)	3474 (38.1)
Previous stroke — no. (%)	351 (3.8)	346 (3.8)	335 (3.7)
Geographic region — no. (%)			
North America	1304 (14.2)	1305 (14.3)	1309 (14.3)
South America	2054 (22.4)	2036 (22.3)	2054 (22.5)
Western Europe, Israel, Australia, or South Africa	2855 (31.2)	2845 (31.2)	2855 (31.3)
Eastern Europe	1607 (17.6)	1612 (17.7)	1604 (17.6)
Asia–Pacific	1332 (14.6)	1319 (14.5)	1304 (14.3)
Medication — no. (%)			
ACE inhibitor or ARB	6475 (70.7)	6581 (72.2)	6462 (70.8)
Calcium-channel blocker	2413 (26.4)	2374 (26.0)	2482 (27.2)
Diuretic	2727 (29.8)	2666 (29.2)	2746 (30.1)
Beta-blocker	6389 (69.8)	6401 (70.2)	6394 (70.1)
Lipid-lowering agent	8239 (90.0)	8204 (90.0)	8158 (89.4)
NSAID	531 (5.8)	466 (5.1)	473 (5.2)
Nontrial PPI	3268 (35.7)	3266 (35.8)	3264 (35.8)



Entre los pacientes con enfermedad vascular aterosclerótica estable, el resultado primario (muerte cardiovascular, accidente cerebrovascular o IAM) fue inferior en un 24% con rivaroxaban (2,5 mg dos veces al día) más aspirina que con aspirina sola (4,1% frente a 5,4%), pero la tasa de hemorragia fue mayor en un 70% (3.1% vs. 1.9%).

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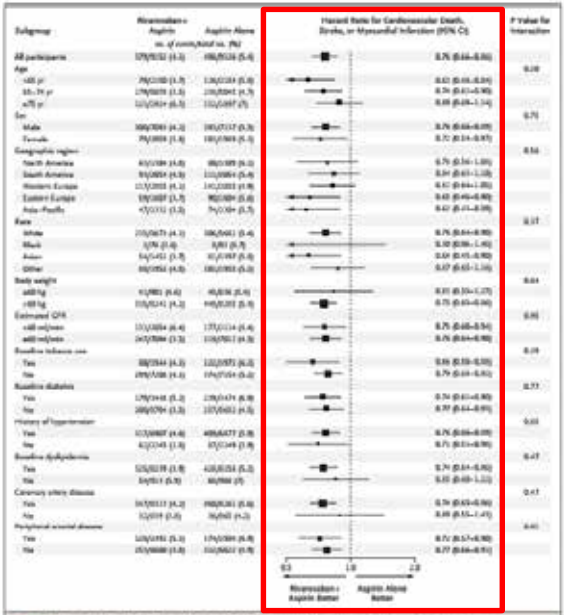

Figure 2. Subgroup Analyses for the Primary Outcome for the Comparison of Rivaroxaban plus Aspirin with Aspirin Alone.

Conclusiones

- **Rivaroxaban 2,5 mg más aspirina 100 mg**:
  - Reduce la muerte CV, accidente cerebrovascular, I AM
  - > riesgo de sangrado sin un aumento significativo de la hemorragia fatal, intracraneal o de órganos críticos
  - Proporciona un beneficio clínico neto
- **Ningún beneficio significativo del rivaroxabán solo**

-¿rivaroxabán más aspirina de por vida?

El coste adicional del rivaroxaban

¿efecto de otros fármacos: estatinas, bb…?

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rivaroxaban in Patients with Heart Failure, Sinus Rhythm, and Coronary Disease

Faiez Zannad, M.D., Ph.D., Stefan D. Anker, M.D., Ph.D., William M. Byra, M.D., John G.F. Cleland, M.D., Min Fu, Ph.D., Mihai Gheorghiade, M.D.,* Carolyn S.P. Lam, M.D., Ph.D., Mandeep R. Mehra, M.D., James D. Neaton, Ph.D., Christopher C. Nessel, M.D., Theodore E. Spiro, M.D., Dirk J. van Veldhuisen, M.D., Ph.D., and Barry Greenberg, M.D., for the COMMANDER HF Investigators†

N Engl J Med 2018;379:1332-42.

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- **OBJETIVO PRIMARIO**
  - EFICACIA: Mortalidad total, IAM o ACV isquémico
  - SEGURIDAD: sangrado fatal o sangrado en espacio crítico potencialmente incapacitante
- **CRITERIOS DE INCLUSIÓN**
  - IC crónica (>meses) con FEVI ≤ 40%
  - Post-descompensación (<3 semanas)
  - BNP ≥200 pg/ml o NT-proBNP ≥800 pg/ml
  - Enfermedad coronaria
  - Bajo tratamiento optimo según GPC
  - No anticoagulación

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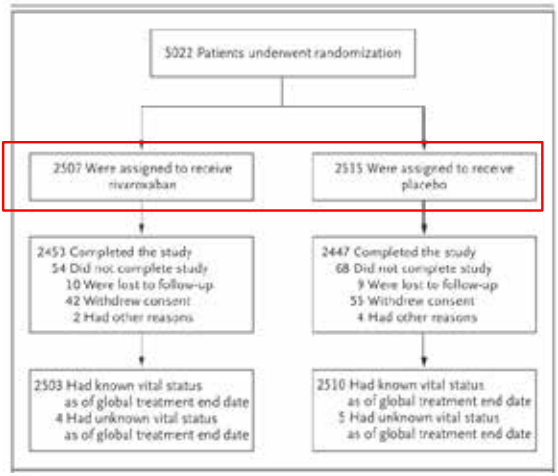

