

6 - Juliol - 2021



# NOVES GUIES D'INSUFICIÈNCIA CARDÍACA DE L'ESC-HFA: REPTES I NECESSITATS NO COBERTES: INSUFICIÈNCIA CARDÍACA CRÒNICA

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Organised by the Heart Failure Association of the ESC .



Heart Failure Guidelines 2021: pharmacological treatment

#### The ESC 2021 Heart Failure Guideline

Process

Heart Failure 2021

- · Summarize the main new evidence (underpinning the pharmacological recommendations)
- Central Algorithm for HFrEF
- · Marco Metra (Chair)- recommendations

Marco Metra



#### #HeartFailure2021

#### Drugs recommended in all patients with heart failure with reduced ejection fraction

Recommendations	Class*	Level
ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	0.01	*
Beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.	- i	
MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	1.00	A
Dapagifilozin or empagifilozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.		
Sacubitril/valuartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death.		

Heart Failure 2021

#HeartFailure2021

\*Class of recommendation. \*Level of evidence

Heart Failure Guidelines 2021: pharmacological treatment





European Journal of Heart Failure (2021) **23**, 352–380 y doi:10.1002/ejhf.2115 **POSITION PAPER** 



Universal definition and classification of heart failure: a report of the Heart Failure Society of **America, Heart Failure Association of the European Society of Cardiology, Japanese** Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure **Endorsed by the Canadian Heart Failure Society, Heart** Failure Association of India, Cardiac Society of Australia

and New Zealand, and Chinese Heart Failure Association

ESC European Society of Cardiology

doi:10.1002/eihf.2115

European Journal of Heart Failure (2021) 23, 352–380 POSITION PAPER

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Endorsed by the Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese Heart Failure Association

#### Natriuretic Peptide Levels Supporting Definition of HF

	Ambulatory	Hospitalized/ Decompensated
BNP, pg/mL	35	100
NT-proBNP, pg/r	nL 125	300

Symptoms and/or signs of HF caused by a structural and/or functional cardiac abnormality and corroborated by *at* least one of the following Elevated natriuretic peptide levels or Objective evidence of cardiogenic pulmonary or systemic congestion

Bozkurt B, et al. Eur J Heart Fail. 2021;23:352-380

ESC Exception Society of Caroline Society doi:10.1002/spir2115

Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure Endorsed by the Canadian Heart Failure Society, Heart

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Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese Heart Failure Association

### New classification of HF according to LVEF





European Journal of Heart Failure (2021) **23**, 381–383 doi:10.1002/ejhf.2129

#### The path to universality

#### Eugene Braunwald\* and Elliott M. Antman

TIMI Study Group, Division of Cardiovascular Medicine, Brigham and Women's Hospital, Department of Medicine, Harvard Medical School, Boston, MA, USA

Time-line for important treatments and definitions of heart failure between 1950 and 2020 (horizontal lines) and dates of heart failure definitions and/or practice guidelines (rectangles)

EDITORIAL COMMENT

"An essential component of the trials that led to these recent advances was a clear definition of HF in the populations studied"





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### Management of patients with HFrEF – Therapeutic algorithm



#HeartFailure2021





### **ICFE reducida**

# Drugs recommended in all patients with heart failure with reduced ejection fraction

Recommendations	Classa	Levelb
ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	1	А
Beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.	1	A
MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	1	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	1	A
Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death.	1	в

Initiation of sacubitril/valsartan in ACE inhibitor naive (i.e. de novo) patients with HFrEF may be considered (class of recommendation IIb, level of evidence B).



<sup>a</sup>Class of recommendation. <sup>b</sup>Level of evidence



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## Ivabradina



### Other drugs to be considered in selected patients with heart failure with reduced ejection fraction

Recommendations	Class*	Level
l <sub>/</sub> -channel inhibitor		
Ivabradine should be considered in symptomatic patients with LVEF ≤35%, in SR and a resting heart rate ≥70 bpm despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE-I/(or ARNI) and an MRA, to reduce the risk of HF hospitalization and CV death. <sup>139</sup>	Ita	в
Ivabradine should be considered in symptomatic patients with LVEF ≤35%, in SR and a resting heart rate ≥70 bpm who are unable to tolerate or have contraindications for a beta-blocker to reduce the risk of HF hospitalization and CV death. Patients should also receive an ACE-I (or ARNI) and an MRA. <sup>149</sup>	lla	c
Soluble Guanylate Cyclase Receptor Stimulator		
Vericiguat may be considered in patients in NYHA Class II–IV who have had worsening HF despite treatment with an ACE-I (or ARNI), a beta-blocker and an MRA to reduce the risk of CV mortality or HF hospitalization. <sup>341</sup>	шь	8



