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Nous abordatges en el tractament de la insuficiència cardíaca crònica

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Guió

- Causes de mort en IC
- Diagnòstic HFpEF
- Tractament farmacològic:
  - HFrEF: DAPA-HF, PIONEER-HF, PROVE-HF
  - HFpEF: PARAGON-HF
- Tractament no farmacològic:
  - CARDIOMEMS
  - Moduladors contractilitat cardíaca.
- Cures Pal·liatives
- Futur
- Conclusions

ESC European Society of Cardiology

European Journal of Heart Failure (2019)
doi:10.1002/ejhf.1569

RESEARCH ARTICLE

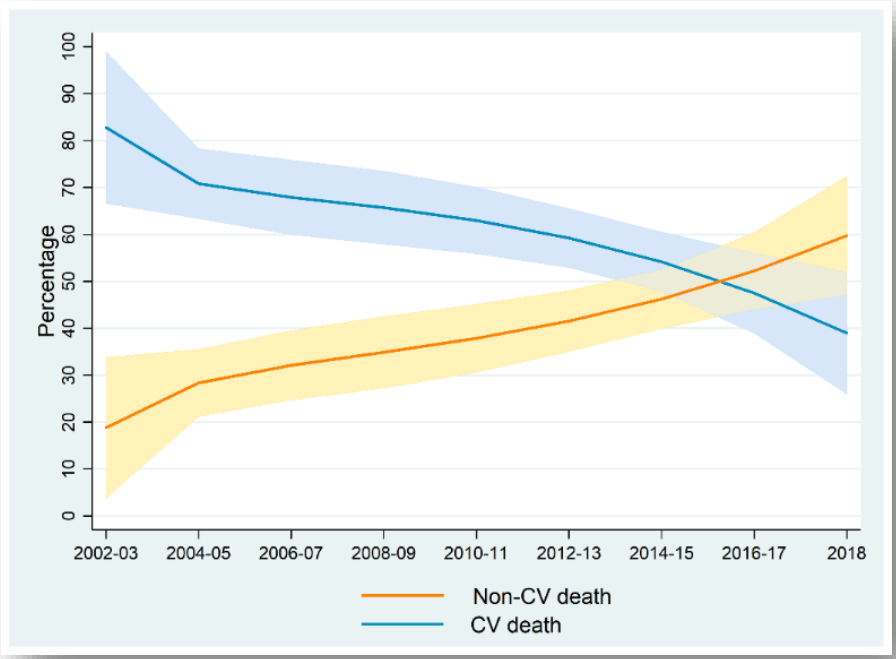
Trends in modes of death in heart failure over the last two decades: less sudden death but cancer deaths on the rise

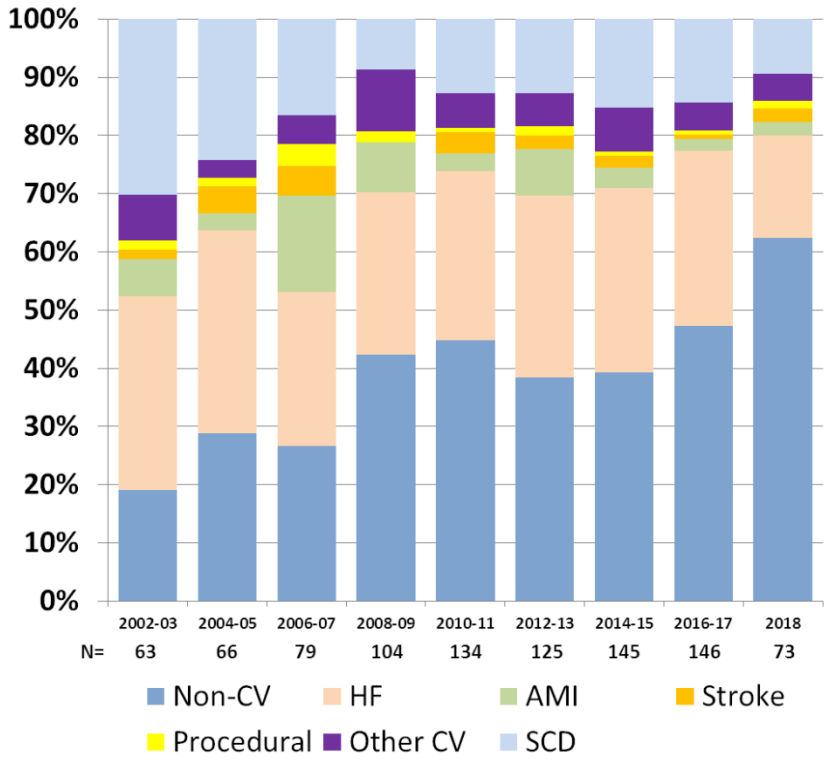
**Pedro Moliner[1,2], Josep Lupón[1,2,3], Marta de Antonio[1,3], Mar Domingo[1], Evelyn Santiago-Vacas[1,4], Elisabet Zamora[1,2,3], Germán Cediel[1,2], Javier Santesmases[1,2], Crisanto Díez-Quevedo[1], Maria Isabel Troya[1], Maria Boldó[1], Salvador Altmir[1], Nuria Alonso[1], Beatriz González[1], Julio Núñez[5,6], and Antoni Bayes-Genis[1,2,3]*

- 2002-2018.
- 1876 pts. 935 morts.
- Exclusió 74 pacients (7,3%) casusa desconeguda

Moliner et al. Trends in modes of death in heart failure over the last two decades: less sudden death but cancer deaths on the rise. Eur J Heart Fail. 2019

Causes de mort en IC





Reducció de la mort cardiovascular

- ↓ Mort sobtada (p = 0,03) primers 10 a (p < 0,001)
- No canvis significatius en la progressió IC com a causa de mort (p = 0,26)

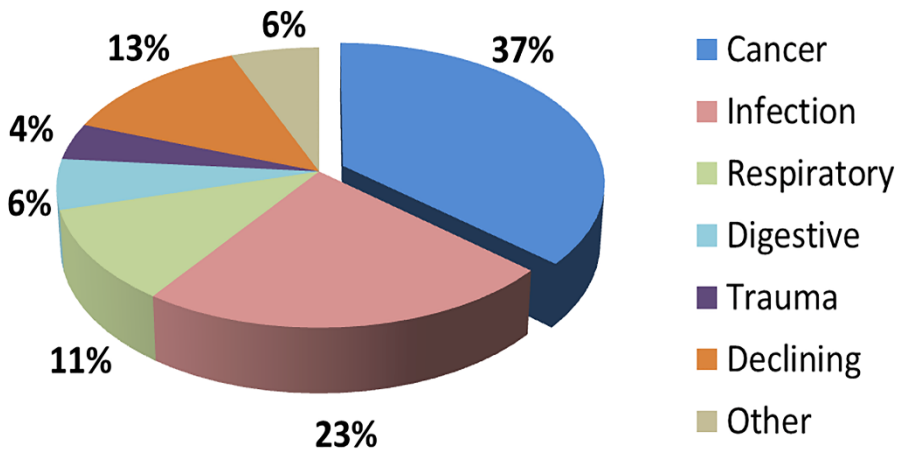
Increment de la mortalitat no cardiovascular

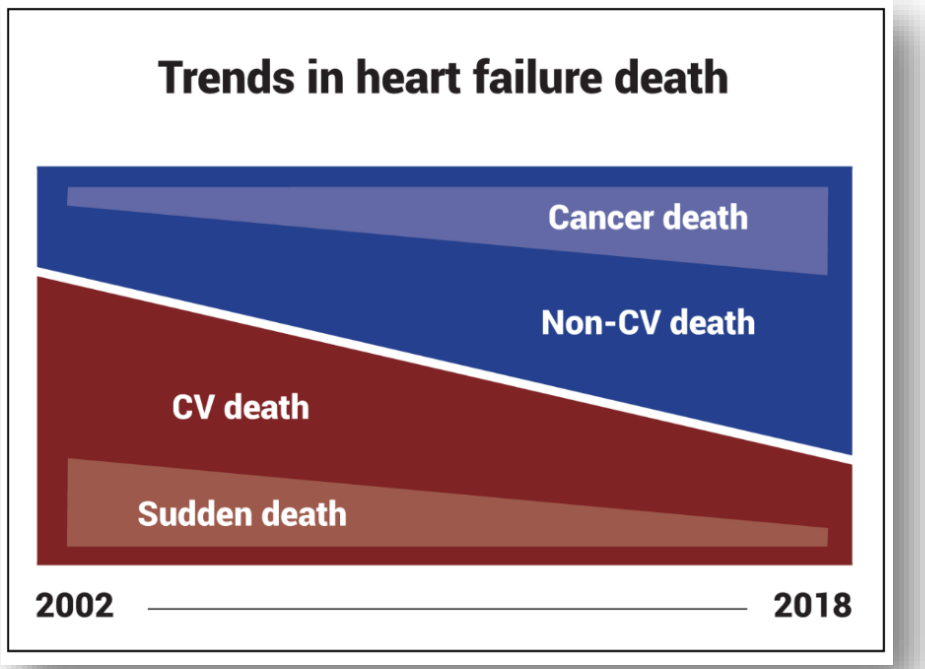
Moliner et al. Trends in modes of death in heart failure over the last two decades: less sudden death but cancer deaths on the rise. Eur J Heart Fail. 2019

Causes de mort en IC

Increment de la mortalitat no cardiovascular

- Augment líneal molt significatiu (p <0,001)
- El càncer va ser la causa més freqüent de mortalitat cardiovascular.





Moliner et al. Trends in modes of death in heart failure over the last two decades: less sudden death but cancer deaths on the rise. Eur J Heart Fail. 2019

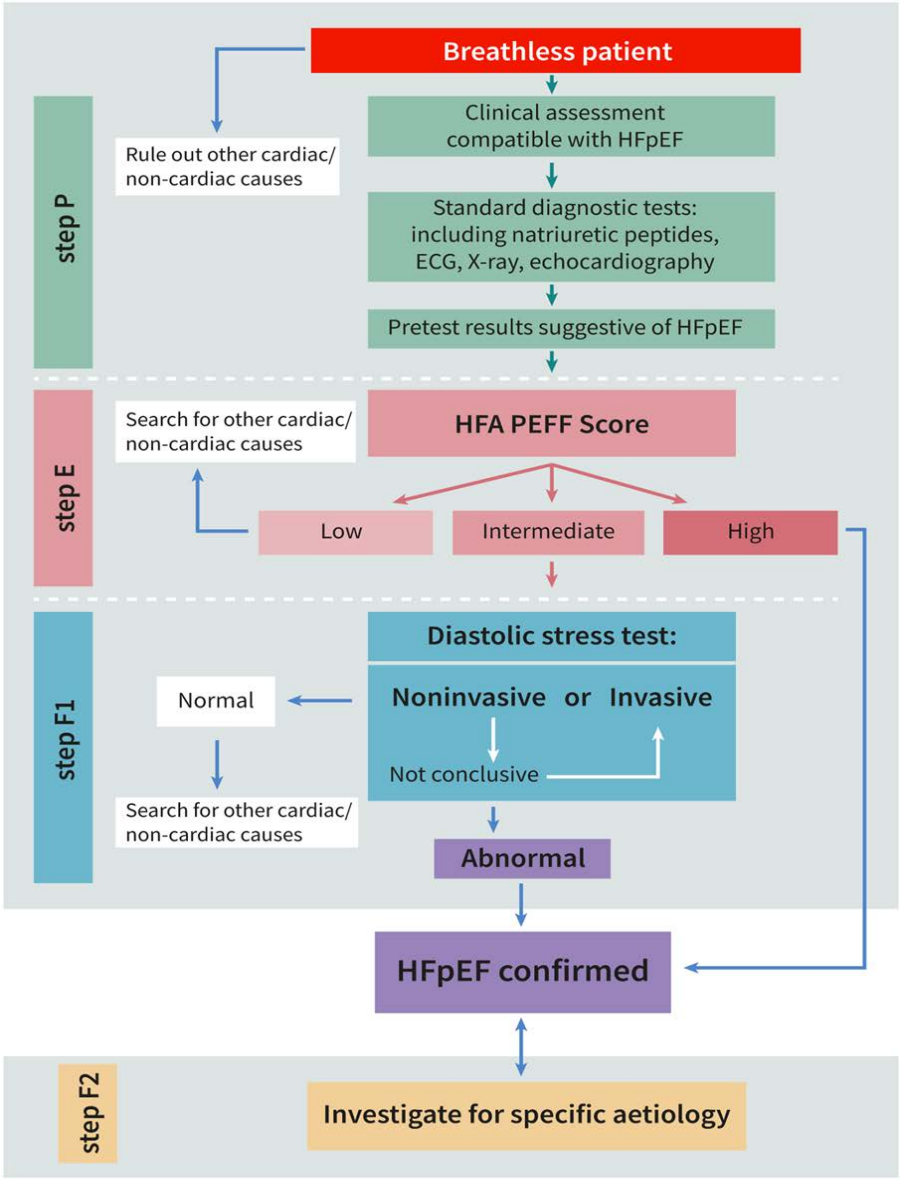
Diagnòstic HFpEF

ESC European Society of Cardiology
European Heart Journal (2019) **40**, 3297–3317
doi:10.1093/eurheartj/ehz641

FASTTRACK CLINICAL RESEARCH
Heart failure/cardiomyopathy

How to diagnose heart failure with preserved ejection fraction: the HFA–PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC)

Burkert Pieske[1,2,3,4]*, Carsten Tschöpe[1,2,5], Rudolf A. de Boer[6], Alan G. Fraser[7], Stefan D. Anker[1,2,5,8], Erwan Donal[9], Frank Edelmann[1,2], Michael Fu[10], Marco Guazzi[11,12], Carolyn S.P. Lam[13,14], Patrizio Lancellotti[15], Vojtech Melenovsky[16], Daniel A. Morris[1], Eike Nagel[17,18], Elisabeth Pieske-Kraigher[1], Piotr Ponikowski[19], Scott D. Solomon[20], Ramachandran S. Vasan[21], Frans H. Rutten[22], Adriaan A. Voors[6], Frank Ruschitzka[23], Walter J. Paulus[24], Petar Seferovic[25], and Gerasimos Filippatos[26,27]