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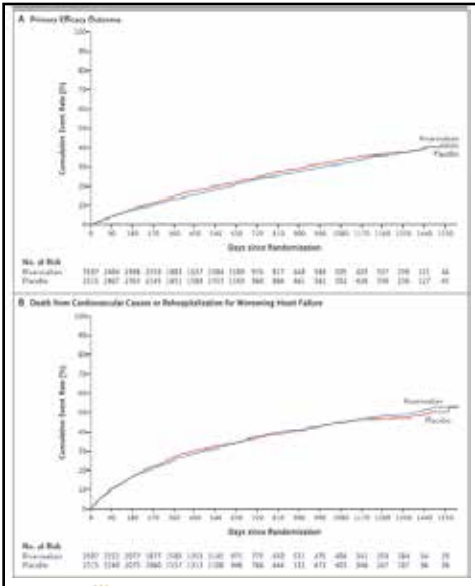
Characteristic	Rivaroxaban (N=2507)	Placebo (N=2515)
Age — yr	66.5±10.1	66.3±10.3
Female sex — no. (%)	551 (22.0)	599 (23.8)
Race — no. (%)†		
White	2063 (82.3)	2065 (82.1)
Black	29 (1.2)	36 (1.4)
Asian	362 (14.4)	365 (14.5)
Other	53 (2.1)	49 (1.9)
Region — no. (%)		
Eastern Europe	1610 (64.2)	1614 (64.2)
North America	74 (3.0)	75 (3.0)
Asia-Pacific	367 (14.6)	366 (14.6)
Latin America	229 (9.1)	229 (9.1)
Western Europe or South Africa	227 (9.1)	231 (9.2)
Body-mass index‡	27.6±5.1	27.8±5.3
eGFR — no. (%)		
<30 ml/min/1.73 m^2	81 (3.2)	82 (3.3)
30 to <60 ml/min/1.73 m^2	884 (35.3)	898 (35.7)
60 to <90 ml/min/1.73 m^2	1101 (43.9)	1137 (45.2)
≥90 ml/min/1.73 m^2	441 (17.6)	398 (15.8)
Clinical features of heart failure		
Median BNP level (IQR) — pg/ml§	702.0 (403.4–1237.0)	695.5 (380.0–1266.3)
Median NT-proBNP level (IQR) — pg/ml§	2840.0 (1537.0–6304.0)	2900.0 (1520.6–6270.5)
Median D-dimer level (IQR) — µg/liter	360 (215–690)	360 (215–655)
Median ejection fraction (IQR) — %	35 (28–38)	34 (27–38)
New York Heart Association classification — no. (%)		
I	80 (3.2)	69 (2.7)
II	1123 (44.8)	1096 (43.6)
III	1208 (48.2)	1254 (49.9)
IV	96 (3.8)	96 (3.8)
Medical history — no. (%)		
Myocardial infarction	1911 (76.2)	1892 (75.2)
Stroke	208 (8.3)	245 (9.7)
Diabetes	1024 (40.8)	1028 (40.9)

Seguimiento 21 meses

IECA/ARA II 93%
BB 92%
ARM 72%

ANTIAGREGANTES 98%
(DOBLE) 36%

N Engl J Med 2018;379:1332-42.



HR (95% CI), 0,94 (0.84, 1.05); P=0.27

N Engl J Med 2018;379:1332-42.

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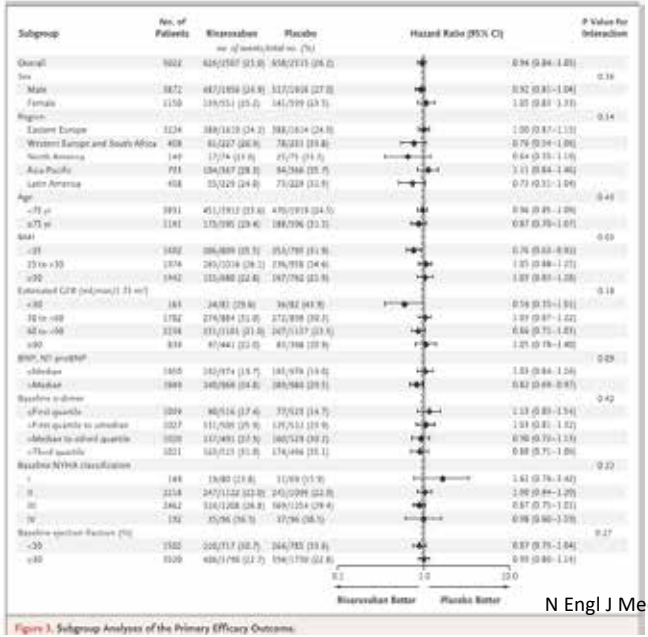

Figure 3. Subgroup Analyses of the Primary Efficacy Outcome.

N Engl J Med 2018;379:1332-42.