\*Class of recommendation. \*Level of evidence

## **ICFE ligeramente reducida**

#HeartFailure2021

### Pharmacological treatments in patients with (NYHA class II-IV) heart failure with mildly reduced ejection fraction

Recommendations	Class <sup>a</sup>	Levelb
Diuretics are recommended in patients with congestion and HFmrEF in order to alleviate symptoms and signs.		lew!
An ACE-I may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death.	IIb	С
An ARB may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death.	пь	с
A beta-blocker may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death.	пь	с
A MRA may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death.	ПЬ	с
Sacubitril/valsartan may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death.	IIb	с



<sup>a</sup>Class of recommendation. <sup>b</sup>Level of evidence



Organised by the Heart Failure Association of the ESC .



### Recomendaciones de tratamiento farmacológico

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Screening for, and treatment of, aetiologies, and cardiovascular and non-cardiovascular comorbidities is recommended in patients with HFpEF (see relevant sections of this document).	1	с
Diuretics are recommended in congested patients with HFpEF in order to alleviate symptoms and signs.	1	с

## 6 de julio 2021: el dia de la ICFE preservada

#### - Tweet



Empagliflozina : Estamos ante el nuevo paradigma de tratamiento de la IC con FEVI preservada y la consolidación de los iSGLT2 en todos los perfiles de IC . Great news for our patients!!

Cristobal Morales @CristobMorales · 2h

investor.lilly.com/news-releases/... Breakthrough results for Jardiance® (empagliflozin) confirm EMPEROR-Preserved as first and only successful trial for heart failure with preserved ejection fraction @ValleAlfonso @almucastro01 @DrDoblas @JTLLERGO @Dr\_Manito @clara\_clarais @fjavesc

Menu =

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Breakthrough results for Jardiance® (empagliflozin) confirm EMPEROR-Preserved as first and only successful trial for heart failure with preserved ejection fraction

July 6, 2021

#### Download PDF

- The EMPEROR-Preserved phase III trial met its primary endpoint and demonstrated significant risk



News Release

Breakthrough results for Jardiance® (empagliflozin) confirm EMPEROR-Preserved as first and only successful trial for heart failure with preserved ejection fraction

- The EMPEROR-Preserved phase III trial met its primary endpoint and demonstrated significant risk reduction with Jardiance for the composite of cardiovascular death or hospitalization for heart failure in adults with heart failure with preserved ejection fraction

- Heart failure with preserved ejection fraction has been classified as "the single largest unmet need in cardiovascular medicine" based on prevalence, poor outcomes and absence of clinically proven therapies to date

- With approval, Jardiance would become the first and only clinically proven therapy to improve outcomes for the full spectrum of heart failure patients regardless of ejection fraction

NEWS PROVIDED BY Eli Lilly and Company → Jul 06, 2021, 06:25 ET SHARE THIS ARTICLE

Boehringer Ingelheim

(PRNewsfoto/Boehringer Ingelheim)



12:52 p. m. · 6 jul. 2021 · Twitter for iPhone

# Baseline characteristics of patients with heart failure with preserved ejection fraction in the EMPEROR-Preserved trial

### **EMPEROR-Preserved**

#### Phase III randomised double-blind placebo-controlled event driven trial

**Key Inclusion Criteria:** T2D and non-T2D, aged ≥18 years, chronic HF (NYHA class II–IV) with LVEF >40%, elevated NT-proBNP concentrations and structural heart changes or documented HHF within 12 months.

Key Exclusion Criteria: Symptomatic hypotension and eGFR <20 mL/min/1.73m2.