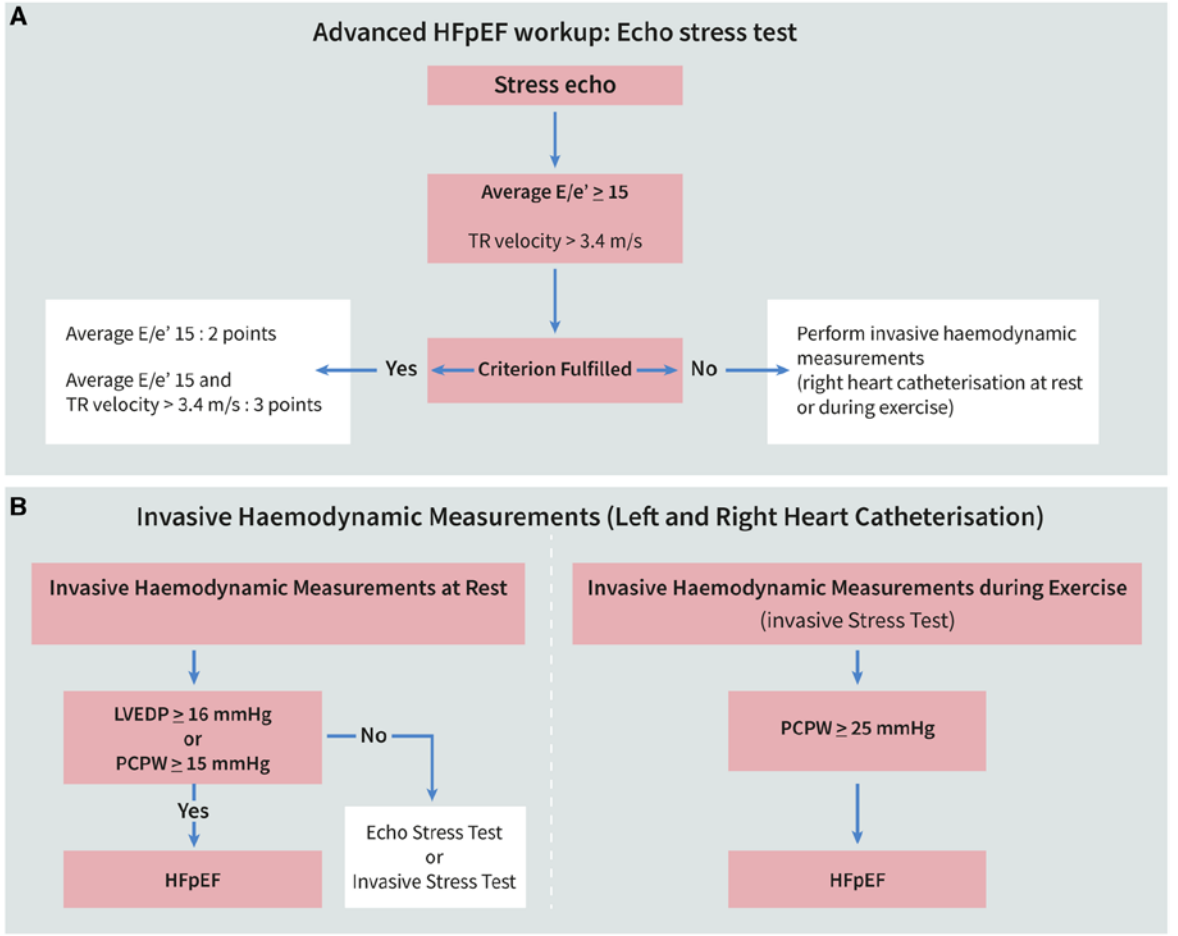


Pieske. Eur Heart J 2019; 40:3297-3317

Diagnòstic HFpEF

	Functional	Morphological	Biomarker (SR)	Biomarker (AF)
Major	septal e' < 7 cm/s or lateral e' < 10 cm/s or Average E/e' ≥ 15 or TR velocity > 2.8 m/s (PASP > 35 mmHg)	LAVI > 34 ml/m² or LVMI ≥ 149/122 g/m² (m/w) and RWT > 0,42 #	NT-proBNP > 220 pg/ml or BNP > 80 pg/ml	NT-proBNP > 660 pg/ml or BNP > 240 pg/ml
Minor	Average E/e' 9 -14 or GLS < 16 %	LAVI 29-34 ml/m² or LVMI > 115/95 g/m² (m/w) or RWT > 0,42 or LV wall thickness ≥ 12 mm	NT-proBNP 125-220 pg/ml or BNP 35-80 pg/ml	NT-proBNP 365-660 pg/ml or BNP 105-240 pg/ml

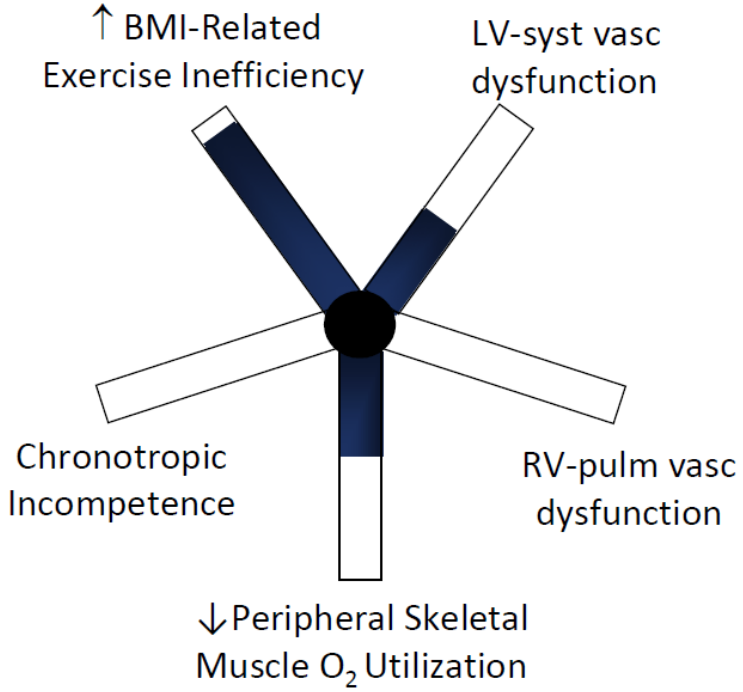
Major Criteria: 2 points	≥ 5 points: HFpEF
Minor Criteria: 1 point	2-4 points: Diastolic Stress Test or Invasive Haemodynamic Measurements



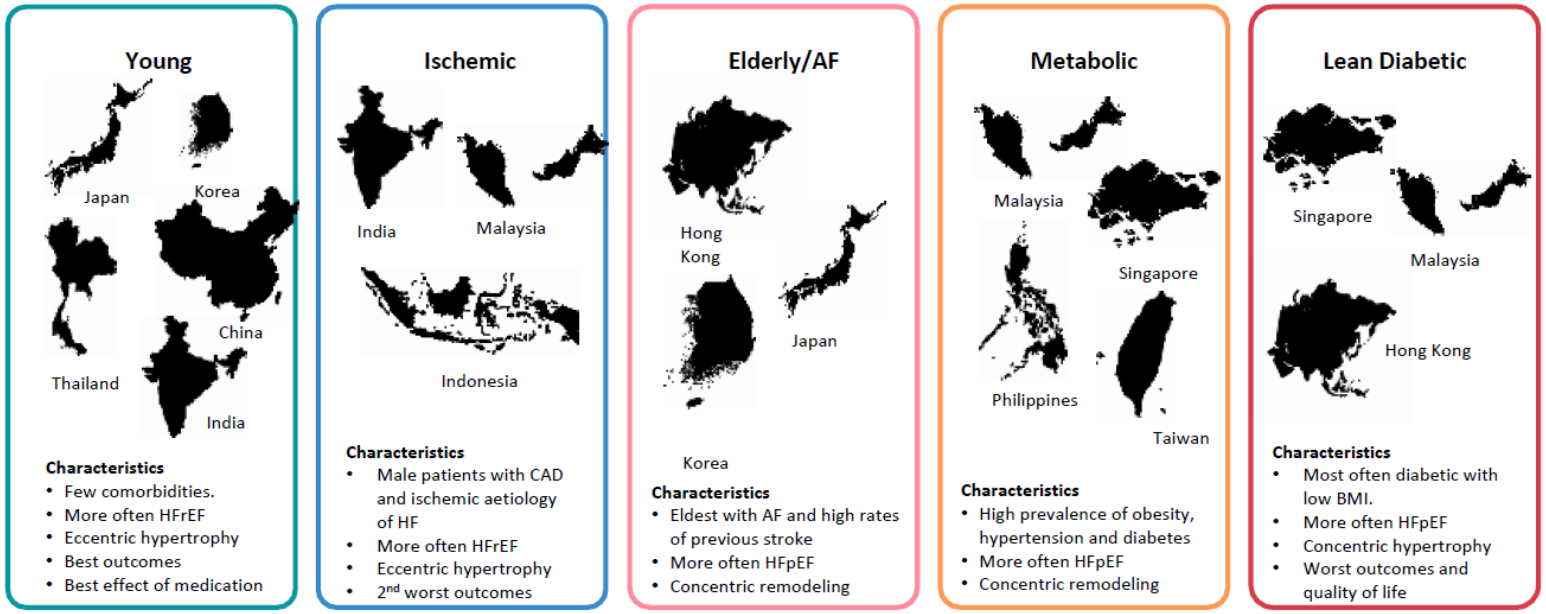
Pieske. Eur Heart J 2019; 40:3297-3317

Diagnòstic HFpEF

Heterogeneïtat. Diferents fenotips



Comorbidity clusters in ASIAN-HF.



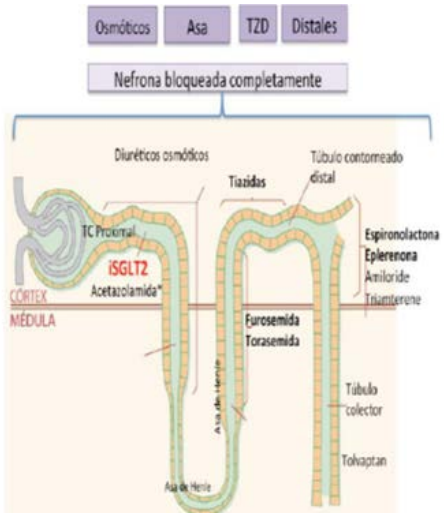
Tromp. PLOS MED. 2018

TRACTAMENT FARMACOLÒGIC HFrEF

ISGLT2

Assaigs en DM ISGLT2 redueixen el risc hospitalització per IC i preserven funció renal:

- EMPA-REG (Empaglifozina)
- CANVAS (Canaglifozina)
- DECLARE-TIMI 58 (Dapglifozina)



ESC European Society of Cardiology

European Journal of Heart Failure (2019)
doi:10.1002/ejhf.1531

CONSENSUS DOCUME

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

Petar M. Seferovic[1], Piotr Ponikowski[2], Stefan D. Anker[3]*, Johann Bauersachs[4], Ovidiu Chioncel[5], John G.F. Cleland[6], Rudolf A. de Boer[7], Heinz Drexel[8], Tuvia Ben Gal[9], Loreena Hill[10], Tiny Jaarsma[11], Ewa A. Jankowska[2], Markus S. Anker[12], Mitja Lainscak[13], Basil S. Lewis[14], Theresa McDonagh[15], Marco Metra[16], Davor Milicic[17], Wilfried Mullens[18], Massimo F. Piepoli[19], Giuseppe Rosano[20], Frank Ruschitzka[21], Maurizio Volterrani[22], Adriaan A. Voors[7], Gerasimos Filippatos[23], and Andrew J.S. Coats[24]*

Sodium–glucose co-transporter 2 inhibitors

Consensus recommendation

The 2016 guidelines indicated that empagliflozin *should be considered* in patients with type 2 diabetes mellitus (T2DM) in order to prevent or delay the onset of HF or prolong life.[8]

The 2019 expert consensus was that canagliflozin and dapagliflozin *should also be considered* for patients with T2DM and either established cardiovascular (CV) disease or at high CV risk in order to prevent or delay the onset of and hospitalizations for HF.

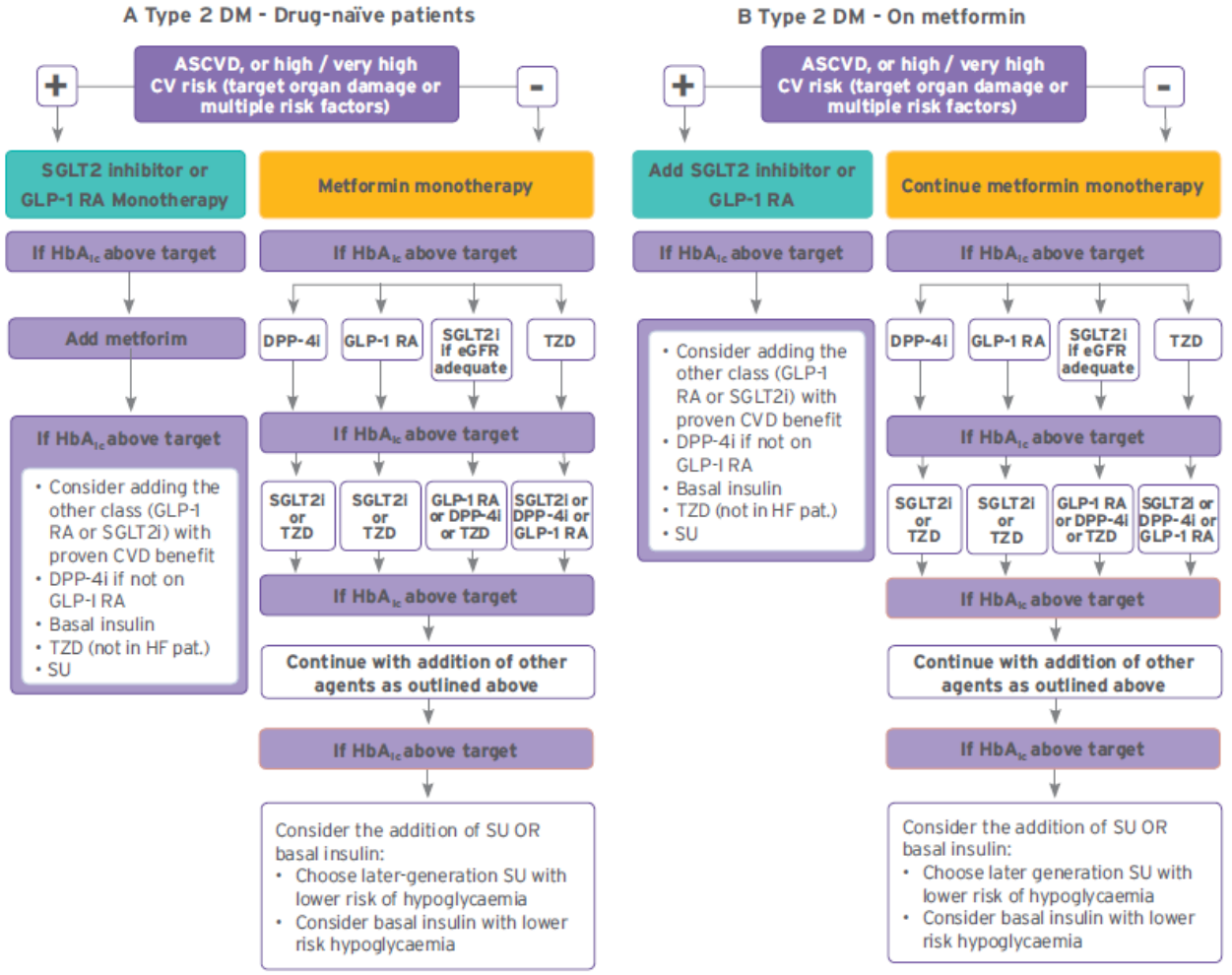
At this stage, no specific recommendations for the use of sodium–glucose co-transporter 2 (SGLT2) inhibitors in patients with established HF can be made.

Seferovic F et al. 2019 Clinical practice update no heart failure 20198 . *Eur J Heart Failure*. 2019.

ISGLT2

Table 6. Recommendations for Glucose-Lowering Treatment for Patients with Diabetes

Recommendations	Class[a]	Level[b]
SGLT2 inhibitors		
Empagliflozin, canagliflozin, or dapagliflozin are recommended in patients with T2DM and CVD, or at very high/high CV risk, to reduce CV events.	I	A
Empagliflozin is recommended in patients with T2DM and CVD to reduce the risk of death.	I	B



Cosentino F et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. *Eur Heart J*. 2019.

DAPA-HF

The NEW ENGLAND JOURNAL of MEDICINE

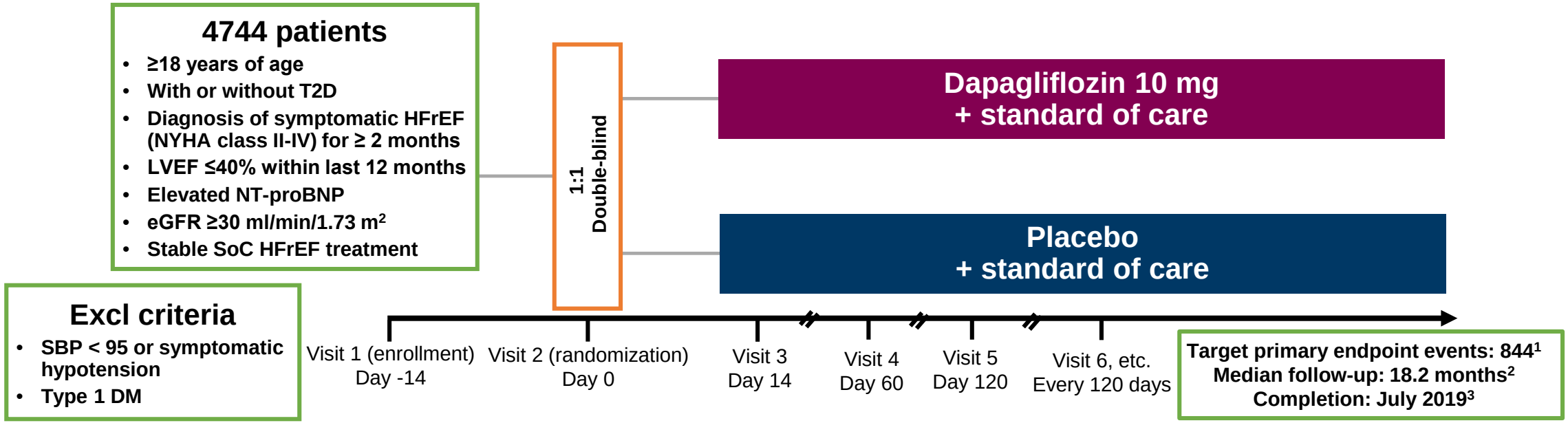
ORIGINAL ARTICLE

Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

J.J.V. McMurray, S.D. Solomon, S.E. Inzucchi, L. Køber, M.N. Kosiborod, F.A. Martinez, P. Ponikowski, M.S. Sabatine, I.S. Anand, J. Bělohlávek, M. Böhm, C.-E. Chiang, V.K. Chopra, R.A. de Boer, A.S. Desai, M. Diez, J. Drozdz, A. Dukát, J. Ge, J.G. Howlett, T. Katova, M. Kitakaze, C.E.A. Ljungman, B. Merkely, J.C. Nicolau, E. O'Meara, M.C. Petrie, P.N. Vinh, M. Schou, S. Tereshchenko, S. Verma, C. Held, D.L. DeMets, K.F. Docherty, P.S. Jhund, O. Bengtsson, M. Sjöstrand, and A.-M. Langkilde, for the DAPA-HF Trial Committees and Investigators*

1. McMurray JJV et al. Dapagliflozin in patients with heart failure and reduced ejection fraction.N Engl J Med2019;381:1995–2008.