Table 2. Efficacy and Safety Outcomes.*

Outcome	Rivaroxaban (N = 2587)		Placebo (N = 2515)		Rivaroxaban vs. Placebo†	
	No. (%)	Events/ 100 Patient-Yr	No. (%)	Events/ 100 Patient-Yr	Hazard Ratio (95% CI)	P Value
Efficacy outcomes‡						
Composite primary efficacy outcome	626 (25.0)	13.44	659 (26.2)	14.27	0.94 (0.84–1.05)	0.27
Death from any cause	546 (21.8)	11.41	556 (22.1)	11.63	0.98 (0.87–1.10)	—
Myocardial infarction	98 (3.9)	2.08	118 (4.7)	2.52	0.83 (0.63–1.08)	—
Stroke	51 (2.0)	1.08	76 (3.0)	1.62	0.66 (0.47–0.95)	—
Secondary and exploratory efficacy outcomes						
Death from a cardiovascular cause or rehospitalization for worsening of heart failure	932 (37.2)	23.32	929 (36.9)	23.46	0.99 (0.91–1.09)	—
Death from a cardiovascular cause	453 (18.1)	9.46	476 (18.9)	9.96	0.95 (0.84–1.08)	—
Rehospitalization for worsening of heart failure	689 (27.5)	17.24	691 (27.5)	17.45	0.98 (0.89–1.09)	—
Rehospitalization for cardiovascular event other than worsening of heart failure	543 (21.7)	13.30	572 (22.7)	14.04	0.95 (0.84–1.07)	—
Death from any cause or rehospitalization for worsening of heart failure	993 (39.6)	24.84	973 (38.7)	24.57	1.01 (0.92–1.10)	—
Symptomatic deep-vein thrombosis	5 (0.2)	0.10	7 (0.3)	0.15	0.71 (0.23–2.24)	—
Symptomatic pulmonary embolism	11 (0.4)	0.23	9 (0.4)	0.19	1.23 (0.51–2.96)	—
	Rivaroxaban (N = 2499)		**Placebo (N = 2509)**		**Rivaroxaban vs. Placebo†**	
	No. (%)	Events/ 100 Patient-Yr	No. (%)	Events/ 100 Patient-Yr	Hazard Ratio (95% CI)	P Value
Safety outcomes§						
Composite principal safety outcome	18 (0.7)	0.44	23 (0.9)	0.55	0.80 (0.43–1.49)	0.48
Fatal bleeding	9 (0.4)	0.22	9 (0.4)	0.22	1.00 (0.41–2.39)	0.95
Bleeding into a critical space with potential for causing permanent disability	13 (0.5)	0.32	20 (0.8)	0.48	0.67 (0.33–1.34)	0.25
ISTH-defined major bleeding¶	82 (3.3)	2.04	50 (2.0)	1.21	1.68 (1.18–2.39)	0.003
Hemoglobin decrease of ≥2 g/dl	55 (2.2)	1.37	30 (1.2)	0.73	1.87 (1.20–2.91)	0.005
Transfusion of ≥2 units of packed red cells or whole blood	31 (1.2)	0.77	18 (0.7)	0.43	1.74 (0.98–3.12)	0.06
Bleeding at a critical site	25 (1.0)	0.62	23 (0.9)	0.56	1.12 (0.63–1.97)	0.70
Fatal bleeding	3 (0.1)	0.07	7 (0.3)	0.17	0.45 (0.12–1.72)	0.23
Bleeding requiring hospitalization	61 (2.4)	1.52	48 (1.9)	1.16	1.30 (0.89–1.90)	0.17

N Engl J Med 2018;379:1332-42.

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RIVAROXABÁN a dosis bajas (2.5 mg bid) NO mejora el pronóstico en pacientes con IC crónica y enfermedad coronaria en ritmo sinusal

1. COMMANDER-HF ha descartado el beneficio en pacientes con ingreso reciente por IC y NYHA III-IV
2. COMPASS avala el beneficio de rivaroxabán a dosis bajas junto con ácido acetilsalicílico (AAS) reduciendo la aparición de eventos vasculares en pacientes con IC leve o sin IC.

Además, las dosis bajas de rivaroxabán (no disponibles en el mercado europeo) no tienen beneficio en reducir eventos trombóticos, y los estudios disponibles no parece que vayan a cambiar las recomendaciones sobre el manejo de los pacientes con IC.

N Engl J Med 2018;379:1332-42.

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6.Diuréticos

- Edad
- Pluripatológico
- Cardiopatía estructural
- Congestión refractaria

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N Engl J Med 2017;377:1964 -75.

Circulation. 2019;139:e840–e878.

Resistencia a los diuréticos

ESC

POSITION PAPER

The use of diuretics in heart failure with congestion — a position statement from the Heart Failure Association of the European Society of Cardiology

Wilfried Mullens[1,2]*, Kevin Damman[3], Veli-Pekka Harjola[4], Alexandre Mebazaa[5], Hans-Peter Brunner-La Rocca[6], Pieter Martens[7,8], Jeffrey M. Testani[9], W.H. Wilson Tang[9], Francesco Orso[9], Patrick Rossignol[10], Manu Metra[11], Gerasimos Filippatos[12,13], Peter M. Seferovic[14], Frank Ruschitzka[15], and Andrew J. Coats[16]

Diuretic response and resistance in heart failure

In achieving euvolaemia, the degree of volume overload and diuretic response will determine the success of therapy.[15] The capacity of inducing natriuresis or diuresis following diuretic administration is defined as diuretic response. Diuretic resistance is defined as an impaired sensitivity to diuretics resulting in reduced natriuresis and diuresis limiting the possibilty to achieve euvolaemia.[16] Diuretic response should always be interpreted in light of the dose and type of the diuretic agent administered and the degree of volume overload, body composition and kidney function. As loop diuretics

Sensibilidad disminuida a los diuréticos

natriuresis y diuresis reducida que imposibilitan un estado euvolémico

- Tipo y dosis de diurético administrado
- Grado de sobrecarga
- Composición corporal
- Función renal

- En la práctica clínica, resistencia a los diureticos =resistencia a diuréticos de asa

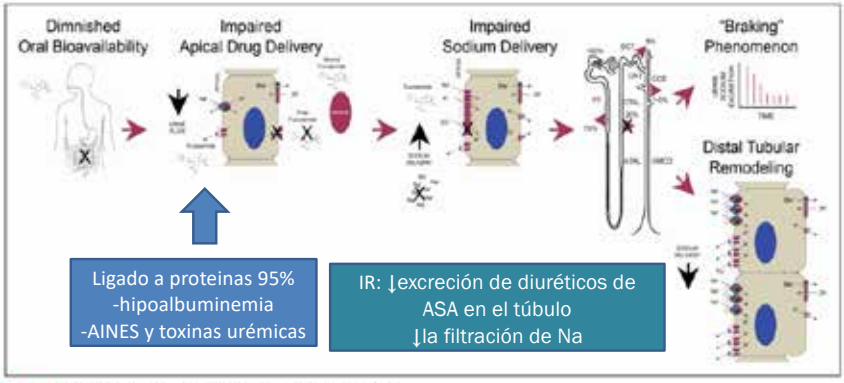

Figure 3. Mechanisms of diuretic resistance in cardiorenal syndrome.

IC ↑la reabsorción de Na en el TCProximal

IC ↑la reabsorción de Na en el TCDistal

Circulation. 2019;139:e840–e878.