In EMPEROR-Preserved, however, all patients had to have raised NT-proBNP levels to be eligible with NT-proBNP >300 pg/mL (or >900 pg/mL, if in AF at screening)

#### COMPOSITE PRIMARY ENDPOINT Time to first event of adjudicated CV death or adjudicated HHF CONFIRMATORY KEY SECONDARY ENDPOINTS • First and recurrent adjudicated HHF events • Slope of change in eGFR (CKD-EPI) from baseline

 Table 1 Comparison of baseline demographic and clinical characteristics of patients enrolled in EMPEROR-Preserved and previous heart failure with preserved ejection fraction trials

	EMPEROR- Preserved (n = 5988)	PARAGON-HF (n = 4822)	TOPCAT (n = 3445)	I-PRESERVE (n = 4128)	CHARM- Preserved (n = 3023)	PEP-CHF (n = 850)
Age (years) <sup>a</sup>	72±9	73 ± 8	69 ± 10	72±7	67±11	75 (72–79)
Women (%)	45	52	52	60	40	56
Obese (%) Race (%)	45	49	55	41	38	NR
White	76	82	89	93	92	N/A
Black	4	2	9	2	4	N/A
Asian	14	13	1	1	2	N/A
Native American/other	6	1	<1	NR	0	N/A
NYHA class (%)						
II	82	72	63	22	61	NR
III	18	27	33	77	38	NR
IV	0.3	0.6	<1	3	2	NR
Hypertension (%)	90	96	91	89	64	79
Diabetes (%)	49	43	32	27	28	21
Chronic kidney disease (%)	50	47	39	31	35	NR
Obstructive/central sleep apnoea (%)	7 / 1	NR	NR	NR	NR	NR
COPD (%)	13	14	12	NR	NR	NR
Current smoker (%)	7	7	10	NR	14	NR
Anaemia (%)	14	NR	NR	15	27	NR
History of CAD (%)	35	43	59	13	33	NR
History of myocardial infarction (%)	29	23	26	24	44	27
History of atrial fibrillation/flutter (%)	52	52	35	29	29	NR
History of malignancy	10	NR	NR	NR	NR	NR
Stroke (%)	10	10	8	10	9	NR

### Table 1 Comparison of baseline demographic and clinical characteristics of patients enrolled in EMPEROR-Preserved and previous heart failure with preserved ejection fraction trials

	EMPEROR- Preserved (n = 5988)	PARAGON-HF ( <i>n</i> = 4822)	TOPCAT (n = 3445)	I-PRESERVE (n = 4128)	CHARM- Preserved (n = 3023)	PEP-CHF (n = 850)
Prior HF hospitalization within 12 months before visit 1 (%)	23	48	72	23	69	NR
ICD (%)	4	0.4	1	NR	0.8	NR
MAGGIC risk score	19.1 ± 5.6	20 ± 6	NR	NR	NR	NR
Medications (%)						
Diuretics	86	96	82	Loop = 83;	75	Loop = 46;
				thiazide = 5	52	thiazide = 55
ACE inhibitors	40	40	65	26	19ª	-
ARBs	39	45	20	N/A	N/A	-
ARNI	2	-	NR	NR	NR	NR
MRA	37	24	-	15	12	NR
Beta-blockers	86	75	78	59	56	55
CCB	30	36	38	40	31	33
Nitrates	12	17	15	27	33	51
Aspirin	42	40	65	NR	58	66
Antiplatelet (except aspirin)	16	13	NR	59	5	NR
Anticoagulants	48	27	23	19	10	16
Statins	69	62	53	NR	NR	NR
Cardiac glycosides	9	9	NR	14	28	12

 Table 2 Comparison of baseline physical examination, laboratory, echocardiographic and electrocardiographic characteristics of patients enrolled in EMPEROR-Preserved and previous heart failure with preserved ejection fraction trials

	EMPEROR- Preserved (n = 5988)	PARAGON-HF (n = 4822)	TOPCAT (n = 3445)	I-PRESERVE (n = 4128)	CHARM- Preserved (n = 3023)	PEP-CHF (n = 850)
BMI (kg/m <sup>2</sup> ) <sup>a</sup>	30±6	30 ± 5	32±7	30 ± 5	29±6	28 (25-30)
Atrial fibrillation/flutter (%, at screening) <sup>b</sup>	35	32	28	29	29	21
LBBB (%)	9	/	8	8	NR	NK
RBBB (%)	9	NR	11	NR	NR	NR
LV hypertrophy (%)	10	NR	29	31	15	NR
Paced rhythm (%)	8	NR	7	NR	NR	NR
E/e' ≥13 (%)	13	NR	NR	NR	NR	NR
Any LA size/volume increase at baseline (%)	82	92°	NR	NR	NR	NR
LA width $\geq$ 4 cm (%)	59	NR	NR	NR	NR	NR
LA length $\geq$ 5 cm (%)	21	NR	NR	NR	NR	NR
LA area $\geq 20 \text{ cm}^2$ (%)	23	NR	NR	NR	NR	NR
LA volume≥55 mL (%)	15	NR	NR	NR	NR	NR
LA volume index $\geq$ 34 mL/m <sup>2</sup> (%)	20	NR	NR	NR	NR	NR