DAPA-HF



Primary Endpoint

- **Time to first occurrence of any of the components of the composite: CV death or hHF or an urgent HF visit**

Secondary Endpoints

- **Time to first occurrence of either of the components of the composite: CV death or hHF**
- **Total number of (first and recurrent) hHF and CV death**
- **Change from baseline measured at 8 months in the total symptom score of the KCCQ**
- **Time to first occurrence of any of the components of the composite: ≥50% sustained decline in eGFR or reaching ESRD or renal death**
- **Time to death from any cause**

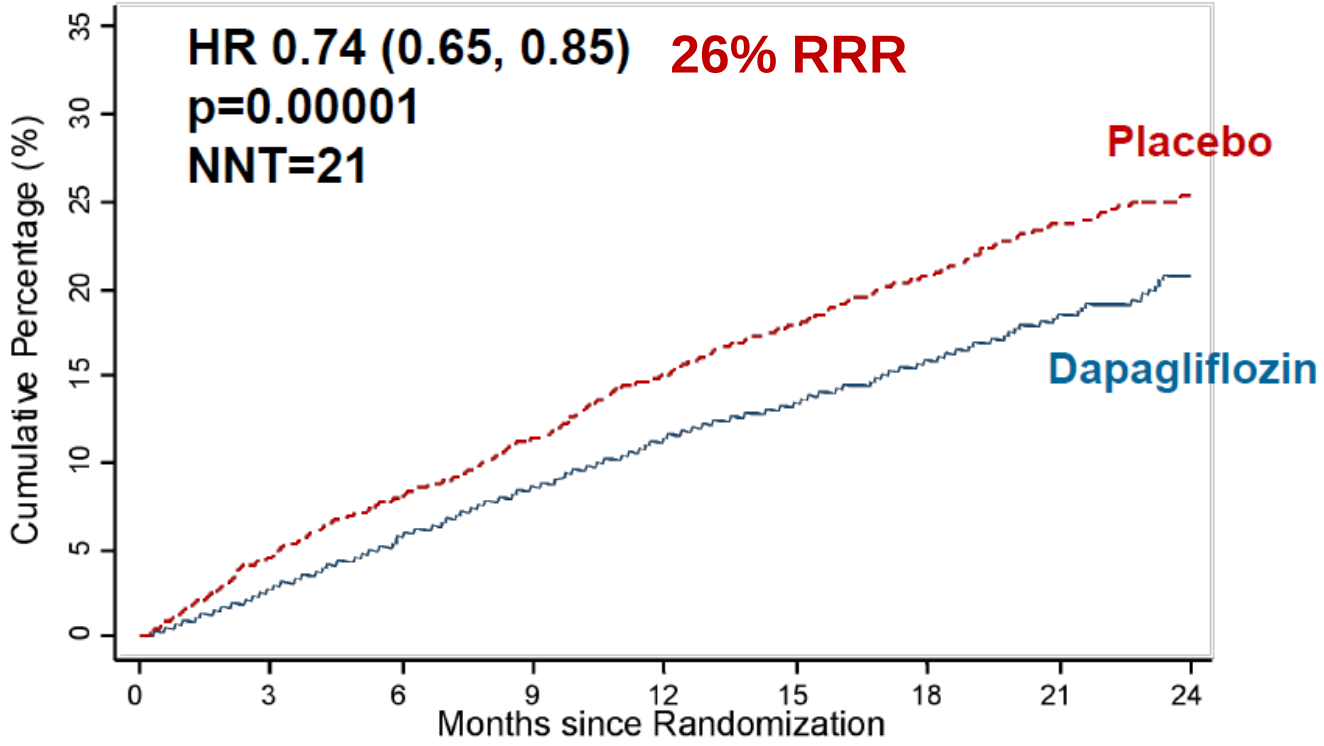
CV = cardiovascular; eGFR = estimated glomerular filtration rate; ESRD = end stage renal disease; HbA1c = glycated hemoglobin; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; hHF = hospitalization for heart failure; KCCQ = Kansas City Cardiomyopathy Questionnaire; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro B-type natriuretic peptide; NYHA = New York Heart Association; SoC = standard of care; T2D = type 2 diabetes.

1. McMurray JJV et al. Dapagliflozin in patients with heart failureand reduced ejection fraction.N Engl J Med2019;381:1995–2008.

DAPA-HF

Primary composite outcome

CV Death/HF hospitalization/Urgent HF visit



Number at Risk

Dapagliflozin	2373	2305	2221	2147	2002	1560	1146	612	210
Placebo	2371	2258	2163	2075	1917	1478	1096	593	210

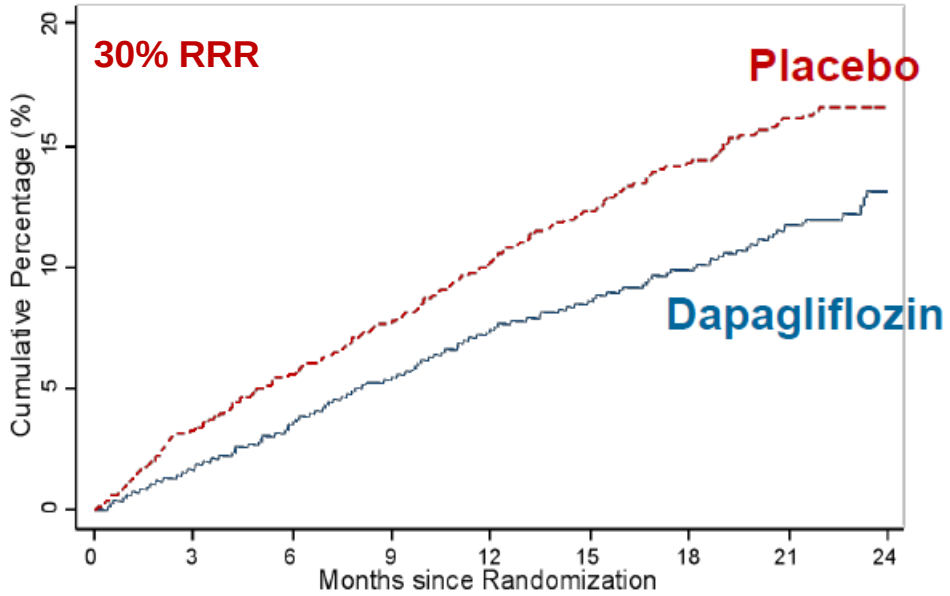
1. McMurray JJV et al. Dapagliflozin in patients with heart failure and reduced ejection fraction.N Engl J Med2019;381:1995–2008.

DAPA-HF

Components of primary outcome

Worsening HF event

HR 0.70 (0.59, 0.83); p=0.00003

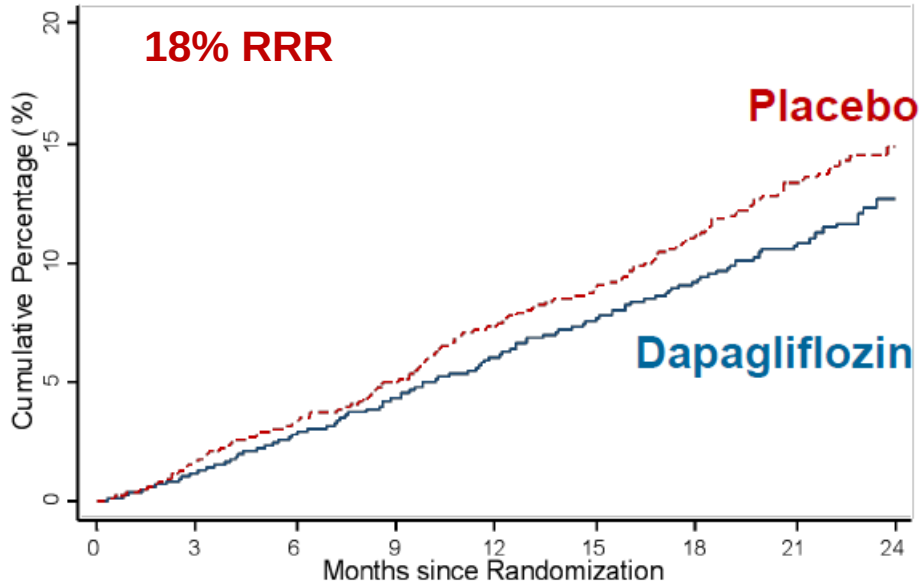


Number at Risk

Dapagliflozin	2373	2305	2221	2147	2002	1560	1146	612	210
Placebo	2371	2258	2163	2075	1917	1478	1096	593	210

Cardiovascular death

HR 0.82 (0.69, 0.98); p=0.029

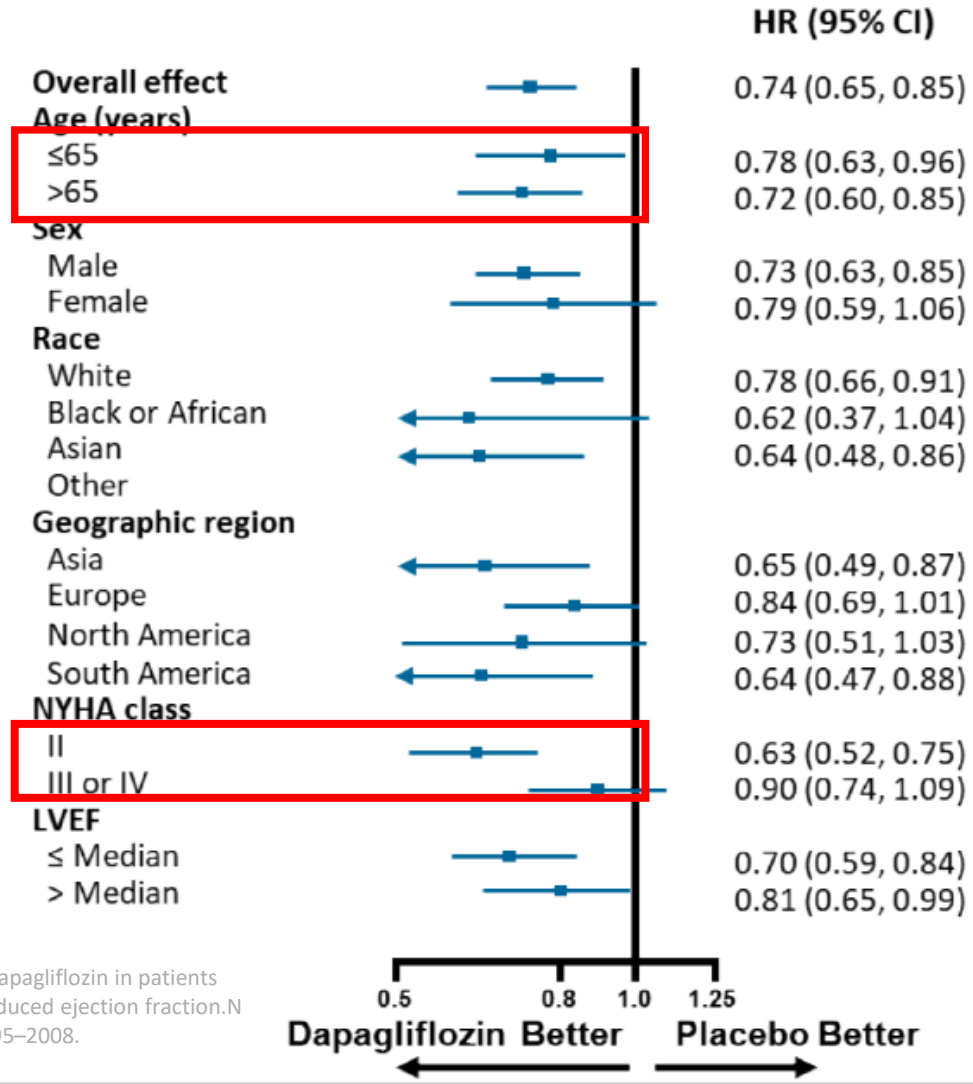


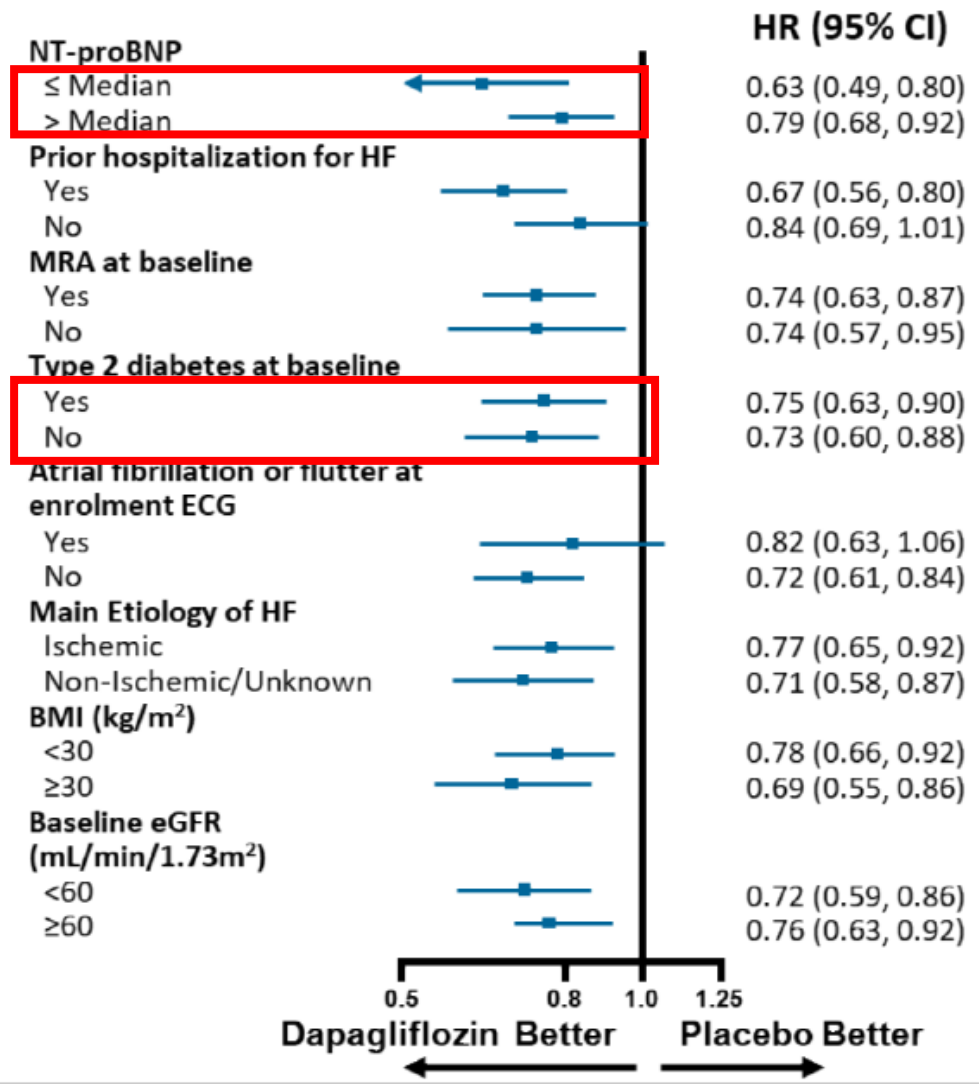
	2373	2339	2293	2248	2127	1664	1242	671	232
	2371	2330	2279	2230	2091	1636	1219	664	234

1. McMurray JJV et al. Dapagliflozin in patients with heart failure and reduced ejection fraction.N Engl J Med2019;381:1995–2008.