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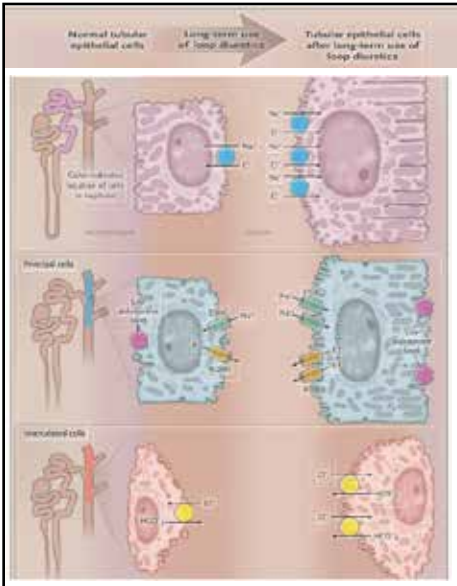

Table 1. Causes of Diuretic Resistance.

Inadequate dose of diuretic
Nonadherence
Not taking drug
High sodium intake
Pharmacokinetic factors
Slow absorption of diuretic because of gut edema
Impaired secretion of diuretic into the tubule lumen
Chronic kidney disease
Aging
Drugs
Nonsteroidal antiinflammatory drugs*
Probenecid
Hypoproteinemia
Hypotension
Nephrotic syndrome
Antinatriuretic drugs
Nonsteroidal antiinflammatory drugs*
Antihypertensive agents
Low renal blood flow
Nephron remodeling
Neurohormonal activation

N Engl J Med 2017;377:1964 -75.

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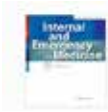
RESISTENCIA A LOS DIURETICOS



Internal and Emergency Medicine

June 2018, Volume 13, Issue 4, pp 541–632 | Cite as

Prevalence and outcome of diuretic resistance in heart failure: comment

2607 PACIENTES (RICA): 21%
RTD: > 80 MG FUROSEMIDA
AUMENTO DE MORTALIDAD A 1 AÑO
HR:1,37 (IC 95%: 1.06-1.79; P=0,018)

American Heart Journal

Volume 144, Issue 1, July 2002, Pages 31–38

Clinical Investigations: Congestive Heart Failure

Diuretic resistance predicts mortality in patients with advanced heart failure * **

Gerald W. Neuberg MD*, Alan B. Miller MD*, Chris M. O'Connor MD*, Robert N. Sellers MD*, Carson MD*, Anne B. Cropp PharmD*, David J. Frid MD*, Regina G. Nye MPH†, Milton L. Prosser MD*, John

1153 PACIENTES CON FEVI BAJA: 35%
RTD: > 80 MG FUROSEMIDA
AUMENTO DE MORTALIDAD
HR:1,37 (P=0,004)

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European Journal of Heart Failure (2014) 16, 1330–1340
doi:10.1002/ejhf.170

Diuretic response in patients with acute decompensated heart failure: characteristics and clinical outcome—an analysis from RELAX-AHF

Adriaan A. Voors[1]*, Beth A. Davison[2], John R. Teerlink[3], G. Michael Felker[4], Gad Cotter[2], Gerasimos Filippatos[5], Barry H. Greenberg[6], Peter S. Pang[7], Bruce Levin[8], Tsushung A. Hua[9], Thomas Severin[9], Piotr Ponikowski[10], Marco Metra[11], for the RELAX-AHF Investigators

PÉRDIDA DE PESO POR 40 MG DE FUROSEMIDA

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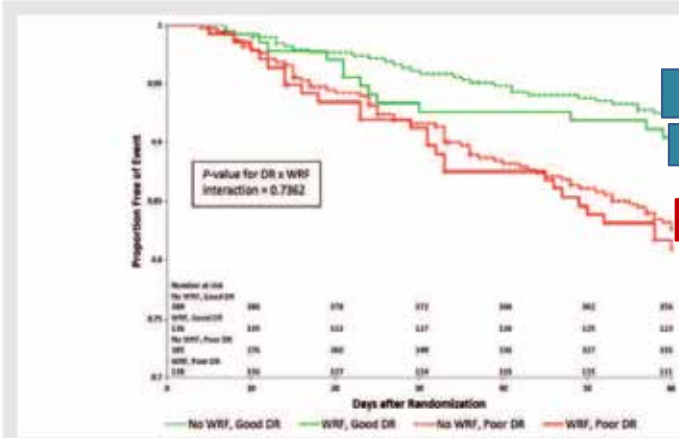

Figure 3 Kaplan–Meier survival curves presenting death or HF/RF readmission through day 60 in 1) patients with WRF and a poor diuretic response (<median); 2) patients with WRF and a good diuretic response (>median); 3) patients without WRF and a poor diuretic response (<median); 4) patients without WRF and a good diuretic response (>median). P = 0.7362 for Wald chi-square test of diuretic response- by-WRF interaction.

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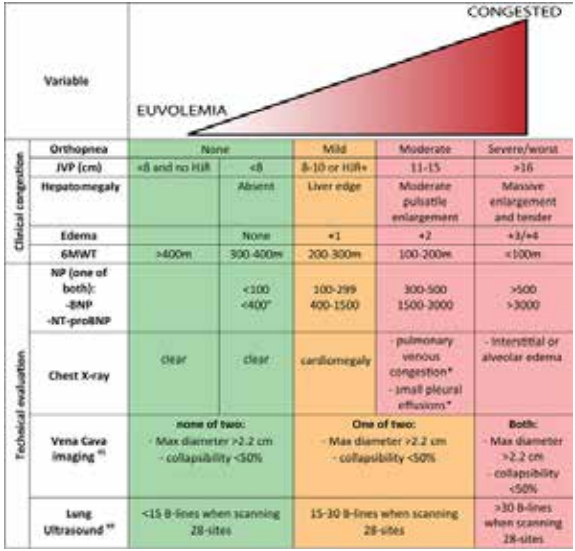
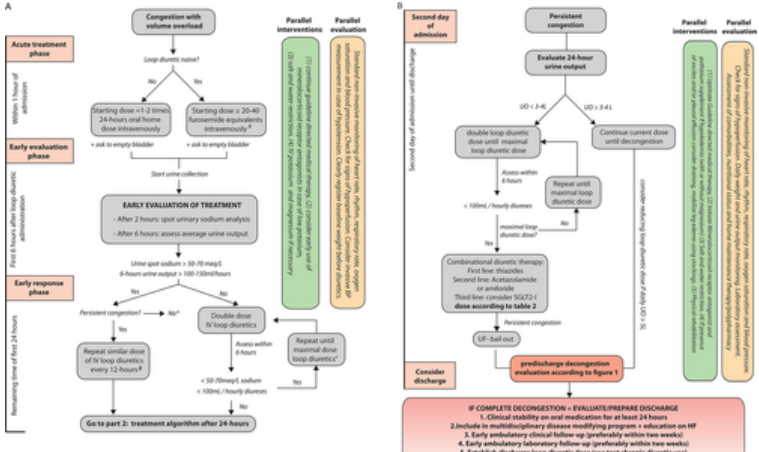


