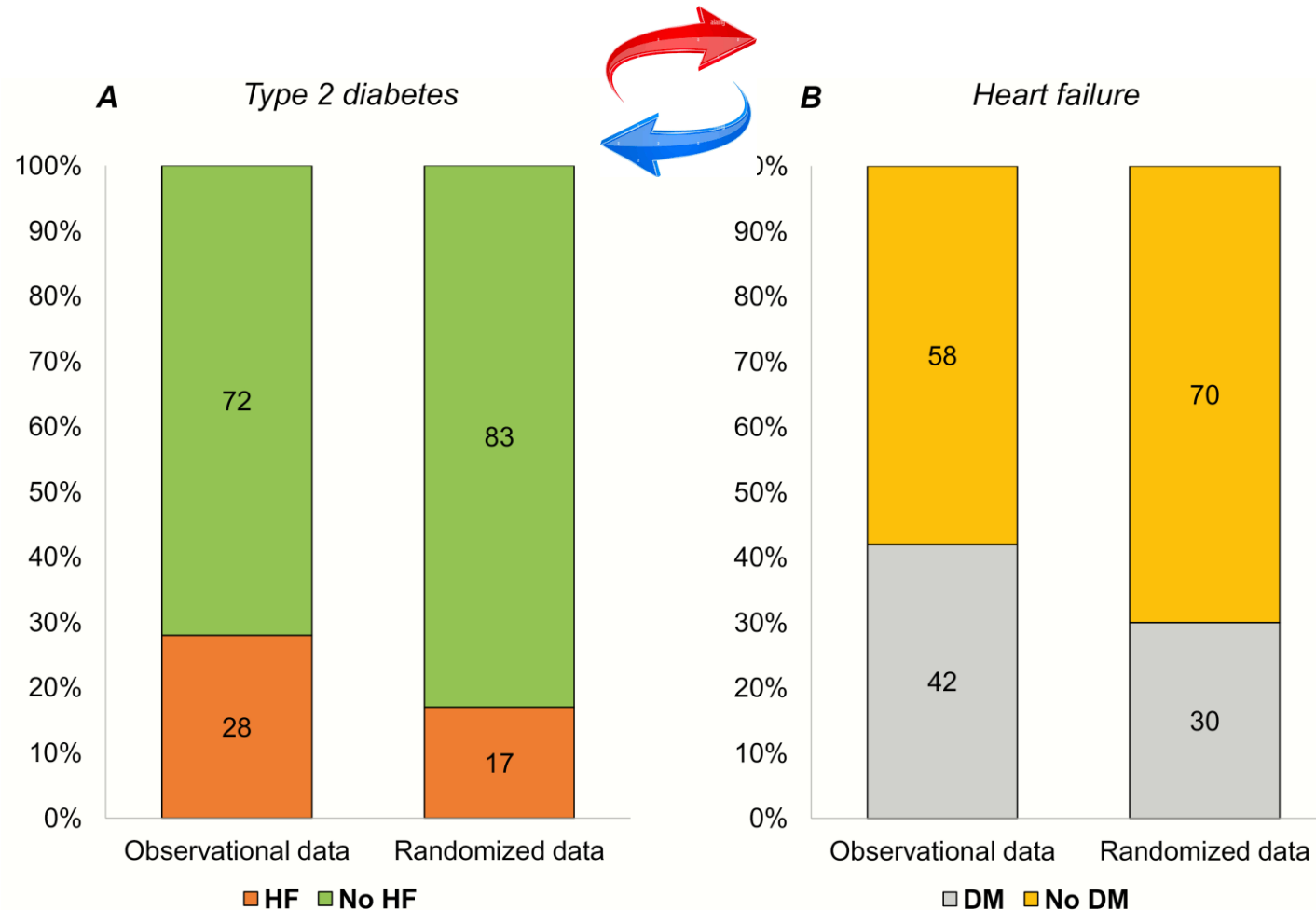


INSUFFISANCE CARDIAQUE  
CHEZ LE DIABETIQUE  
TRAITEMENT MEDICAL

A. TALAMALI – CARDIOLOGUE LIBERAL

# Épidémiologie

IC et DT2 deux maladies étroitement liées

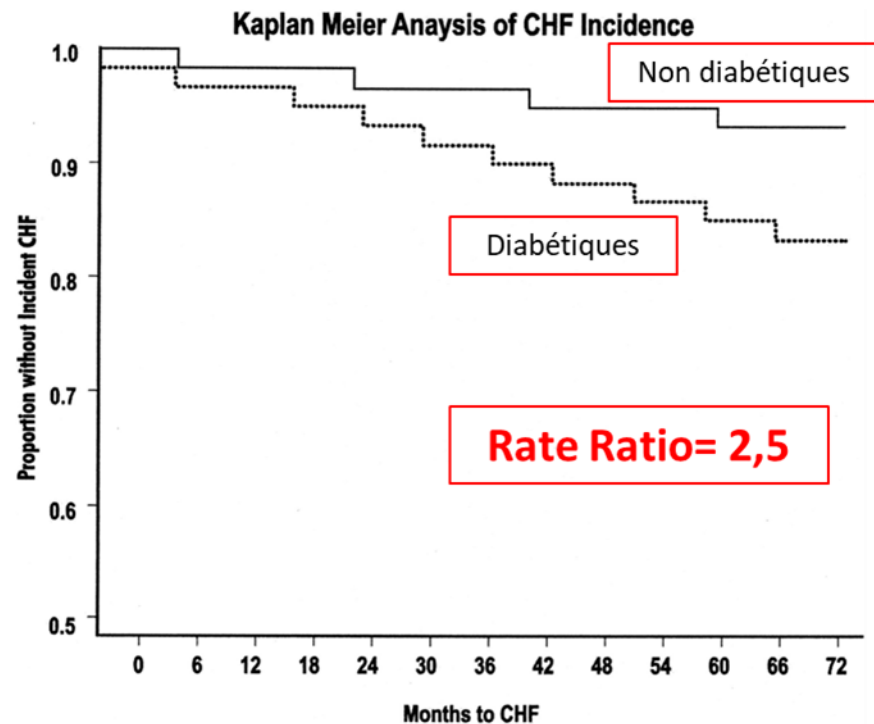


- Environ 17% à 28% des DT2 ont une IC déjà connue.
- À l'inverse, 30% à 40% des IC sont des DT2
- IC aiguës, 50% sont DT2