DAPA-HF

Primary Endpoint: Prespecified subgroups





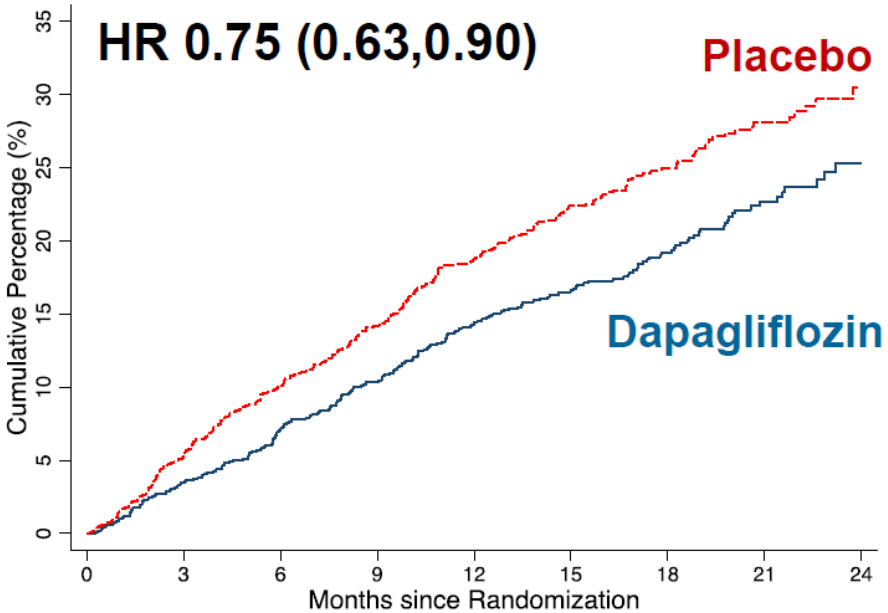
1. McMurray JJV et al. Dapagliflozin in patients with heart failureand reduced ejection fraction.N Engl J Med2019;381:1995–2008.

DAPA-HF

Primary composite outcome

CV Death/HF hospitalization/Urgent HF visit

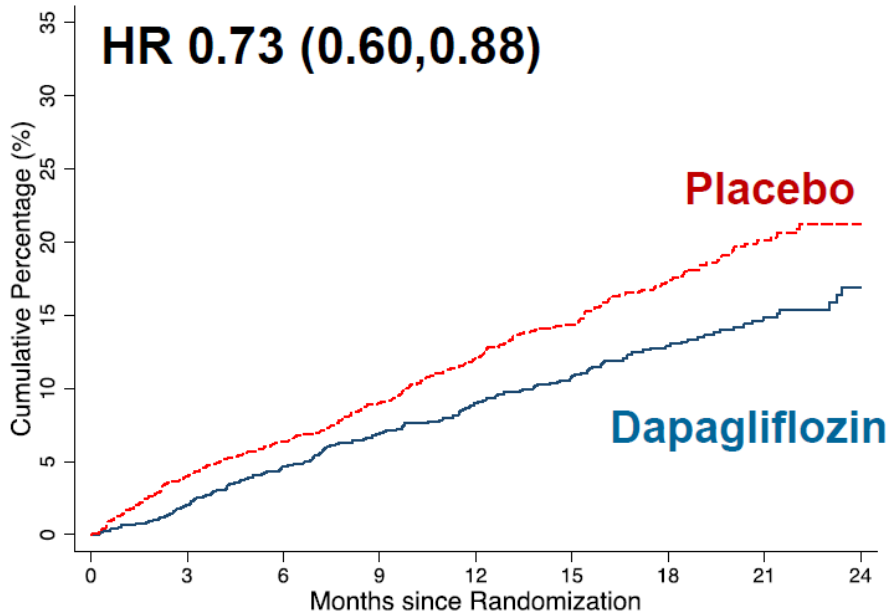
Diabetes



Number at Risk

Dapagliflozin	1075	1037	994	955	876	678	500	259	88
Placebo	1064	1005	949	899	816	630	469	253	89

No Diabetes



Number at Risk

Dapagliflozin	1298	1268	1227	1192	1126	882	646	353	122
Placebo	1307	1253	1214	1176	1101	848	627	340	121

P interaction 0.80

1. McMurray JJV et al. Dapagliflozin in patients with heart failureand reduced ejection fraction.N Engl J Med2019;381:1995–2008.

Secondary Endpoint: Kansas City Cardiomyopathy Questionnaire (KCCQ)

Total Symptom Score (TSS): Change from baseline to 8 months*

Treatment	Change	Difference
DAPA	+6.1 ± 18.6	2.8 points (95% CI 1.6, 4.0) p<0.001†
Placebo	+3.3 ± 19.2	

Total Symptom Score: Proportion with ≥5 point change from baseline to 8 months‡

Treatment	Dapagliflozin	Placebo	Odds ratio (95% CI)
≥5 point improvement	58%	51%	1.15 (1.08, 1.23) p<0.001
≥5 point deterioration	25%	33%	0.84 (0.78, 0.90) p<0.001

*Increase in score indicates an improvement

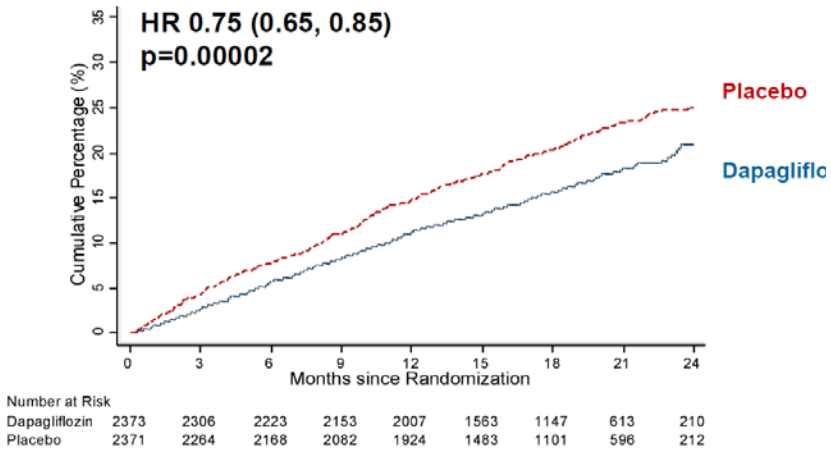
†Calculated from win ratio, incorporating death. Win ratio = 1.18 (CI 1.11, 1.26). Win ratio >1 indicates superiority of dapagliflozin over placebo.

‡Taking account of death CI = confidence interval; DAPA = dapagliflozin.

1. McMurray JJV et al. Dapagliflozin in patients with heart failureand reduced ejection fraction.N Engl J Med2019;381:1995.

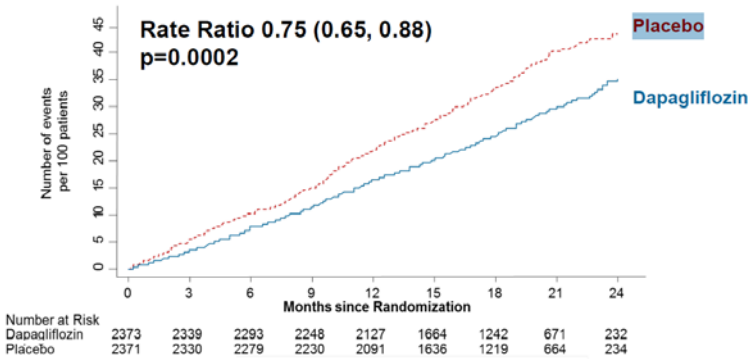
DAPA-HF

CV death or HF hospitalization

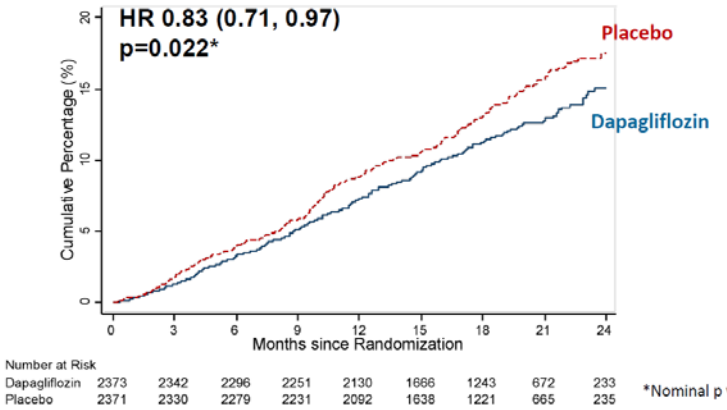


Total HF hospitalizations and CV death

Including first and repeat hospitalizations



All-cause death



*Nominal p value

Worsening renal function endpoint

Composite of: Sustained* ≥50% reduction in eGFR, end-stage renal disease (ESRD) or death from renal causes

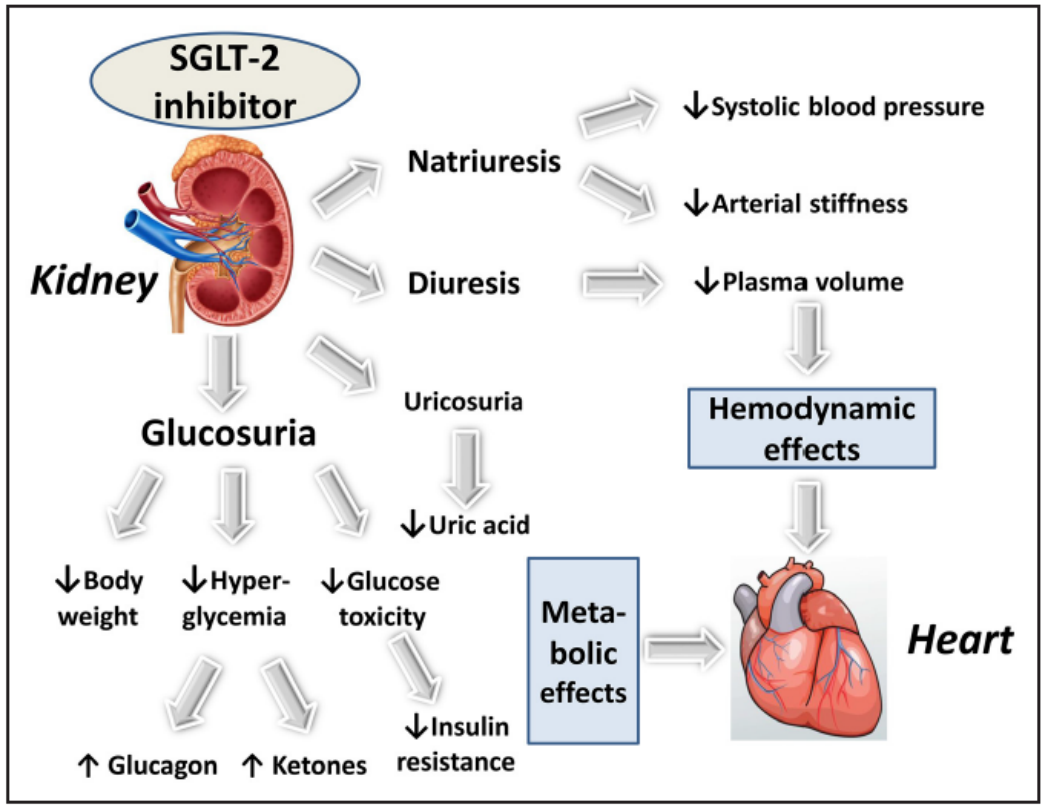
Treatment	No. (%)
Dapagliflozin	28 (1.2)
Placebo	39 (1.6)

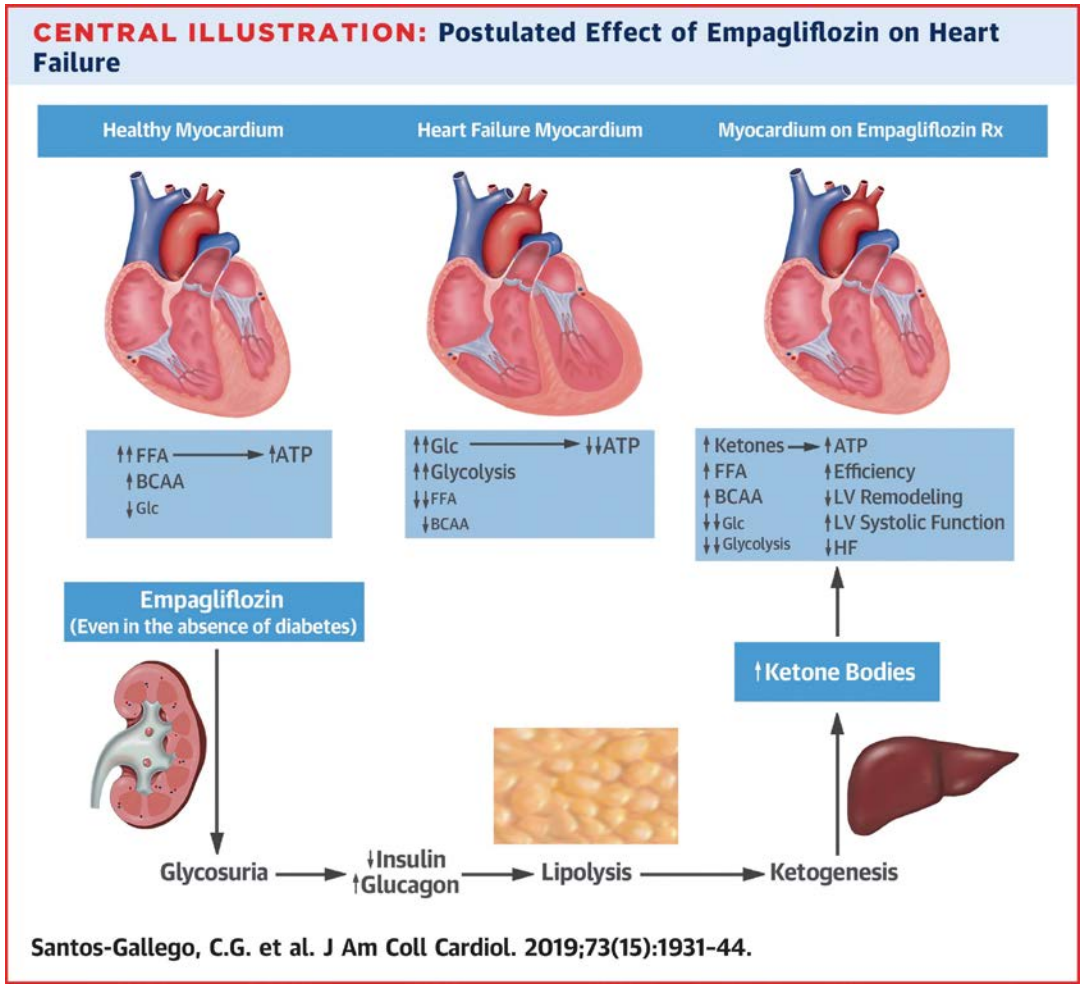
Hazard ratio (95% CI)
0.71 (0.44, 1.16)
p=0.17

Patients exposed to at least one dose of study drug	Dapagliflozin (n=2368)	Placebo (n=2368)	p-value
Adverse events (AE) of interest (%)			
Volume depletion⁺	7.5	6.8	0.40
Renal AE‡	6.5	7.2	0.36
Fracture	2.1	2.1	1.00
Amputation	0.5	0.5	1.00
Major hypoglycaemia	0.2	0.2	-
Diabetic ketoacidosis	0.1	0.0	-
AE leading to treatment discontinuation (%)	4.7	4.9	0.79
Any serious adverse event (incl. death) (%)	38	42	<0.01

1. McMurray JJV et al. Dapagliflozin in patients with heart failureand reduced ejection fraction.N Engl J Med2019;381:1995–2008.