European Journal of Heart Failure, Volume: 21, Issue: 2, Pages: 137-155

The use of diuretics in heart failure with congestion — a position statement from the Heart Failure Association of the European Society of Cardiology



European Journal of Heart Failure, Volume: 21, Issue: 2, Pages: 137-155, First published: 01 January 2019, DOI: (10.1002/ejhf.1369)

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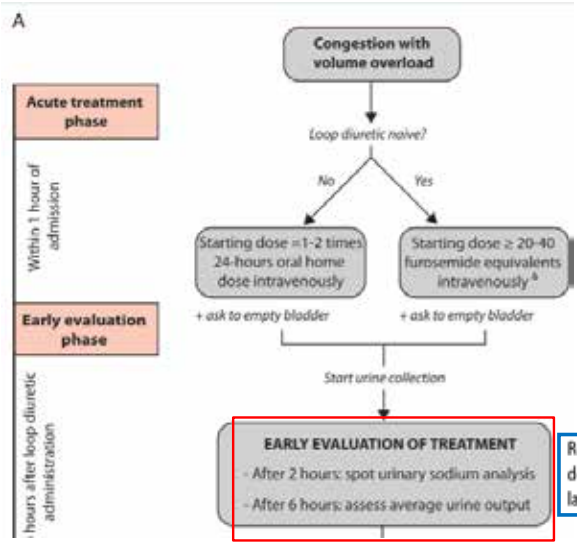

Requiere una evaluación inicial de la diuresis y la natriuresis en las primeras 6 horas

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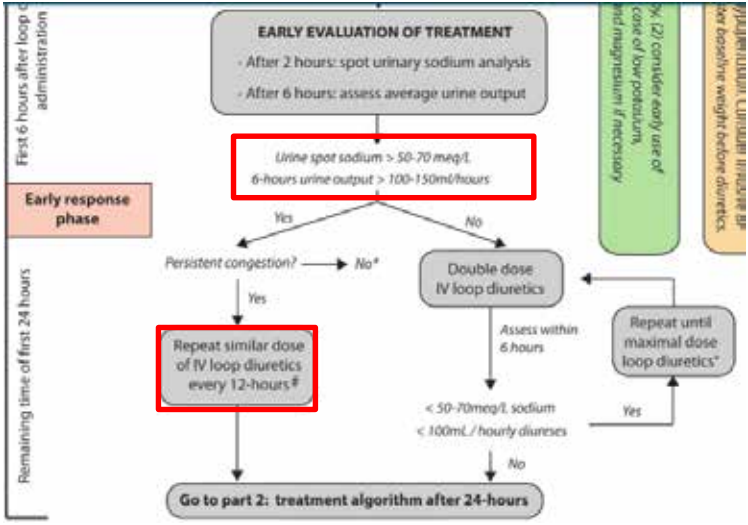

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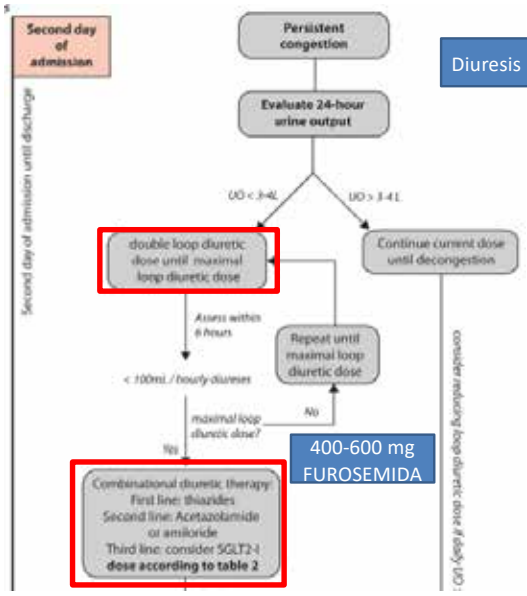
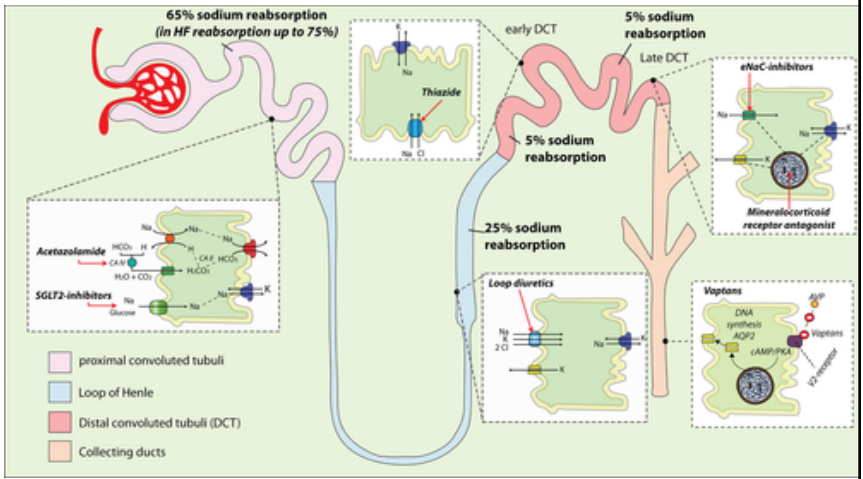