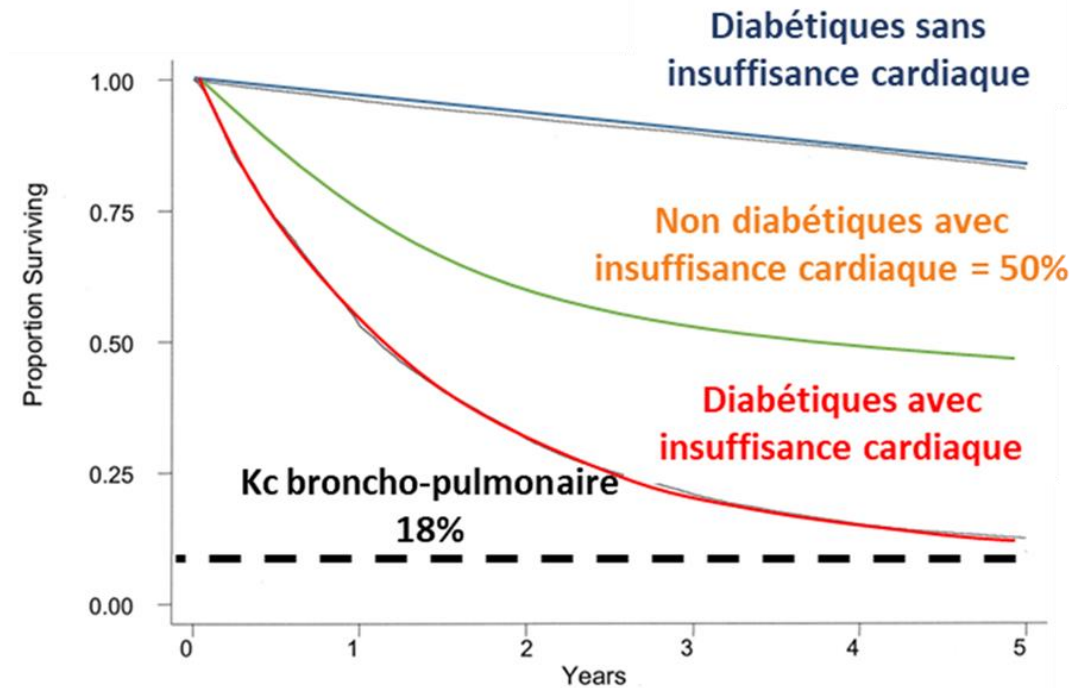
# Épidémiologie

IC et DT2: longtemps sous-estimée

incidence 2 fois supérieure, pronostic effroyable

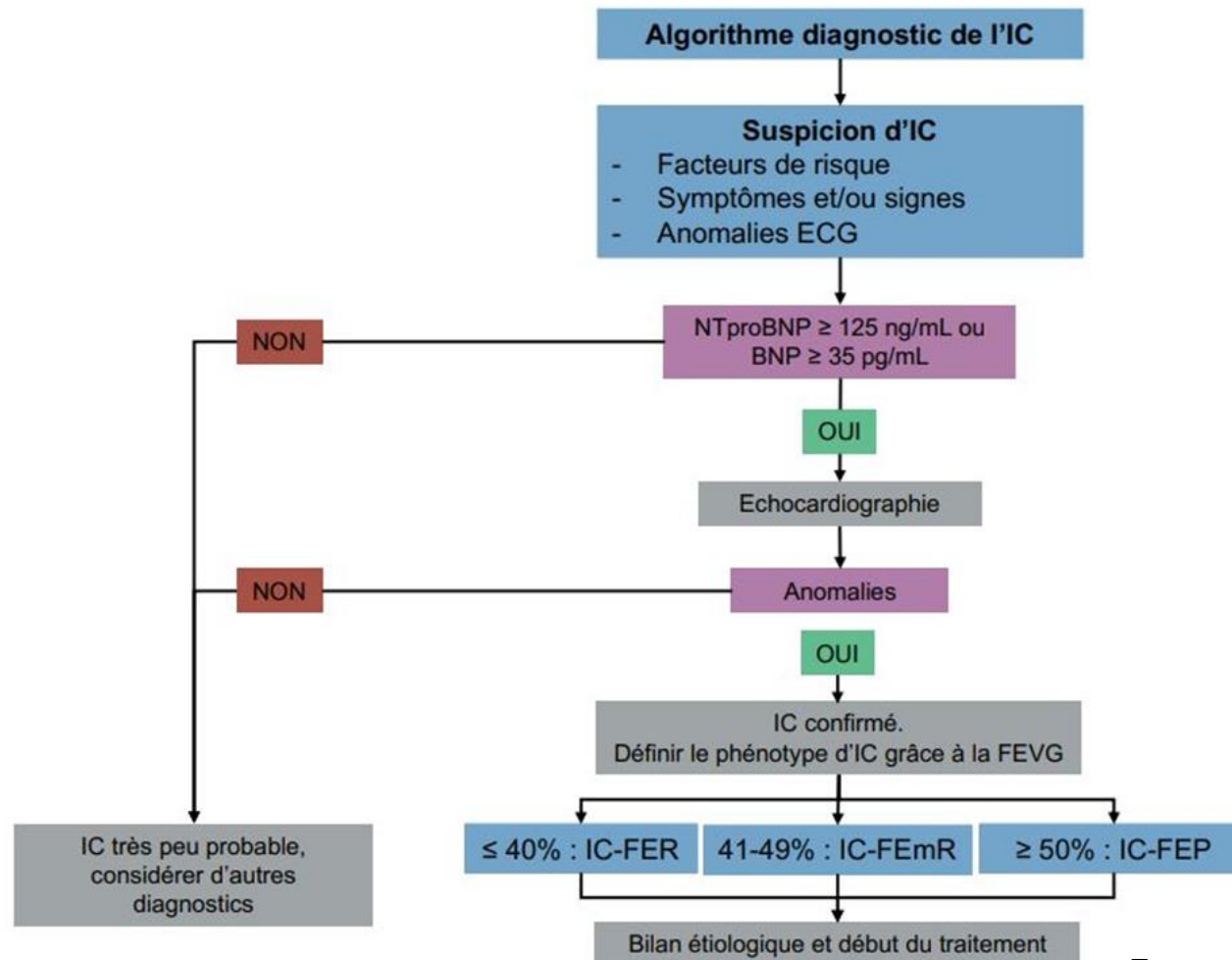


Gregory A. Nichols et al, *Diabetes Care* 27:1879–1884, 2004



Alain G. Bertoni et al, *Diabetes Care* 27:699–703, 2004

# Diagnostic et phénotypes de l'insuffisance cardiaque



Traitement de l'insuffisance  
cardiaque à FE réduite



ESC

European Society  
of Cardiology

European Heart Journal (2021) 42, 3599–3726

doi:10.1093/eurheartj/ehab368

ESC GUIDELINES

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



### Management of HFrEF



To reduce mortality - for all patients

ACE-I/ARNI

BB

MRA

SGLT2i

# Efficacy of Angiotensin-Converting Enzyme Inhibitors and Beta-Blockers in the Management of Left Ventricular Systolic Dysfunction According to Race, Gender, and Diabetic Status

## A Meta-Analysis of Major Clinical Trials

- Les IEC ont été la première classe de médicaments à démontrer une réduction de la mortalité chez les patients souffrant d'ICFER.
- Bénéfices observés chez les patients avec et sans diabète.