ISGLT2 Mecanisme acció





Santos-Gallego, C.G. et al. J Am Coll Cardiol. 2019;73(15):1931-44.

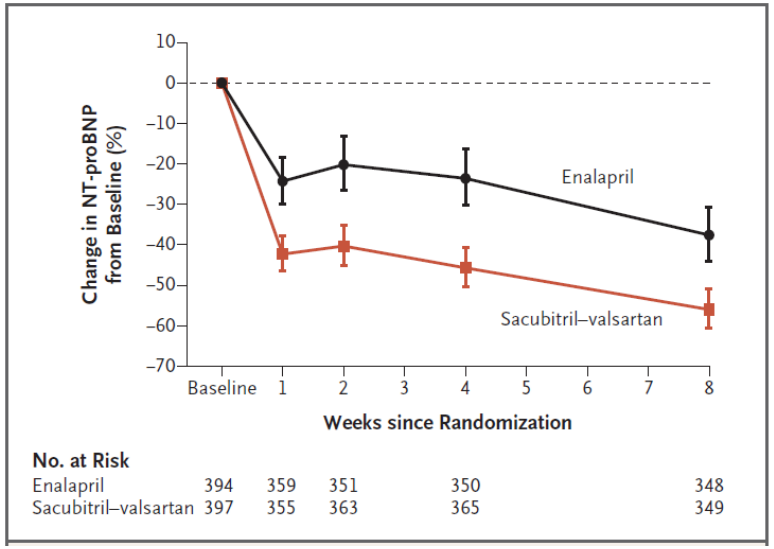
PIONEER-HF

ORIGINAL ARTICLE

Angiotensin–Neprilysin Inhibition in Acute Decompensated Heart Failure

Eric J. Velazquez, M.D., David A. Morrow, M.D., M.P.H., Adam D. DeVore, M.D., M.H.S., Carol I. Duffy, D.O., Andrew P. Ambrosy, M.D., Kevin McCague, M.A., Ricardo Rocha, M.D., and Eugene Braunwald, M.D., for the PIONEER-HF Investigators*

- 881 pts amb FE<40% ingressats per IC
- Randomitzat enalapril vs Sacubitril/Valsartan durant 8 setmanes
- Sacubitril/Valsartan va ser superior a enalapril en reduir NT-proBNP,
- Subgrup de novo i naïve
- Segur

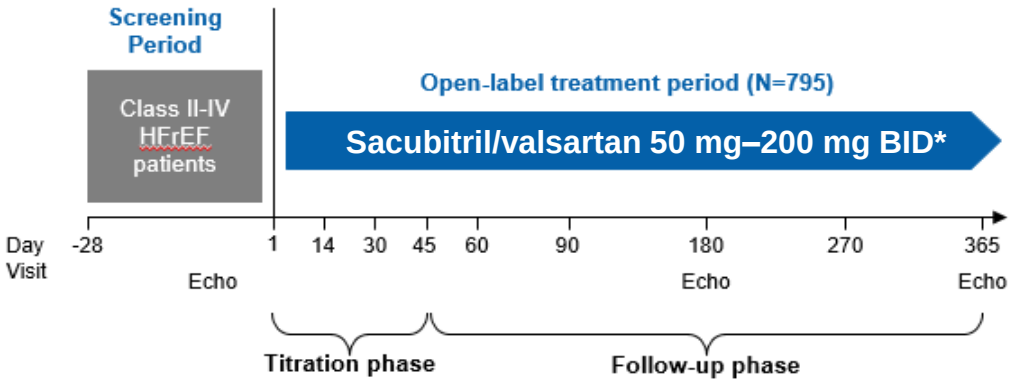


PROVE-HF

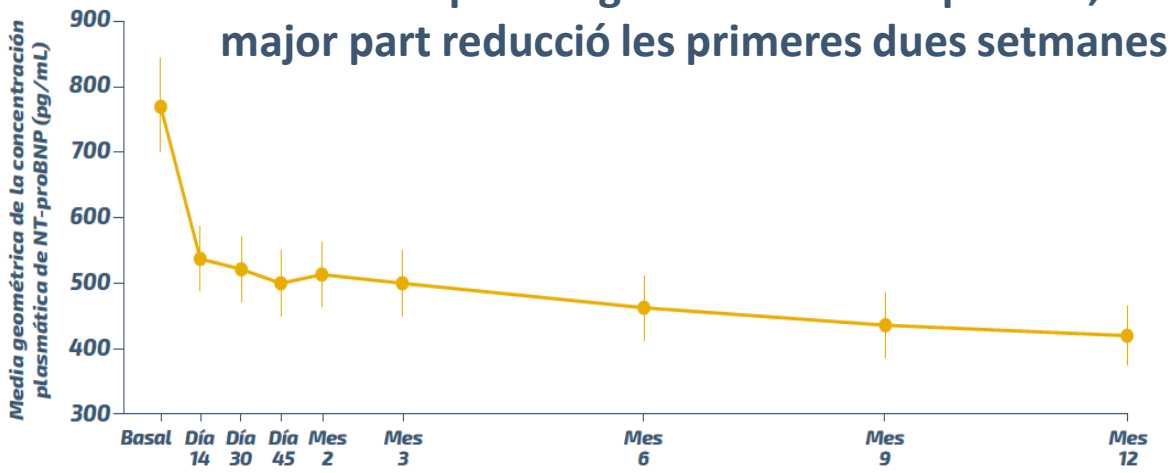
JAMA | Original Investigation

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; Ileana L. Piña, MD, MPH; Ricardo A. Rocha, MD; Amil M. Shah, MD, MPH; Kristin M. Williamson, PharmD; Scott D. Solomon, MD; for the PROVE-HF Investigators



Reducció ràpida i significativa de NT-proBNP, major part reducció les primeres dues setmanes

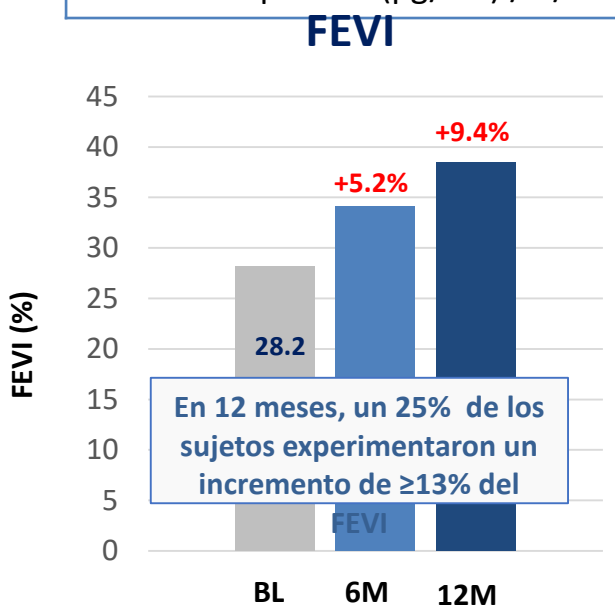


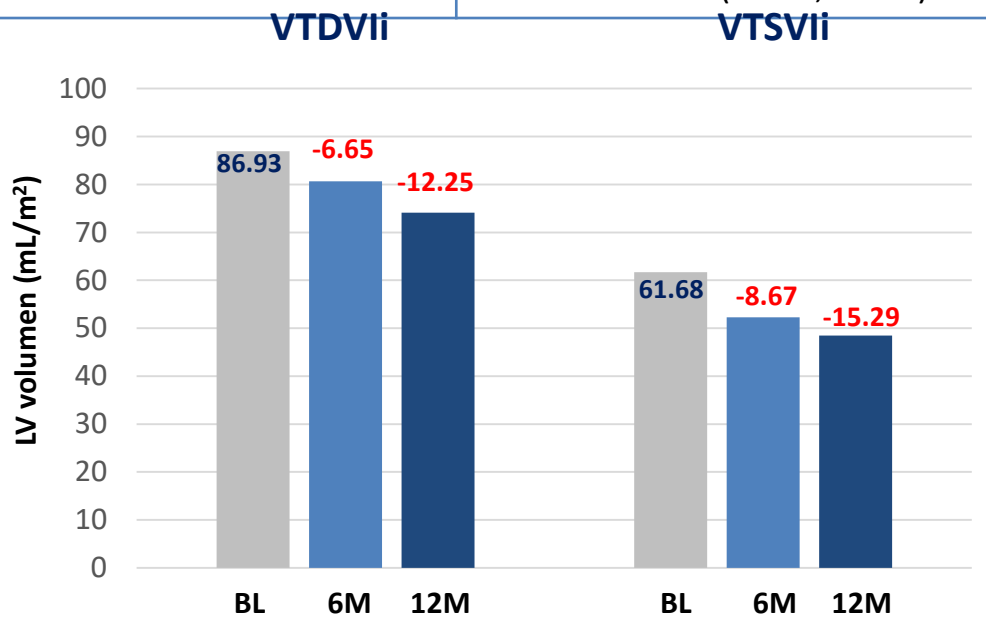
Januzzi JL, et al. Prospective Study of Biomarkers, Symptom Improvement and Ventricular Remodeling During Entresto Therapy for Heart Failure . Presentación oral en la ESC 2019, Paris, France

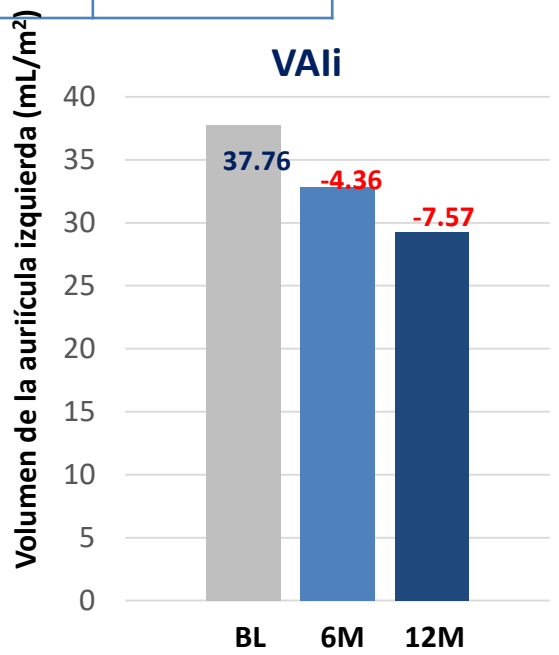
Objetiu primari

PROVE-HF

Parámetro	Pearson r (IQR)	P valor
NT-proBNP (pg/mL) / FEVI (%)	-0.381 (-0.448, -0.310)	<0.0001
NT-proBNP (pg/mL) / VTDVIi (mL/m²)	0.320 (0.246, 0.391)	<0.0001
NT-proBNP (pg/mL) / VTSVIi (mL/m²)	0.405 (0.335, 0.470)	<0.0001
NT-proBNP (pg/mL) / VAIi (mL/m²)	0.263 (0.186, 0.338)	<0.0001
NT-proBNP (pg/mL) / E/e’	0.269 (0.182, 0.353)	<0.0001







E/e’: velocidad de flujo mitral E sobre e’ de Doppler tisular; NT-proBNP: fracción N-terminal del propéptido natriurético tipo B; VTDVIi: volumen telediastólico del ventrículo izquierdo indexado; VTSVIi: volumen telesistólico del ventrículo izquierdo indexado; VAIi: Volumen aurícula izquierda indexado

Januzzi JL, et al. Prospective Study of Biomarkers, Symptom Improvement and Ventricular Remodeling During Entresto Therapy for Heart Failure. Presentación oral en la ESC 2019, Paris, France

PROVE-HF

Subgrups interés prespecificats

15% | 37% | 35%

De novo en IC y naïve en IECA/ARA II (N=118)	
	Cambio medio método MC desde el inicio a los 12 meses (IC 95%)
FEVI (%)	+12.8 (+11.05, +14.5)
VTDVIi (mL/m²)	-13.81 (-15.78, -11.83)
VTSVIi (mL/m²)	-17.88 (-20.07, -15.68)
VAIi (mL/m²)	-8.44 (-9.73, -7.15)
E/e'	-2.60 (-3.83, -1.37)

p<0,001 **FEVI ≥ 12,8 %**

Niveles NT-proBNP < PARADIGM-HF (N=292)	
	Cambio medio método MC desde el inicio a los 12 meses (IC 95%)
FEVI (%)	+9.4 (+8.6, +10.3)
VTDVIi (mL/m²)	-11.32 (-12.24, -10.40)
VTSVIi (mL/m²)	-14.15 (-15.15, -13.15)
VAIi (mL/m²)	-7.06 (-7.54, -6.58)
E/e'	-0.93 (-1.43, -0.43)

p<0,001 **FEVI ≥ 9,4 %**

Con dosis inferior a dosis objetivo (N=278)	
	Cambio medio método MC desde el inicio a los 12 meses (IC 95%)
FEVI (%)	+9.4 (+8.4, +10.3)
VTDVIi (mL/m²)	-10.99 (-12.21, -9.77)
VTSVIi (mL/m²)	-14.32 (-15.67, -12.97)
VAIi (mL/m²)	-7.23 (-7.97, -6.50)
E/e'	-0.46 (-1.32, +0.40)*

p<0,001, excepto * **FEVI ≥ 9,4 %**

Adaptado de Januzzi JL. JAMA 2019

Januzzi JL, et al. Prospective Study of Biomarkers, Symptom Improvement and Ventricular Remodeling During Entresto Therapy for Heart Failure . Presentación oral en la ESC 2019, Paris, France

Sacubitril/valsartan

Consensus recommendation

Sacubitril/valsartan *is recommended* as a replacement for angiotensin-converting enzyme inhibitors (ACE-I)/angiotensin receptor blockers (ARB) to reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal medical treatment with an ACE-I, a beta-blocker and a mineralocorticoid receptor antagonist (MRA).

Initiation of sacubitril/valsartan rather than an ACE-I or an ARB *may be considered* for patients hospitalized with new-onset HF or decompensated chronic HF to reduce the short-term risk of adverse events and to simplify management (by avoiding the need to titrate ACE-I first and then switch to sacubitril/valsartan).

Seferovic F et al. 2019 Clinical practice update no heart failure 20198 . *Eur J Heart Failure*. 2019.