Diuresis bruta

400-600 mg FUROSEMIDA

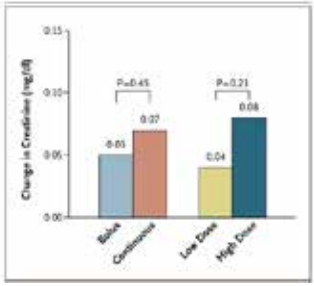


European Journal of Heart Failure, Volume: 21, Issue: 2, Pages: 137-155

Table 1. Baseline Characteristics of the Study Participants, According to Treatment Group.*

Characteristic	Bolus Every 12 Hr (N=156)	Continuous Infusion (N=152)	Low Dose (N=151)	High Dose (N=157)
Age — yr	66.2±13.2	65.8±14.1	65.5±13.3	66.2±13.9
Male sex — no. (%)	115 (74)	111 (73)	113 (75)	116 (74)
White race — no. (%)	114 (73)	108 (71)	106 (70)	116 (74)
Dose of oral furosemide or furosemide equivalent — mg/day	134±51	127±50	137±52	131±51
Ejection fraction (%)	35±18	35±18	31±17	36±18
Hospitalization for heart failure within previous 12 mo — no./total no. (%)	124/155 (74)	111/149 (74)	113/139 (77)	110/154 (71)
Ischemia as cause of heart failure — no. (%)	91 (58)	85 (56)	86 (58)	88 (56)
History of atrial fibrillation or flutter — no. (%)	84 (54)	78 (51)	82 (54)	80 (51)
Diabetes mellitus — no. (%)	81 (52)	77 (51)	77 (51)	81 (52)
Implantable cardioverter–defibrillator — no. (%)	63 (40)	56 (37)	62 (41)	57 (36)
ACE inhibitor or ARB — no. (%)	104 (67)	93 (61)	94 (62)	103 (66)
Beta blocker — no. (%)	130 (83)	123 (81)	125 (83)	131 (83)
Aldosterone antagonist — no. (%)	42 (27)	44 (29)	43 (28)	43 (27)
Systolic blood pressure — mm Hg	118±21	121±22	120±19	119±21
Heart rate — beats/min	76±14	80±17	78±15	79±17
Oxygen saturation — %	96±3	96±3	96±3	96±3
Jugular venous pressure ≥8 cm of water — no./total no. (%)	137/151 (91)	130/141 (92)	128/141 (91)	139/151 (92)
Orthopnea — no./total no. (%)	134/146 (92)	133/146 (90)	137/147 (93)	130/147 (88)
Sodium — mg/dl	138±4	138±4	138±4	138±4
BUN — mg/dl	37±21	38±24	36±23	37±22
Creatinine — mg/dl	1.5±0.5	1.5±0.5	1.5±0.5	1.5±0.5
NT-proBNP — pg/ml	7308±7097	7570±7517	8121±7624	6758±6961
Cystatin C — mg/liter	1.6±0.5	1.6±0.6	1.6±0.5	1.6±0.6

N Engl J Med 2011;364:797-805.



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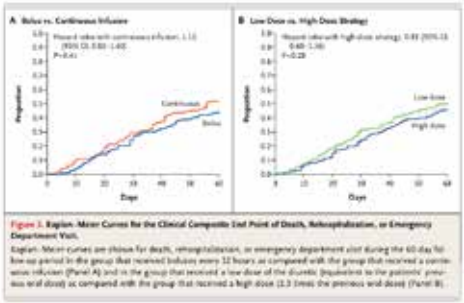

Figure 3. Kaplan–Meier Curves for the Clinical Composite End Point of Death, Rehospitalization, or Emergency Department Visit.

Kaplan–Meier curves are shown for death, rehospitalization, or emergency department visit during the 60-day follow-up period in the group that received boluses every 12 hours as compared with the group that received a continuous infusion (Panel A) and in the group that received a low dose of the diuretic (equivalent to the patients' previous oral dose) as compared with the group that received a high dose (2.5 times the previous oral dose) (Panel B).

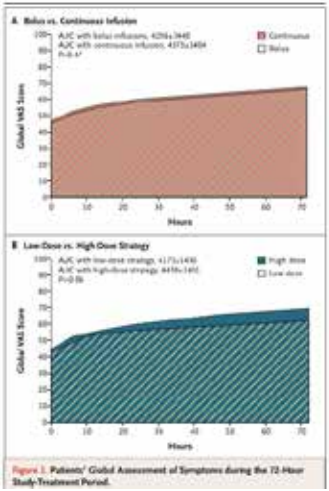

Figure 2. Patients' Global Assessment of Symptoms during the 72-Hour Study-Treatment Period.

Diuréticos de asa en bolo o perfusión continua tiene una efectividad similar respecto al control de los síntomas, pero la utilización de **dosis elevadas** frente a dosis baja favorece una mayor diuresis y existe una tendencia hacia un mejor control de los síntomas, sin diferencias en la función renal a las 72 horas.

N Engl J Med 2011;364:797-805.

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TIAZIDAS

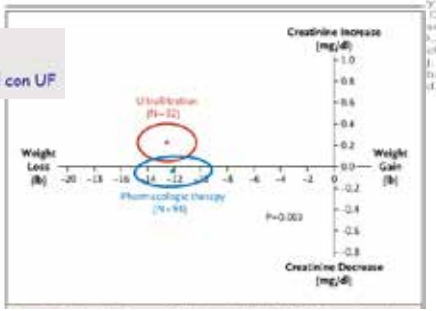
THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ultrafiltration in Decompensated Heart Failure with Cardiorenal Syndrome

Lee, Ph.D., David A. Bull, M.D., Jan L. Rouleau, M.D., M.P.H., Michael Felker, M.D., Anstrom, Ph.D., Harra, R.N., M.S.N., M.D.,

= disnea y pérdida de peso.
= reingresos y mortalidad
> Empeoramiento función renal con UF



	Current Dose		Suggested Dose	
	loop (/day)	thiazide	loop (/day)	thiazide
A	≤ 80	+ or -	40 mg iv bolus+ 5 mg/hr	0
B	81-160	+ or -	80 mg iv bolus+ 10 mg/hr	5 mg metazolone QD
C	161-240	+ or -	80 mg iv bolus+ 20 mg/hr	5 mg metazolone BID
D	> 240	+ or -	80 mg iv bolus+ 30 mg/hr	5 mg metazolone BID