 Table 2 Comparison of baseline physical examination, laboratory, echocardiographic and electrocardiographic characteristics of patients enrolled in EMPEROR-Preserved and previous heart failure with preserved ejection fraction trials

		<b>ARAGON-HF</b> n = 4822)	<b>TOPCAT</b> ( <i>n</i> = 3445)	I-PRESERVE (n = 4128)	CHARM- Preserved (n = 3023)	PEP-CHF (n = 850)
Baseline weight (kg)	82 ± 19	NR	90 ± 22	NR	NR	NR
Baseline heart rate <sup>a</sup>	70 ± 12	70 ± 12	69±10	71 ± 10	71 ± 12	73 (66-82)
Baseline SBP (mmHg) <sup>a</sup>	132 ± 16	136 ± 15	129 ± 14	136 ± 15	136 <u>+</u> 18	139 (129–150)
Baseline DBP (mmHg) <sup>a</sup>	76 <u>+</u> 11	77 <u>+</u> 11	76 <u>+</u> 11	79 <u>+</u> 9	78 <u>+</u> 11	80 (74-86)
Baseline NT-proBNP (pg/mL)	974 (499–1730	) 885 (863-908)	950 (588–	1920) –	-	-
LVEF (%) <sup>a</sup>	54±9	58±8	57±7	59±9	54±9	64 (56-66)
eGFR (mL/min) <sup>a</sup>	60.6 ± 19.8	63 ± 19	$68 \pm 20$	$73 \pm 23$	NR	NR
<45	23.8	18	NR	NR	NR	NR
45 to <60	26.1	30	NR	31	NR	NR
≥60	50.1	53	NR	NR	NR	NR
Baseline haemoglobin (g/dL) <sup>a</sup>	13±2	NR	13±2	14	13	NR
Baseline troponin (ng/mL) <sup>a</sup>	$23.7 \pm 30$	NR	NR	NR	NR	NR
Haemoglobin A1c (%) <sup>a</sup>	7.3 ± 1.5	NR	NR	NR	NR	NR



Organised by the Heart Failure Association of the ESC .



#### Recomendaciones de tratamiento farmacológico

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Tafamidis is recommended in patients with genetic testing proven hereditary hTTR-CMP and NYHA class I or II symptoms to reduce symptoms and CV hospitalization and mortality.	1	в
Tafamidis is recommended in patients with wtTTR-CA and NYHA class I or II symptoms to reduce symptoms and CV hospitalization and mortality.	I	в

Tafamidis in Transthyretin Cardiomyopathy Clinical Trial (ATTR-ACT)



# Heart Failure 2021: pharmacological needs for next future

- Advanced heart failure
- Post-MI
- HFpEF : Emperor-Preserved **V**. Deliver (?)
- HFmrEF
- CKD and HF meds
- Individualization and implementation
- Digital solutions



European Journal of Heart Failure (2021) doi:10.1002/ejhf.2206 **POSITION PAPER** 

Patient profiling in heart failure for tailoring medical therapy. A consensus document of the Heart Failure Association of the European Society of Cardiology

### Important characteristics when considering therapy in heart failure patients



#### Rosano G et al. Eur J Heart Fail. 2021.doi.org/10.1002/ejhf.2206

### Fenotipos clínicos para la individualización en IC



#### Rosano G et al. Eur J Heart Fail. 2021.doi.org/10.1002/ejhf.2206

### ESC/HFA personalized approach for the treatment of heart failure







# Improved Risk Stratification for Ventricular Arrhythmias and Sudden Death in Patients With Nonischemic Dilated Cardiomyopathy