TRACTAMENT FARMACOLÒGIC HFpEF

PARAGON-HF

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 24, 2019 VOL. 381 NO. 17

Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction

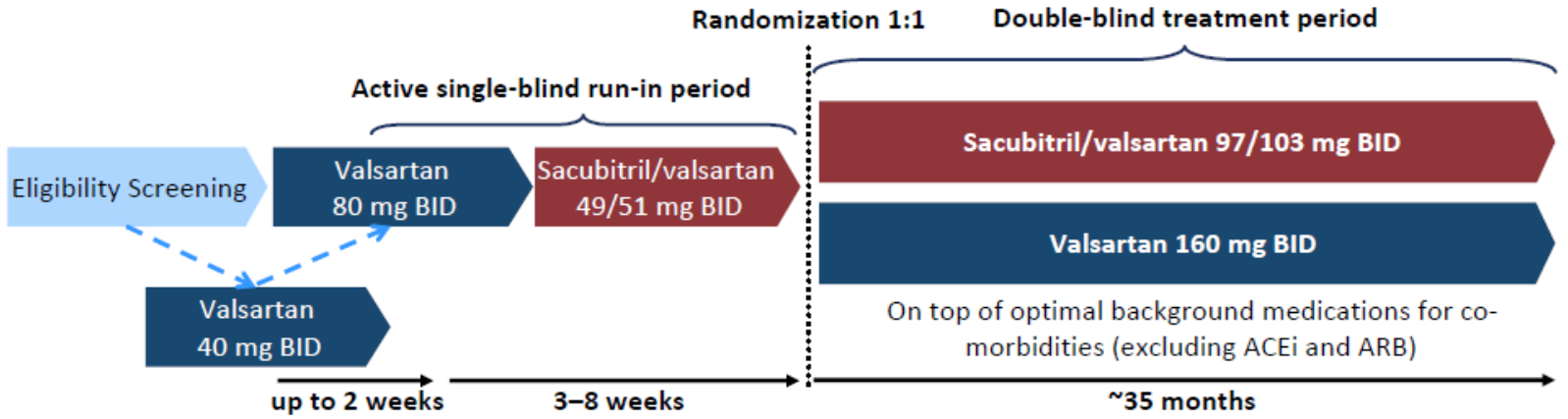
S.D. Solomon, J.J.V. McMurray, I.S. Anand, J. Ge, C.S.P. Lam, A.P. Maggioni, F. Martinez, M. Packer, M.A. Pfeffer, B. Pieske, M.M. Redfield, J.L. Rouleau, D.J. van Veldhuisen, F. Zannad, M.R. Zile, A.S. Desai, B. Claggett, P.S. Jhund, S.A. Boytsov, J. Comin-Colet, J. Cleland, H.-D. Düngen, E. Goncalvesova, 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,

INCLUSIÓ:

- FE> 45%
- IC (II-IV) tt diürètic 30 dies abans
- Patologia estructural (AE dil/HVE)
- Elevació pèptids natriürètics (valors segons ingrés o no)

EXCLUSIÓ:

- Mesura previa EF<40%
- IC aguda
- TA <110 o > 180 mmHg
- FG< 30 K >5,2



4822 pts

Primary Endpoint
Composite of total (first and recurrent) HF hospitalizations and CV death

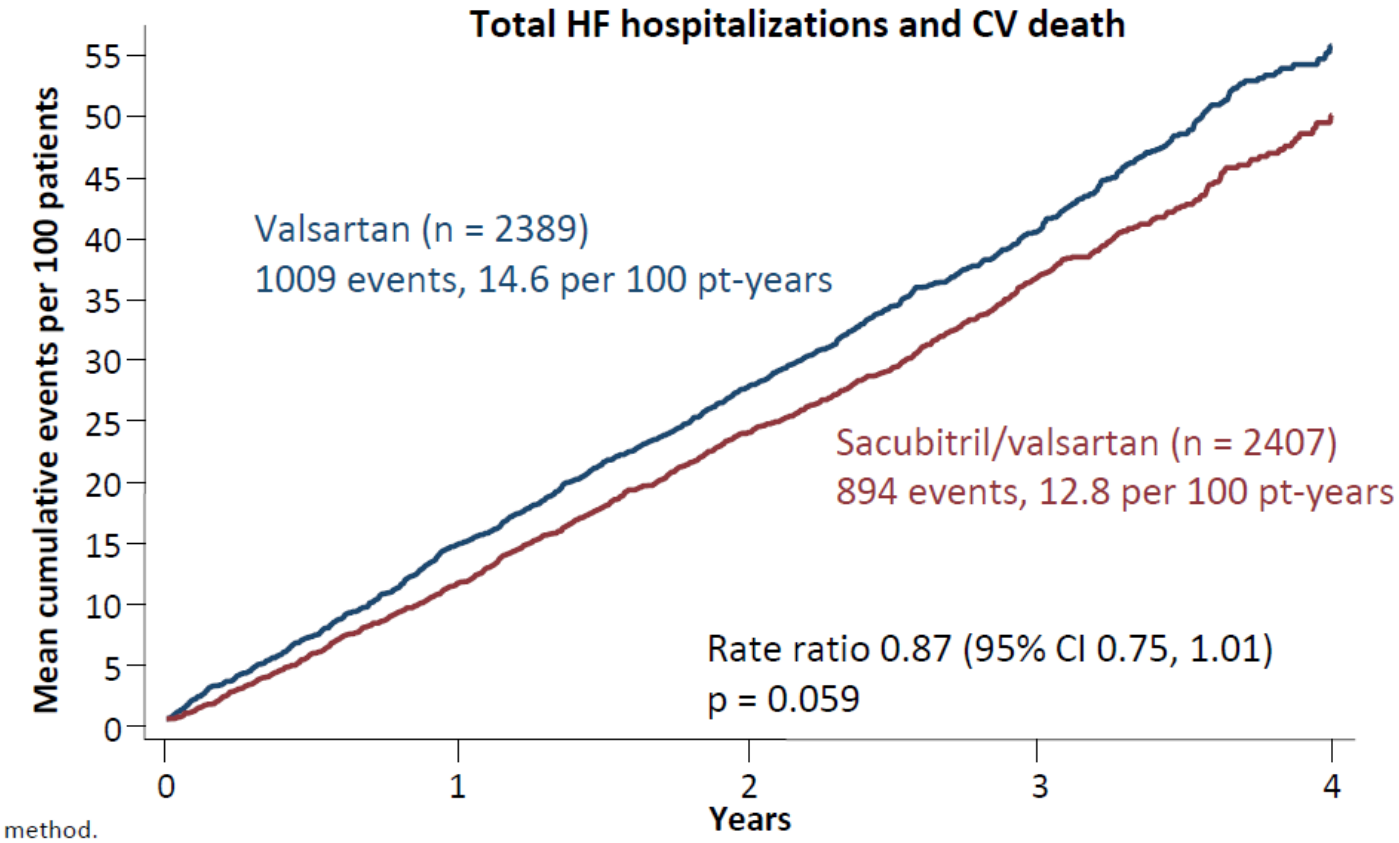
Secondary Endpoints:

- Improvement in NYHA functional classification at 8 months
- Changes in KCCQ clinical summary score at 8 months
- Time to first occurrence of worsening renal function
- Time to all-cause mortality

PARAGON-HF

PARAGON-HF primary results

Recurrent event analysis of total HF hospitalizations and CV death*



*Semiparametric LWYY method.

Solomon SD etal.Angiotensin-neprilysin inhibition in heart failure with preserved ejection fraction. N Engl J Med 2019;381:1609–1620

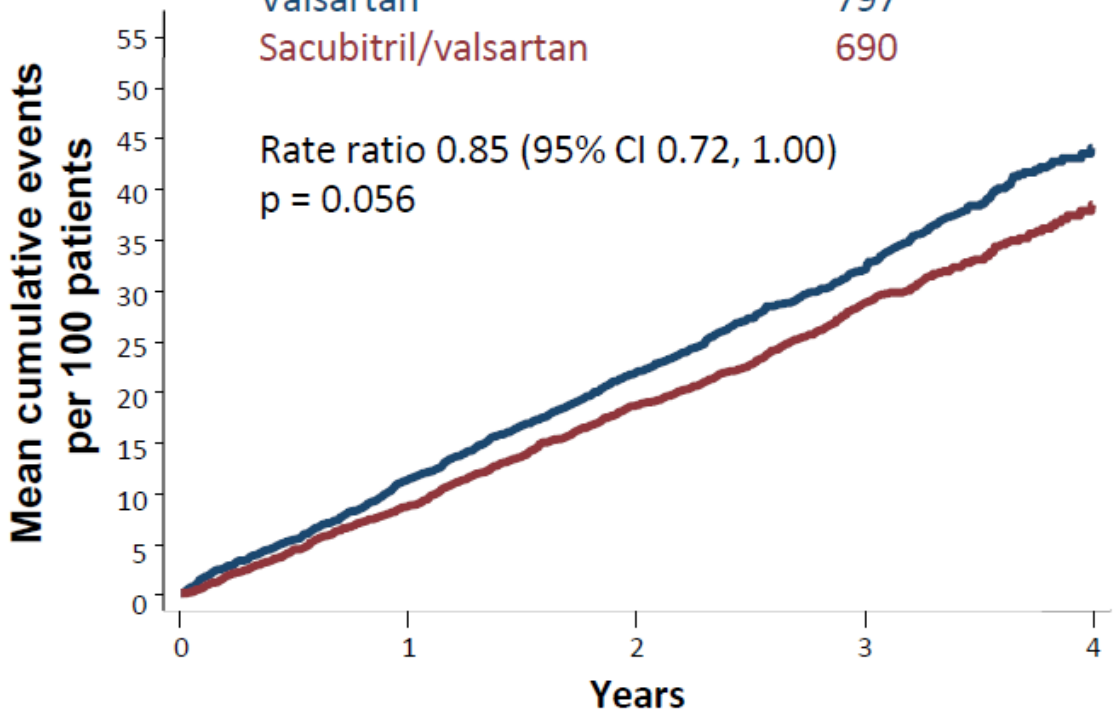
PARAGON-HF

HF hospitalizations and CV death

HF hospitalizations*

	Events
Valsartan	797
Sacubitril/valsartan	690

Rate ratio 0.85 (95% CI 0.72, 1.00)
p = 0.056

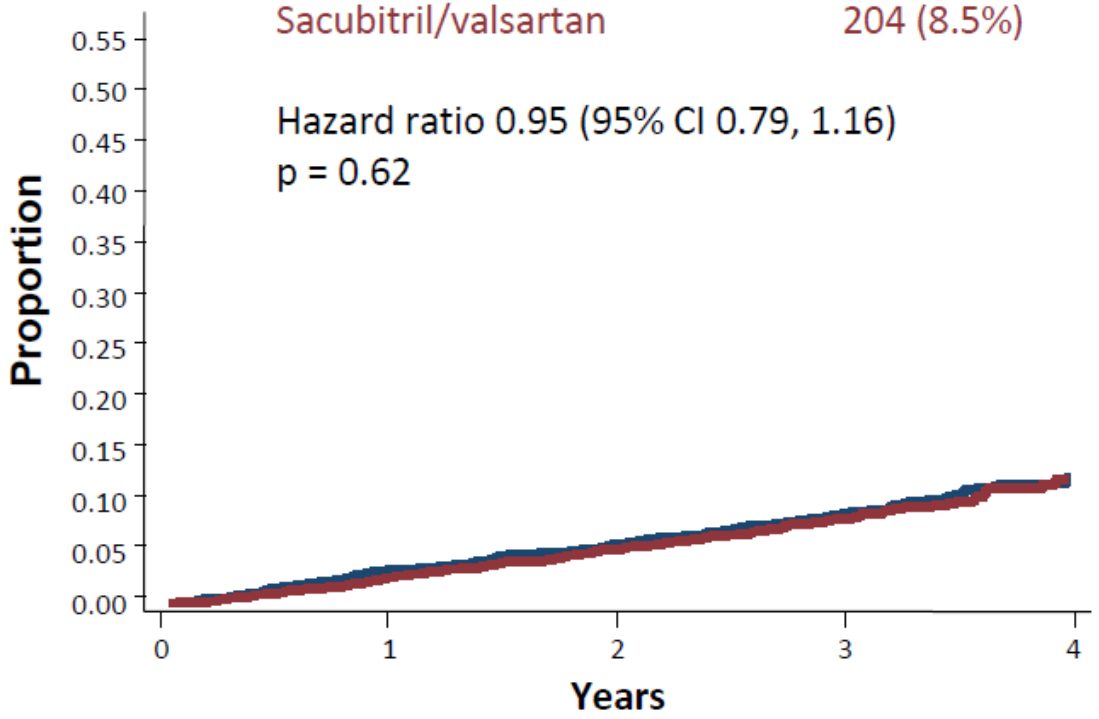


*Semiparametric LWYY method

CV death*

	Patients
Valsartan	212 (8.9%)
Sacubitril/valsartan	204 (8.5%)

Hazard ratio 0.95 (95% CI 0.79, 1.16)
p = 0.62



Solomon SD etal.Angiotensin-neprilysin inhibition in heart failure with preserved ejection fraction. N Engl J Med 2019;381:1609–1620

PARAGON-HF

Secondary endpoints

	Sacubitril/valsartan N = 2316	Valsartan N = 2302	Effect size (95% CI)	Nominal P-value
NYHA functional classification at 8 months – Change from baseline (%) Improved Unchanged Worsened	 15.0% 76.3% 8.7%	 12.6% 77.9% 9.6%	OR for improvement 1.45 (1.13, 1.86)	0.004
KCCQ clinical summary score at 8 months – Change from baseline (SE)	-1.6 (0.4)	-2.6 (0.4)	LSM of difference = 1.03 (0.00, 2.1)	0.051
KCCQ responder (> than 5-point improvement)	33.0%	29.6%	OR = 1.30 (1.04, 1.61)	0.019
Worsening Renal Function Composite of renal death, reaching ESRD, or ≥50% decline in eGFR relative to baseline.	1.4%	2.7%	HR = 0.50 (0.33, 0.77)	0.002
All-cause mortality (%)	14.2%	14.6%	HR = 0.97 (0.84, 1.13)	0.68

Solomon SD etal.Angiotensin-neprilysin inhibition in heart failure with preserved ejection fraction. N Engl J Med 2019;381:1609–1620

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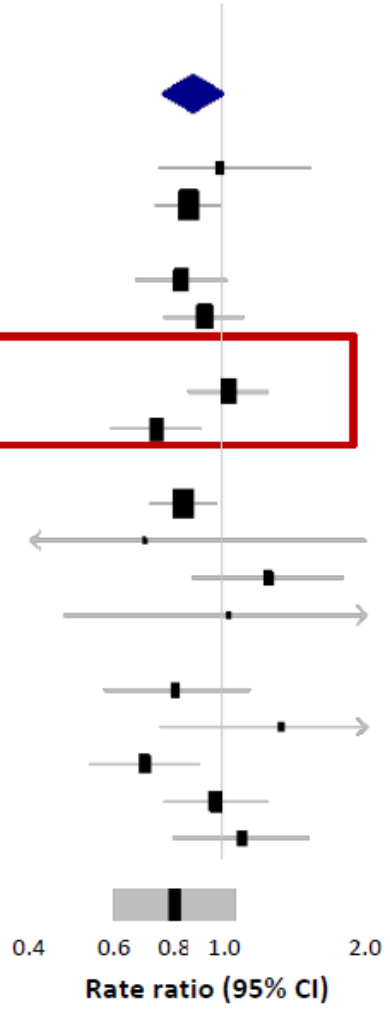
Pre-specified subgroups for primary endpoint

Evidence for overall heterogeneity

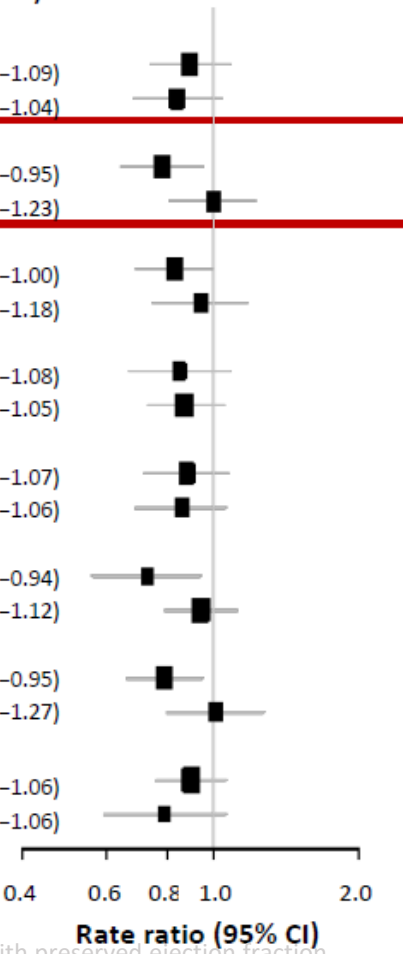
Subgroup	No. of events /patients	Rate ratio (95% CI)
Overall	**1903/4796**	**0.87 (0.75–1.01)**
Age (years)		
Less than 65 years	276/825	0.99 (0.64–1.53)
65 years or older	1627/3971	0.85 (0.73–0.99)
Age (years)		
Less than 75 years	938/2597	0.82 (0.66–1.02)
75 years or older	965/2199	0.92 (0.76–1.11)
Sex*		
Male	980/2317	1.03 (0.85–1.25)
Female	923/2479	0.73 (0.59–0.90)
Race		
Caucasian	1542/3907	0.83 (0.71–0.97)
Black	89/102	0.69 (0.24–1.99)
Asian	237/607	1.25 (0.87–1.79)
Other	35/180	1.03 (0.47–2.28)
Region		
North America	478/559	0.80 (0.57–1.14)
Latin America	83/370	1.33 (0.75–2.36)
Western Europe	544/1390	0.69 (0.53–0.89)
Central Europe	466/1715	0.97 (0.76–1.24)
Asia/Pacific	332/762	1.10 (0.79–1.52)



Multivariate interaction p < 0.05.