ESPIRONOLACTONA

Efficacy and Safety of Spironolactone in Acute Heart Failure

The ATHENA-HF Randomized Clinical

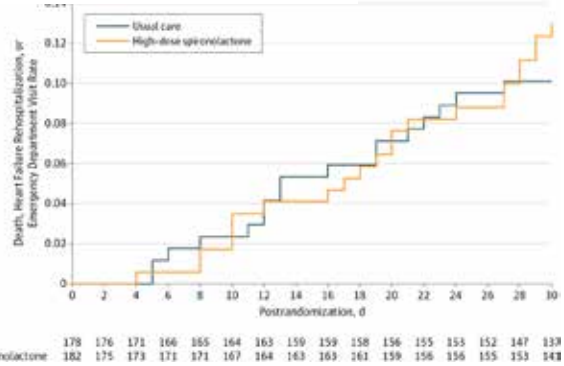
360 pacientes. Multicéntrico. Doble ciego

Espironolactona 100 mg *vs.* placebo (o espironolactona 25 mg) IC aguda

96 horas

= Disnea
= Pérdida de peso
= Diuresis

Sin mayor hiperpotasemia o deterioro función renal



JAMA Cardiol. 2017;2(9):950-958.

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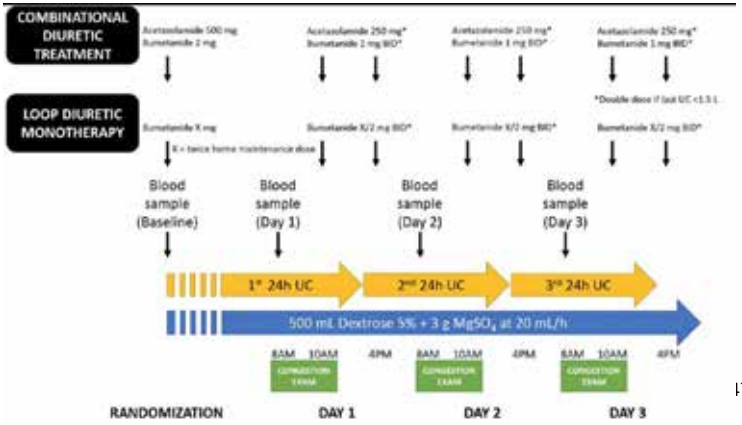
ACETAZOLAMIDA

Research Article

Acetazolamide to increase natriuresis in congestive heart failure at high risk for diuretic resistance



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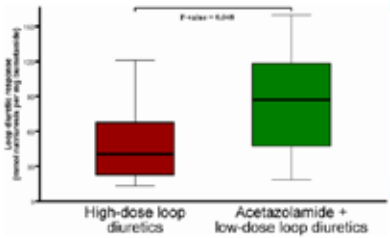

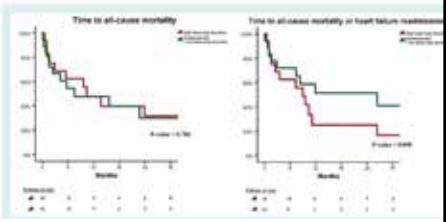

European Journal of
Heart Failure

Study Design

Rationale and design of the ADVOR (Acetazolamide in Decompensated Heart Failure with Volume Overload) trial

Wilfried Mullens, Frederik H. Verbrugge, Petra Nijst, Pieter Martens, Katrien Tartaglia, Evi Theunissen, Liesbeth Bruckers, Walter Droogne, Pierre Troisfontaines, Kevin Damman ... See all authors

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SGTL2

CARDIOVASCULAR DISEASE

Recommendations

Screening

10.34 In asymptomatic patients, routine screening for coronary artery disease is not recommended as it does not improve outcomes as long as atherosclerotic cardiovascular disease risk factors are treated. A

10.35 Consider investigations for coronary artery disease in the presence of any of the following: atypical cardiac symptoms (e.g., unexplained dyspnea, chest discomfort), signs or symptoms of associated vascular disease including carotid bruits, transient ischemic attack, stroke, claudication, or peripheral arterial disease; or electrocardiogram abnormalities (e.g., Q waves). E

STANDARDS OF MEDICAL CARE IN DIABETES—2019

Treatment

10.36 In patients with known atherosclerotic cardiovascular disease, consider ACE inhibitor or angiotensin receptor blocker therapy to reduce the risk of cardiovascular events. B

10.37 In patients with prior myocardial infarction, β-blockers should be continued for at least 2 years after the event. B

10.38 In patients with type 2 diabetes with stable congestive heart failure, metformin may be used if estimated glomerular filtration rate remains >30 mL/min but should be avoided in unstable or hospitalized patients with congestive heart failure. B

10.39 Among patients with type 2 diabetes who have established atherosclerotic cardiovascular disease, sodium-glucose cotransporter 2 inhibitors or glucagon-like peptide 1 receptor agonists with demonstrated cardiovascular disease benefit (Table 9.1) are recommended as part of the antihyperglycemic regimen. A

10.40 Among patients with atherosclerotic cardiovascular disease at high risk of heart failure or in whom heart failure coexists, sodium-glucose cotransporter 2 inhibitors are preferred. C