Schematic Representation of the Proposed New Algorithm



high-risk LGE: epicardial LGE, transmural LGE, or combined septal and free-wall LGE



#### Di Marco A, et al. J Am Coll Cardiol. 2021;77:2890-2905

### **CCS/CHFS HEART FAILURE GUIDELINES UPDATE 2021**

### Simplified treatment algorithm for management of heart failure with reduced ejection fraction (HFrEF)



#### RECOMMENDATION

 We recommend that in the absence of contraindications, patients with HFrEF be treated with combination therapy including 1 evidence-based medication from each of the following categories:

 a. ARNI (or ACEI/ARB);
 b. β-blocker;
 c. MRA; and
 d. SGLT2 inhibitor.
 (Strong Recommendation; Moderate-Quality Evidence).

➤ The "algorithm" has been informed by best available evidence and the consensus of the Primary Panel, but to date, there is no proven superior approach to medication initiation and titration.

➢ On the basis of clinical characteristics, it might be preferable to titrate doses of different classes of medications simultaneously ("in-parallel" approach), rather than fully titrate one medication class before initiating an additional agent ("strict sequential" approach).

# **2021 ACC Expert Consensus Now Includes Dapagliflozin as a Component of First-Line Treatment for Patients With HFrEF**



- ARNIs, beta-blockers<sup>b</sup>, MRAs and SGLT2 inhibitors are first-line medications for all patients with HFrEF.
- SGLT2 inhibitors should be added for patients with chronic HFrEF who are already receiving ARNI/ACEI/ARB, beta-blocker and MRA, if not contraindicated.
- Achieving target or maximally tolerated doses of other HFrEF therapies is not necessary before adding SGLT2 inhibitors.

Maddox TM et al. Online ahead of print. J Am Coll Cardiol. 2021.

# Should we do it differently ? The debate for 2021



Adapted from John J.V. McMurray & Milton Packer. Circulation. 2021;143:875–877

#### Tratamiento del paciente con ICFE reducida en 2021



1. VICTORIA: Vericiguat si TAS  $\geq$  100 mmHg / FG  $\geq$  15 ml/min/1,73m2

2. GALACTIC-HF: Omecamtiv mecarbil si TAS ≥ 85 mmHg / FG ≥ 20 ml/min/1,73m2 (No comercializado)

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#### 22:42

🔊 50 % 🗖

Nicolas Manito 3478 Tweets

377 Siguiendo 4638 Seguidores

Tweets

Tweets y respuestas Multimedia



Nicolas Manito @Dr\_Manito · 2min ····

Very proud of Dr. Toni Bayes-Genis co-charing Highlights of Heart Failure-HFA ESC 2021. Also his team ICOR @lcorCat was the most cited investigator group in this important session. Congratulations Toni and to your excellent group!!! #HeartFailure2021 #CardioTwitter





#### **Clinical Case Award**

## Severe ventricular dysfunction due to a catecholamine-secreting paraganglioma

Luis Manuel Dominguez Rodriguez, María Melendo-Viu, David Dobarro-Pérez, Andrés Íñiguez-Romo

#### What is the current situation?

- 28-year-old male.
- Right hemiplegia and aphasia.
- Severe ventricular dysfunction of unknown etiology.
- Cardiogenic shock with beta-blockers.
- Persistent fever of unknown origin and negative microbiological studies.

#### What should we do now?





Catecholamine-secreting paraganglioma



### HEART FAILURE 2022 Madrid 21-24 Mayo

## **Conclusiones Heart Failure 2021 Guidelines**

- La cuatri-terapia (BB, IECA-Sac/Vals, ARM, iSGLT2) en ICFEr obtiene la máxima recomendación en un esquema horizontal de aplicación clínica
- Dapagliflozina y Empagliflozina son recomendación IA en pacientes con ICFEr para reducir el riesgo de hospitalización por IC y muerte
- Débil recomendación de los tratamientos farmacológicos para los pacientes con ICFE ligeramente reducida
- No hay novedades ni cambios para las recomendaciones en ICFE preservada
- Importancia de la optimización terapéutica durante la hospitalización por IC seguida de la continuidad asistencial pos-alta

Las guías de IC definitivas se presentaran durante el congreso ESC 2021 (27-30 agosto)



# **Moltes gracies !!!**



@ Dr\_Manito