Together with

Subgroup	No. of events /patients	Rate ratio (95% CI)
Diabetic		
Yes	1041/2069	0.89 (0.74–1.09)
No	862/2727	0.84 (0.68–1.04)
LVEF*		
at or below median (57%)	1048/2495	0.78 (0.64–0.95)
above median (57%)	855/2301	1.00 (0.81–1.23)
History of AF		
Yes	1140/2521	0.83 (0.69–1.00)
No	763/2275	0.94 (0.75–1.18)
Screening NT–proBNP		
at or below median (911 pg/mL)	708/2379	0.85 (0.67–1.08)
above median (911 pg/mL)	1183/2378	0.87 (0.73–1.05)
Screening SBP		
at or below median (137 mmHg)	984/2450	0.88 (0.72–1.07)
above median (137 mmHg)	919/2344	0.86 (0.69–1.06)
MRA use		
Yes	543/1238	0.73 (0.56–0.94)
No	1360/3558	0.94 (0.79–1.12)
Baseline eGFR		
<60 mL/min/1.73m²	1115/2341	0.79 (0.66–0.95)
>=60 mL/min/1.73m²	787/2454	1.01 (0.80–1.27)
NYHA class		
I/II	1402/3843	0.90 (0.76–1.06)
III/IV	499/951	0.79 (0.59–1.06)



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PARAGON-HF

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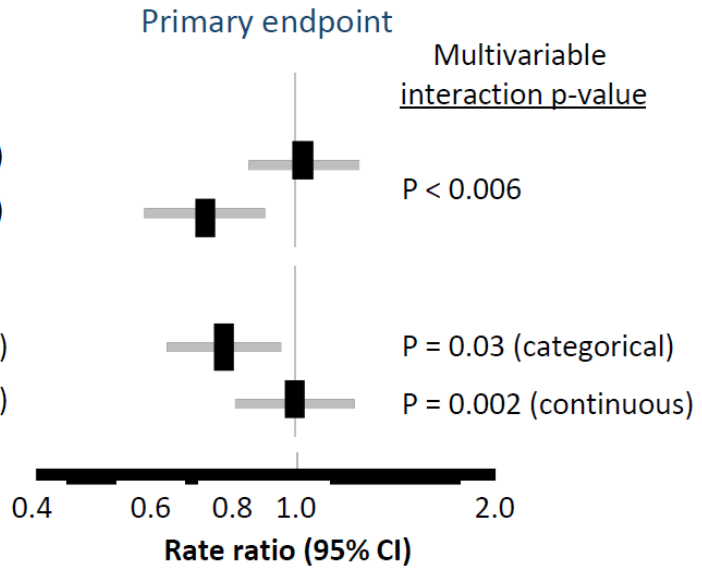
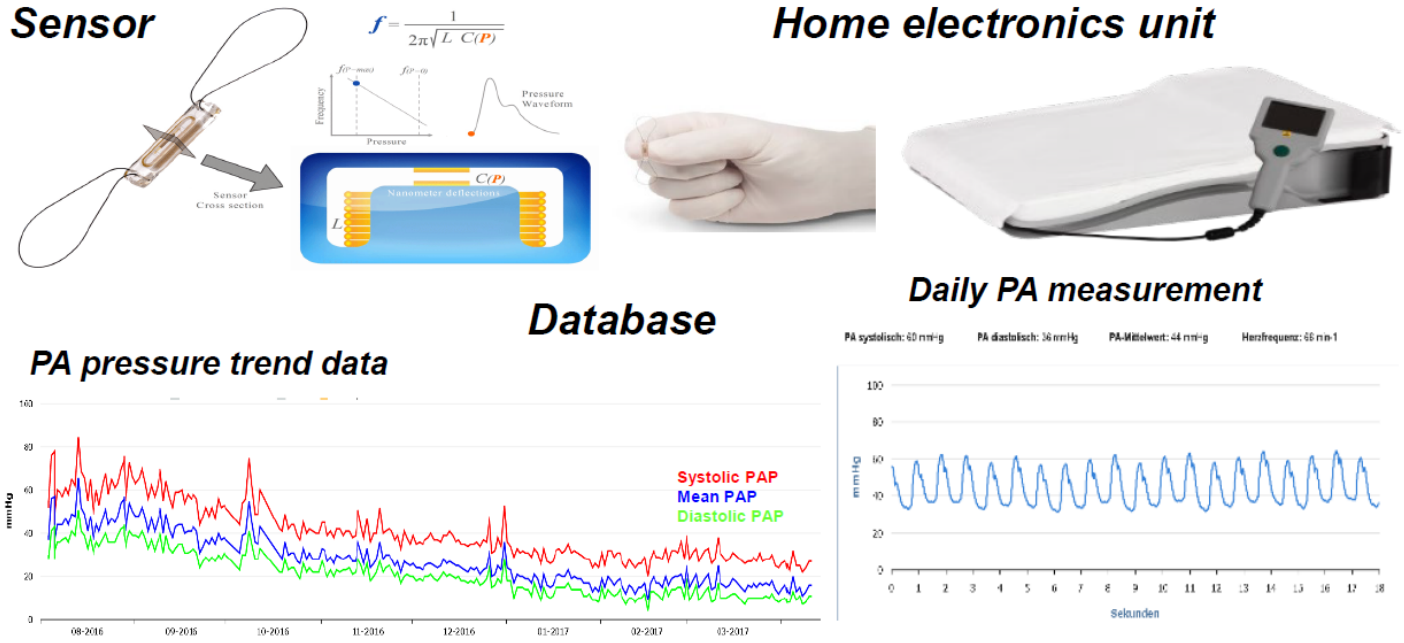


TRACTAMENT NO FARMACOLÒGIC

CARDIOMEMS

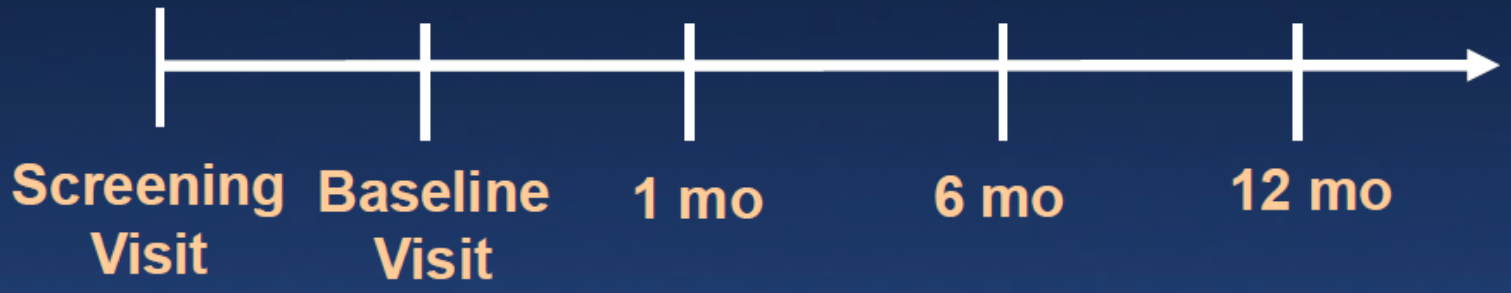


Monitoring of pulmonary artery pressures using a wireless implantable haemodynamic monitoring system (CardioMems) may be considered in symptomatic patients with HF with previous HF hospitalization in order to reduce the risk of recurrent HF hospitalization.	IIb	B	628, 629

Eur Heart J 2016; 37: 2129

CardioMEMS Post Approval Study (PAS): Study Design

A prospective, multi-center, open-label trial in ~1200 patients with NYHA Class III Heart Failure and a HFH within the prior 12 months



Right Heart Catheterization
Baseline Hemodynamics
PA Sensor Implantation

Scheduled Study visits

Patients instructed to transmit PA pressures daily

All hospitalizations submitted to CEC* for adjudication

Primary Efficacy Endpoint:
Reduction in rate of HFH at 1-year post-implant compared with the year prior to enrollment

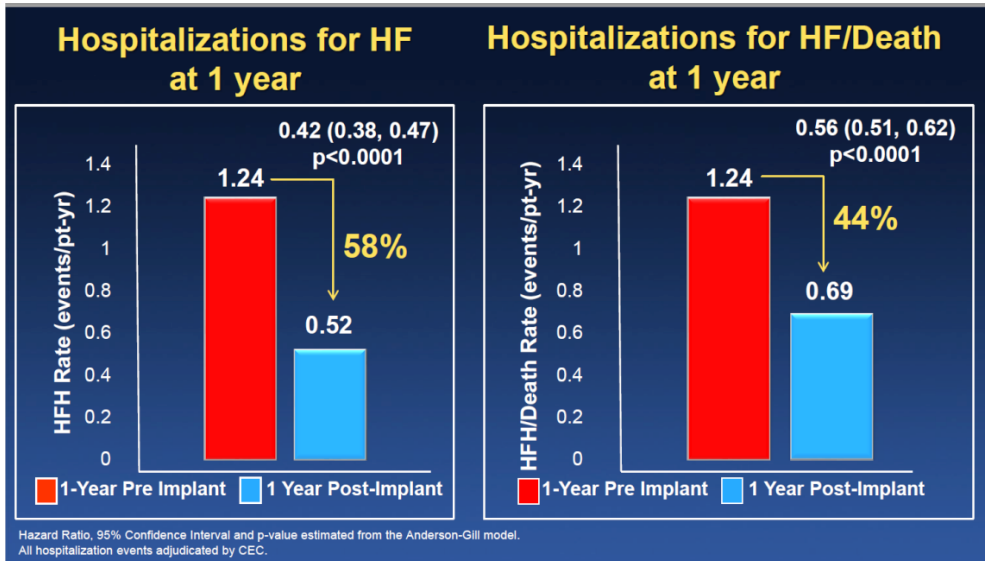
Primary Safety Endpoints:
Freedom from DSRC** > 80% at 2 years
Freedom from Sensor Failure > 90% at 2 years

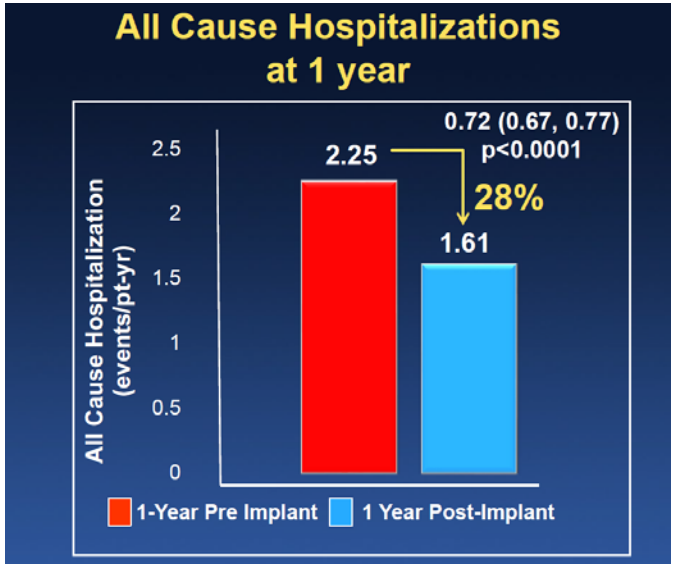
Supplemental Analysis:
HFH or death at 1 year
Death at 1 year
Patient compliance
Outcomes in subgroups

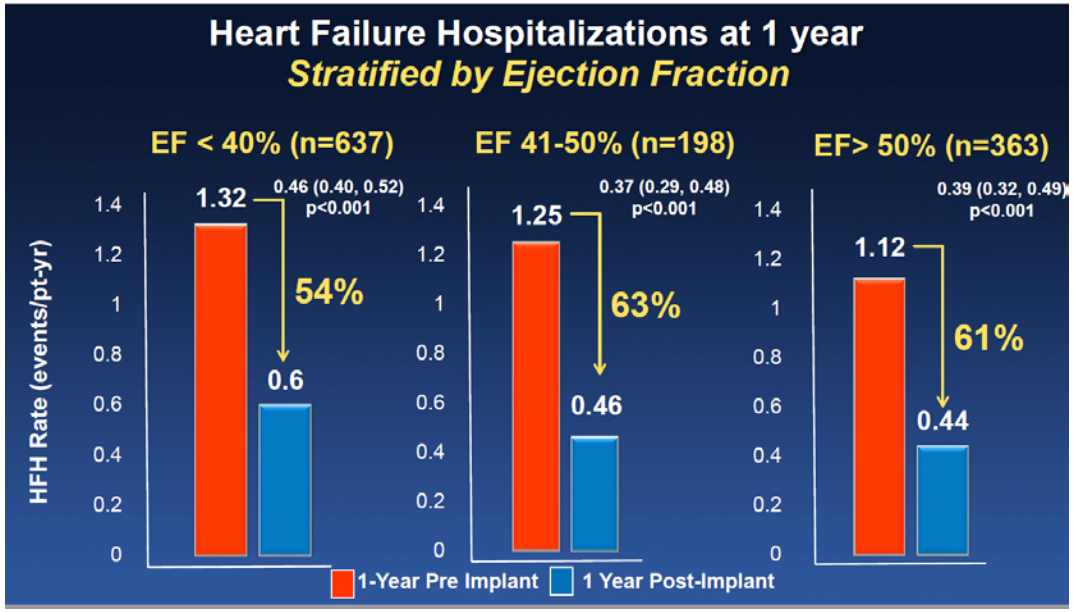
Shavelle. Pulmonary Artery Pressure-Guided Therapy for Ambulatory Heart Failure Patients in Clinical Practice:1-Year Outcomes from the CardioMEMSPost-Approval . ACC 2019

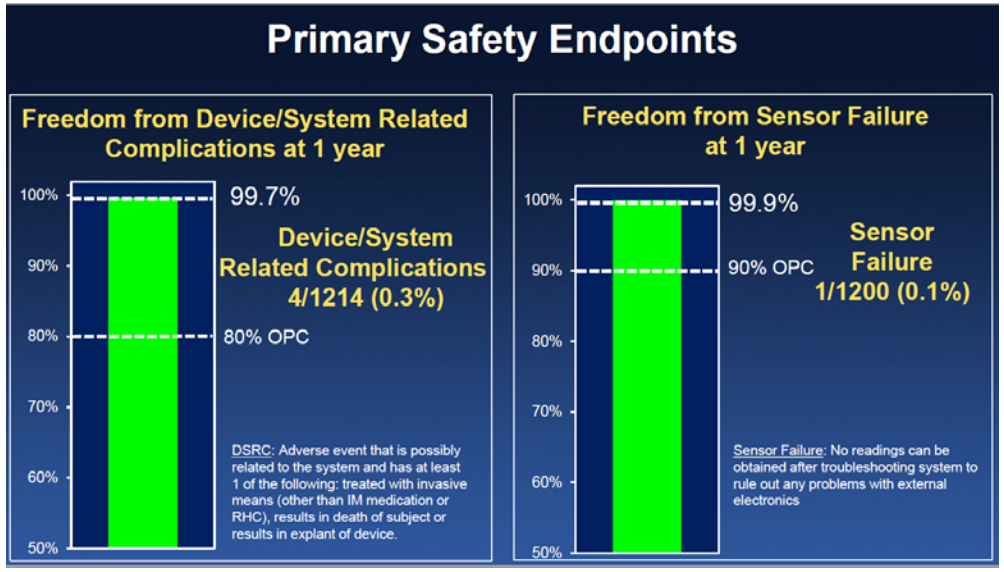
*CEC = Clinical Events Committee; **DSRC = Device and System-Related Complications; HFH = Heart Failure Hospitalization

CARDIOMEMS PAS study









Shavelle. Pulmonary Artery Pressure-Guided Therapy for Ambulatory Heart Failure Patients in Clinical Practice:1-Year Outcomes from the CardioMEMSPost-Approval . ACC 2019

CARDIOMEMS

JAMA Cardiology | Original Investigation

Association of Ambulatory Hemodynamic Monitoring of Heart Failure With Clinical Outcomes in a Concurrent Matched Cohort Analysis