Metformina

I SGTL2
A GLP1

I SGTL2

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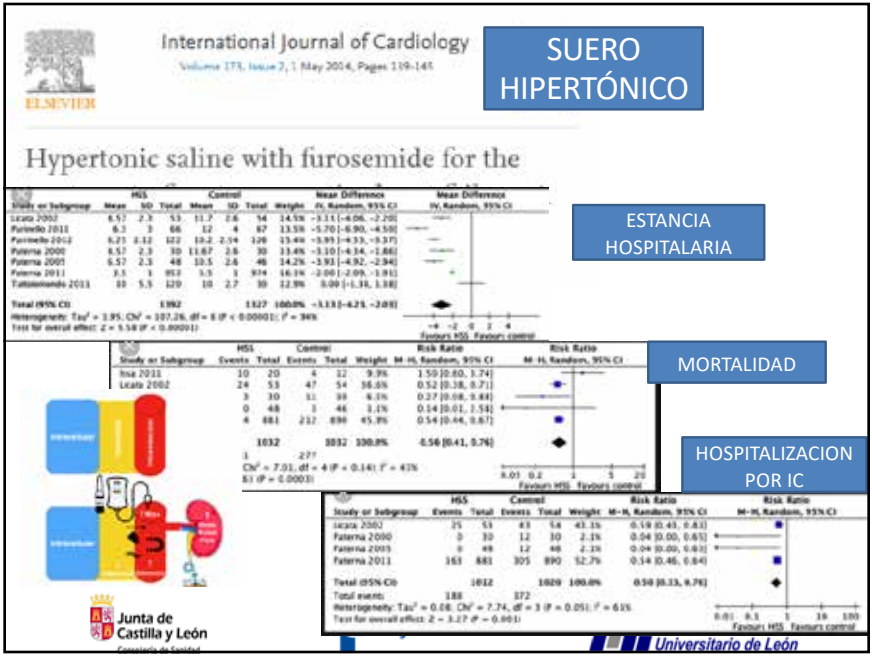
International Journal of Cardiology
Volume 178, Issue 2, 1 May 2014, Pages 139-141
SUERO HIPERTÓNICO
Hypertonic saline with furosemide for the
ESTANCIA HOSPITALARIA
MORTALIDAD
HOSPITALIZACION POR IC
Junta de Castilla y León
Universitario de León

VAPTANES

-La vasopresina promover la retención de fluidos a nivel renal.

-Tolvaptan, un antagonista de los receptores V2, ha sido propuesto como un potencial tratamiento de la insuficiencia cardíaca congestiva,

contrarrestar el efecto antidiurético de la vasopresina y a su vez generar menos trastornos en la función renal o en el medio interno, con relación a los diuréticos de asa.

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Journal of Cardiology 63 (2014) 169–174

Contents lists available at SciVerse ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Tolvaptan reduces the risk of worsening renal function in patients with acute decompensated heart failure in high-risk population

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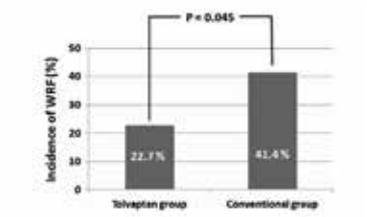

Fig. 2. The incidence of WRF in the tolvaptan group and conventional therapy group. WRF, worsening of renal function.

JAMA. 2007 Mar 28;297(12):1332-43. Epub 2007 Mar 25.

Short-term clinical effects of tolvaptan, an oral vasopressin antagonist, in patients hospitalized for heart failure: the EVEREST Clinical Status Trials.

Gheorghiade M[1], Konstam MA, Burnett JC Jr, Grinfeld L, Maggioni AP, Swedberg K, Udelson JE, Zannad F, Cook T, Ouyang J, Zimmer C, Orlandi C; Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan (EVEREST) Investigators.

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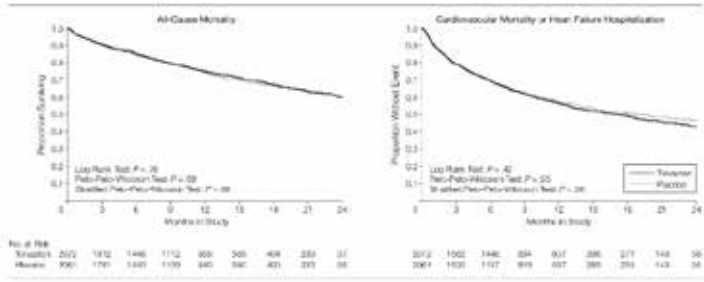

Figure 2. Kaplan-Meier Analyses of All-Cause Mortality and Cardiovascular Mortality or Hospitalization for Heart Failure

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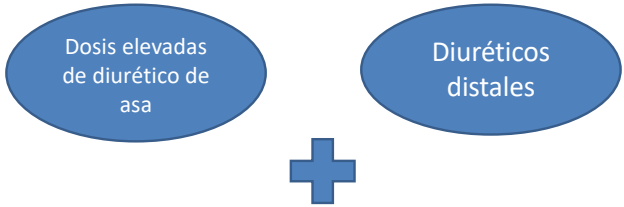

Monitorización paralela de la diuresis y natriuresis, asegurando la perfusión multiorgánica en todo momento

Piedra angular del manejo de los pacientes congestivos y con resistencia a diuréticos.

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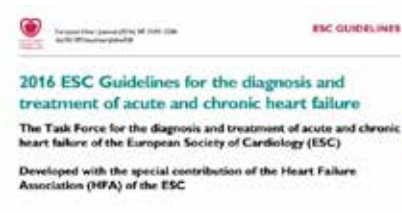
RIESGO DE RESISTENCIA A DIURETICO

INCERTIDUMBRE EN EL TRATAMIENTO

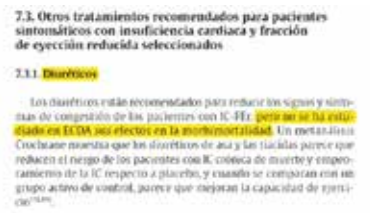


ESC GUIDELINES

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

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

Developed with the special contribution of the Heart Failure Association (HFA) of the ESC



7.3. Otros tratamientos recomendados para pacientes sintomáticos con insuficiencia cardiaca y fracción de eyección reducida seleccionados

7.3.1. Diuréticos

Los diuréticos están recomendados para reducir los signos y síntomas de congestión de los pacientes con IC-FEr, pero no se ha estudiado en ECDA sus efectos en la morbimortalidad. Un metanálisis Cochrane muestra que los diuréticos de asa y las tiacidas parece que reducen el riesgo de los pacientes con IC crónica de muerte y empeoramiento de la IC respecto a placebo, y cuando se comparan con un grupo activo de control, parece que mejoran la capacidad de ejercicio[78,79].

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