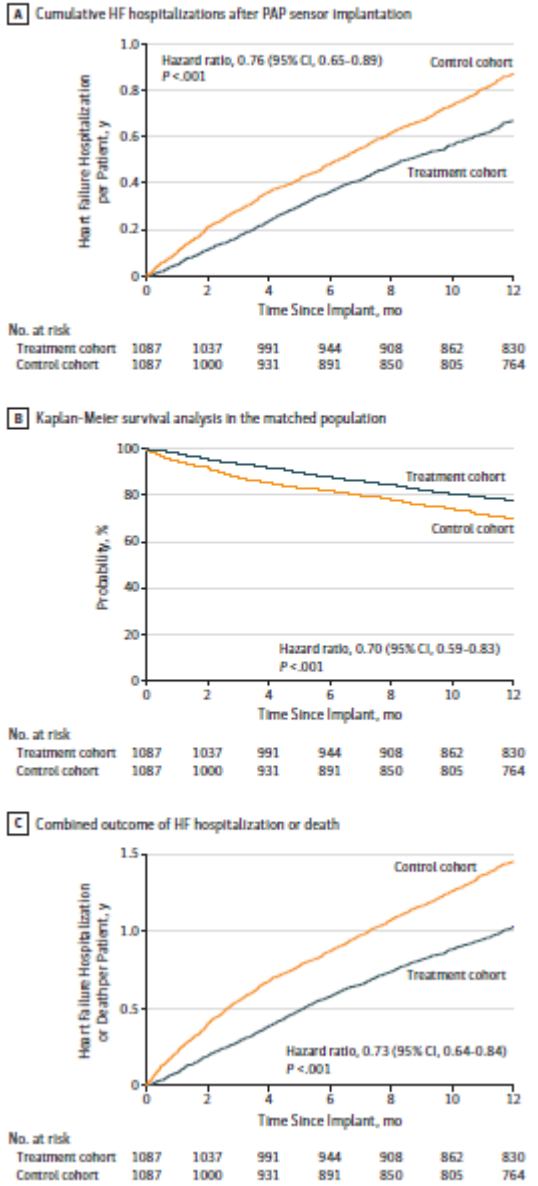
Jacob Abraham, MD; Rupinder Bharmi, MS; Orvar Jonsson, MD; Guilherme H. Oliveira, MD; Andre Artis, MD; Ali Valika, MD; Robert Capodilupo, MD; Philip B. Adamson, MD; Gregory Roberts, BS; Nirav Dalal, MBA; Akshay S. Desai, MD, MPH; Raymond L. Benza, MD

1087 pacients CardioMEMS

Aparellar amb cohort control

Disminució ingressos

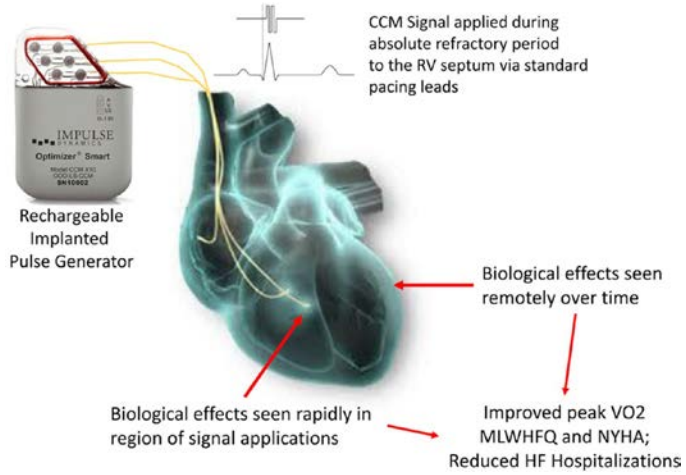
Figure 2. Cumulative Events After Pulmonary Artery Pressure (PAP) Sensor Implant



MODULADORS CONTRACTILITAT CARDÍACA

Consensus recommendation

Cardiac contractility modulation (CCM) *may be considered* in patients with HFrEF (LVEF 25–45%) and a narrow QRS complex (<130 ms) in order to improve exercise capacity, quality of life and alleviate HF symptoms.

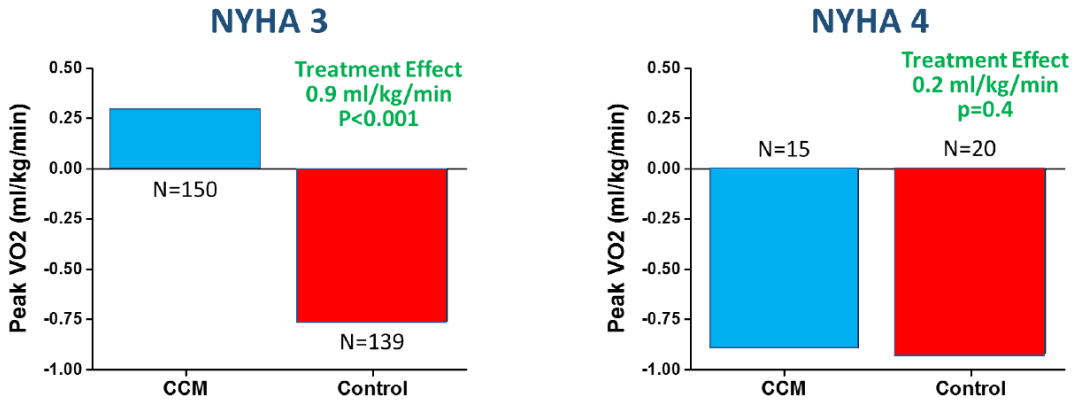


Cardiac Contractility Modulation (CCM) in HFrEF NYHA Class III Patients

Daniel Burkhoff MD PhD
Cardiovascular Research Foundation

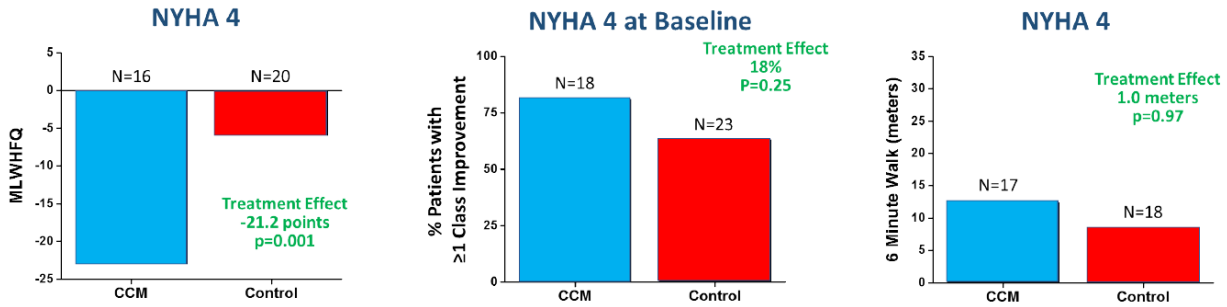
ANÀLISIS SUBGRUP PREESCPECIFICAT PER DETERMINAR SI EL BENEFICI DE LA CCM VARIA EN FUNCIÓ DE LA NYHA III O IV (SUBESTUDI FIX-HF-5C STUDY)

Primary Endpoint: Peak VO2



Burkoff. Late breaking trial III - Innovative and device therapy . HFA 2019

CCM IN NYHA 4



Seferovic F et al. 2019 Clinical practice update no heart failure 20198 . *Eur J Heart Failure*. 2019.

MitraClip

Consensus recommendation

Referral of patients with HF and secondary (i.e. functional) mitral regurgitation to a multidisciplinary HF team that will decide on management *is recommended*.

Reduction in mitral regurgitation using a MitraClip device *may be considered* for patients with HFrEF who fulfil the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation) selection criteria (*Table 3*).[79]

Tractament optimitzat
IM severa desproporcionada

Seferovic F et al. 2019 Clinical practice update no heart failure 20198 . *Eur J Heart Failure*. 2019.

CURES PAL·LIATIVES

Artículo especial

Documento de consenso y recomendaciones sobre cuidados paliativos en insuficiencia cardiaca de las Secciones de Insuficiencia Cardiaca y Cardiología Geriátrica de la Sociedad Española de Cardiología

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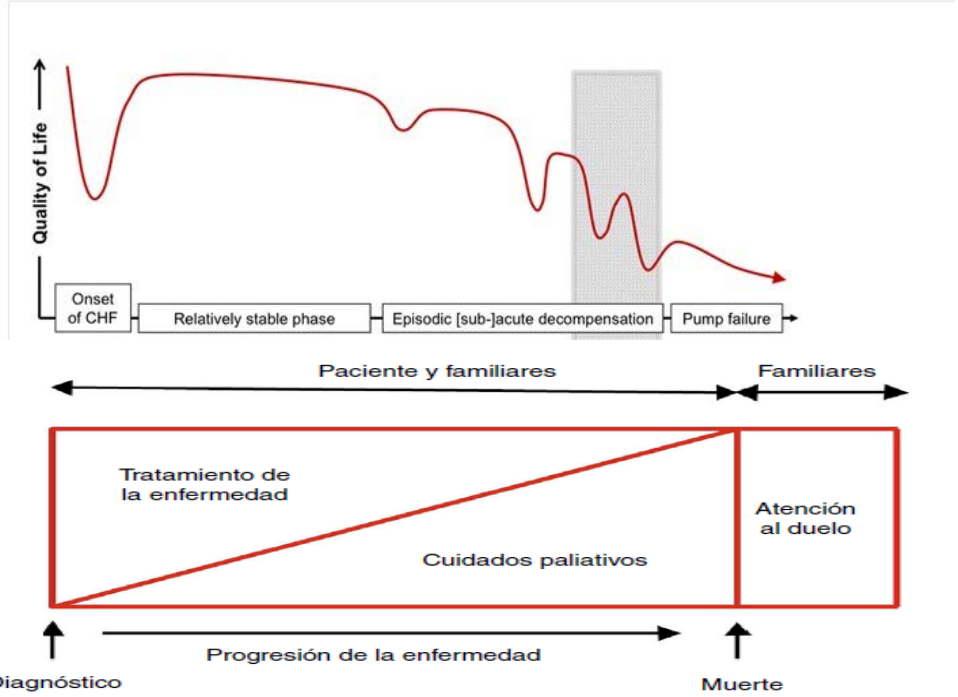
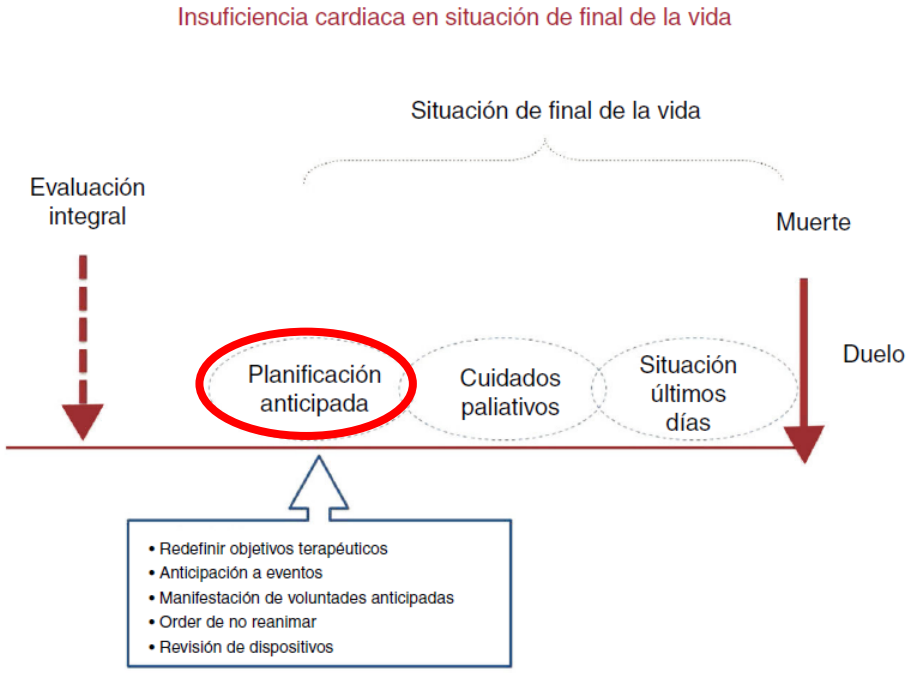




ESTUDIS EN CURS

- **HFrEF**: Vericiguat (VICTORIA)
- **HFpEF**: ISGLT2 (4), 2 estudis ARM, Vericiguat (VITALITY-HFpEF)
- **Dispositius**:
  - RELIEVE-HF (V-Wave shunt interauricular)
  - BeATHF (baroreceptors sinus carotidi)

REPTES DE FUTUR (VISIÓ PERSONAL)

- **Medicina de precisió→Individualitzar tractament→ Qui es beneficia d'una pastilla o dispostiu extra??**
- **Fenotipar millor ICFEp**
- **Estratificar risc de MS en MCD (RM)**
- **Valoració integral geriátrica: fragilitat per cardiopatia o ja no té reserves→ evitar tractaments futils**

CONCLUSIONS

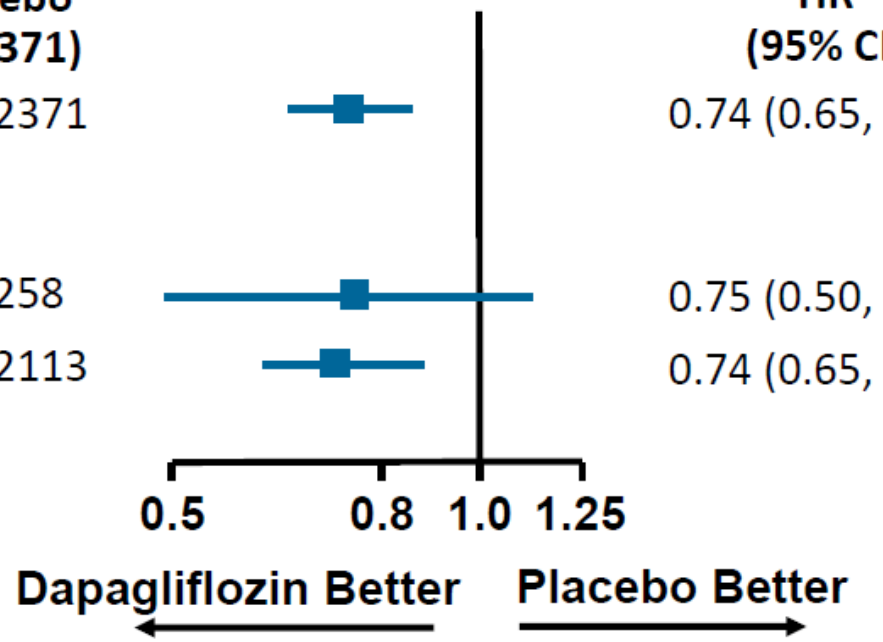
- **Causes de mort** IC 17 anys: increment molt significatiu de la mortalitat no cardiovascular, sent el càncer la més freqüent. La mortalitat CV s'ha reduït a expenses principalment de la MS.
- Nou **algoritme diagnòstic HFpEF** ESC: molt centrat en eco, complexe.
- **HFrEF**:
  - Dapaglifozina (ISGLT2) nou tractament en la IC, mecanisme acció no aclarit. Assaigs popers: Efecte de classe, HFpEF.
  - Sacubitril/Valsartan: és segur iniciar en ingrés per ICA, de novo/naïve i millora el remodelat→ beneficis clínics
- **HFpEF**: PARAGON-HF Sacubitril/Valsartan
  - Reducció modesta de l'objectiu primari que no assoleix significació estadística.
  - Potencial benefici en subgrup de dones i FE < 57% (heterogeneïtat fenotip HFpEF
- **CARDIOMEMS**: estratègia útil per reduir ingressos per IC
- **Moduladors de la contractilitat cardíaca**: no en CF IV
- Importància implementació **cures pal·liatives** de forma precoç, elaboració protocols, multidisciplinar.

Moltes gràcies!

DAPA-HF

ARNI/no ARNI *post hoc* subgroup: Primary endpoint

	Dapagliflozin (n=2373)	Placebo (n=2371)	HR (95% CI)
All patients	386/2373	502/2371	0.74 (0.65, 0.85)
Angiotensin Receptor Neprilysin Inhibitor (ARNI)			
Yes	41/250	56/258	0.75 (0.50, 1.13)
No	345/2123	446/2113	0.74 (0.65, 0.86)



Resultados: análisis de sensibilidad pre-especificado del endpoint primario

Análisis de sensibilidad	Estimación (RR o HR)	P valor nominal
Análisis primario LWYY (estratificado por región) - adjudicado	RR=0.87 (0.75, 1.01)	0.059
Análisis primario (LWYY) incluyendo visitas a urgencias por IC adjudicadas en el *endpoint* compuesto	RR=0.86 (0.75, 0.99)	0.040
Eventos reportados por el investigador (LWYY)	RR=0.84 (0.74, 0.97)	0.014
Modelo binomial negativo	RR=0.87 (0.74, 1.01)	0.066
Análisis primario LWYY (estratificado por país)*	RR=0.86 (0.75, 0.997)	0.045
Tiempo hasta primer evento primario compuesto (muerte CV u hospitalización por IC)	HR=0.92 (0.81, 1.03)	0.15