**Table 4.** Effect of ACE Inhibitors on Mortality From Heart Failure in Diabetic and Nondiabetic Patients

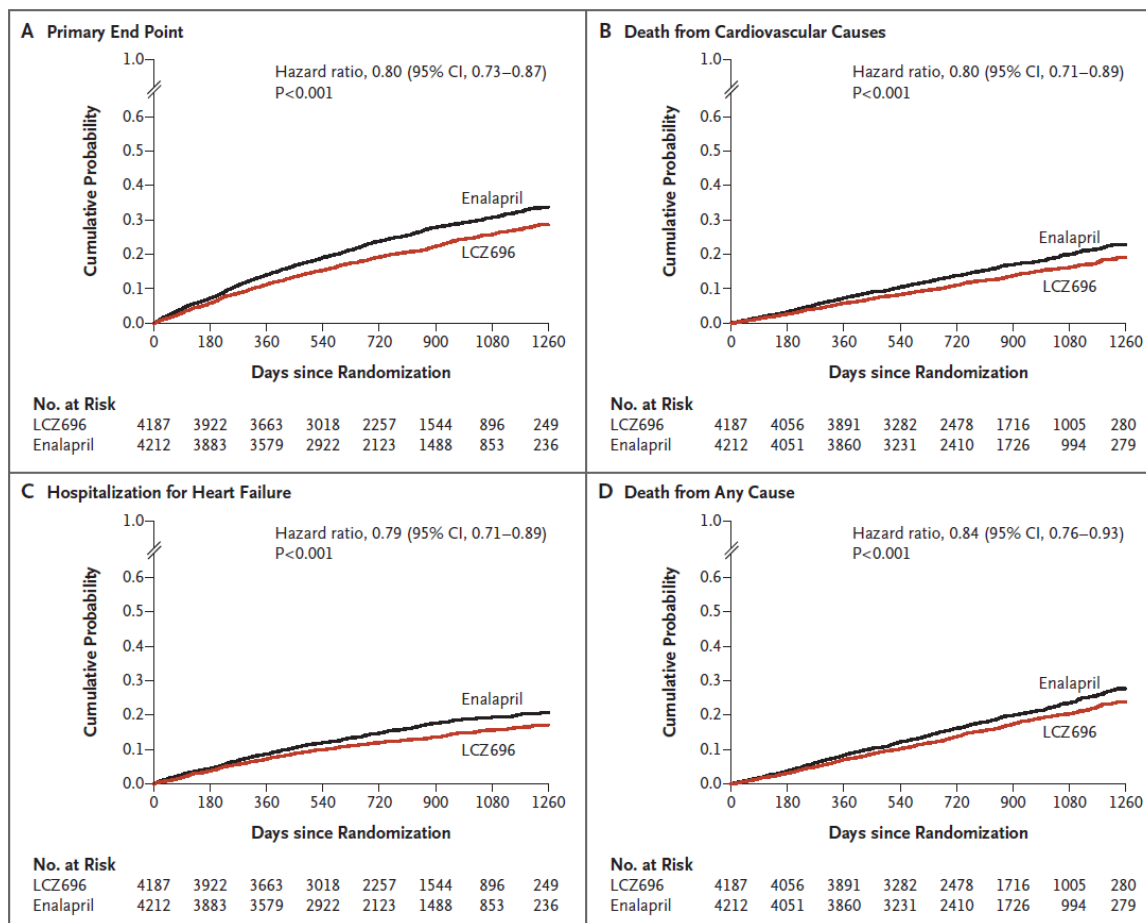
Study Name	RR Analysis					
	Total N	Nondiabetic N	Diabetic N	RR, Nondiabetic (95% CI)	RR, Diabetic (95% CI)	RRR (95% CI)
CONSENSUS	253	197	56	0.64 (0.46–0.88)	1.06 (0.65–1.74)	1.67 (0.93–3.01)
SAVE	2,231	1,739	492	0.82 (0.68–0.99)	0.89 (0.68–1.16)	1.09 (0.79–1.50)
SMILE	1,556	1,253	303	0.79 (0.54–1.15)	0.44 (0.22–0.87)	0.56 (0.25–1.22)
SOLVD-Prevention	4,228	3,581	647	0.97 (0.83–1.15)	0.75 (0.55–1.02)	0.77 (0.54–1.09)
SOLVD-Treatment	2,569	1,906	663	0.84 (0.74–0.95)	1.01 (0.85–1.21)	1.21 (0.97–1.50)
TRACE	1,749	1,512	237	0.85 (0.74–0.97)	0.73 (0.57–0.94)	0.87 (0.65–1.15)
Random effects pooled estimate		10,188	2,398	0.85 (0.78–0.92)	0.84 (0.70–1.00)	1.00 (0.80–1.25)

## Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

the PARADIGM-HF |

sacubitril/valsartan (ARNi)

SRAA /peptide natriurétique



Le sacubitril/valsartan (ARNi) a montré une réduction significative des décès CV et des hospitalisations liées à l'insuffisance cardiaque par rapport aux inhibiteurs de l'ECA

# Risk Related to Pre–Diabetes Mellitus and Diabetes Mellitus in Heart Failure With Reduced Ejection Fraction

## Insights From Prospective Comparison of ARNI With ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial

the PARADIGM-HF I

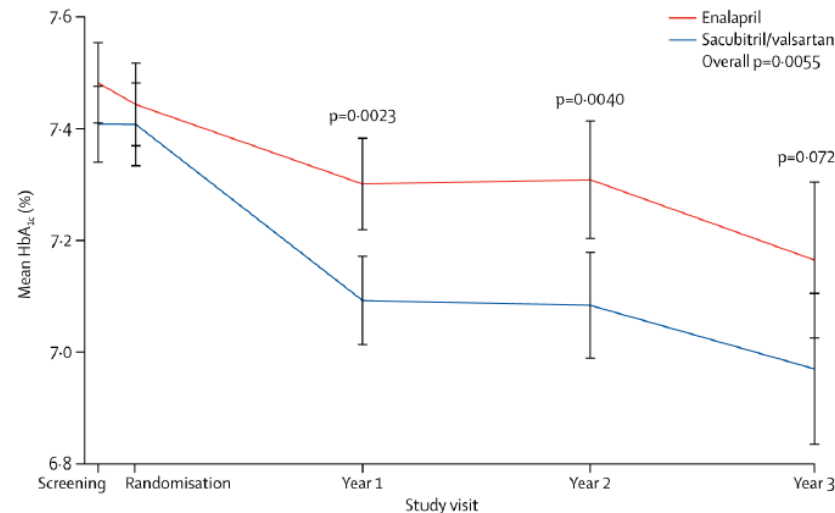
Les effets positifs du sacubitril/valsartan sont cohérents quel que soit le taux d'HbA1c

Table 3. Treatment Effects of LCZ696 (Sacubitril/Valsartan) According to History of Diabetes Mellitus and Glycemic Status

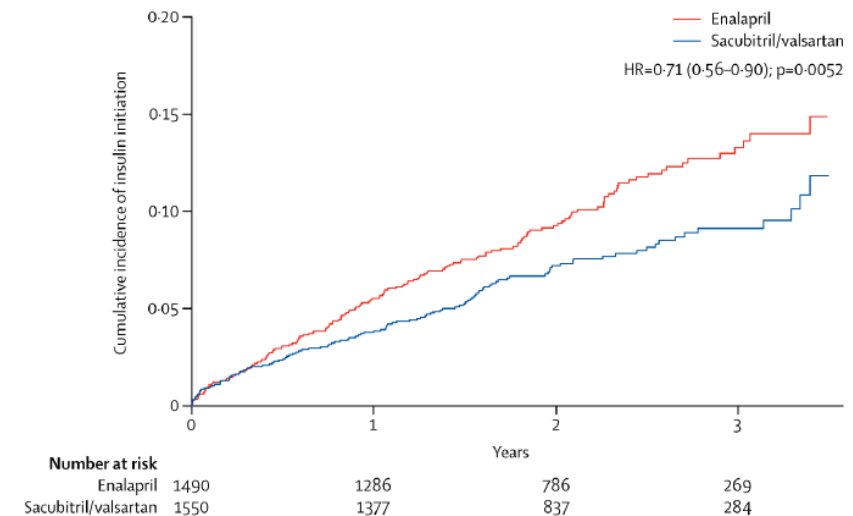
	Overall	Normoglycemia	Pre–Diabetes Mellitus	Undiagnosed Diabetes Mellitus	Diabetes Mellitus	P Values for Interaction
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	
HF hospitalization or cardiovascular death	0.80 (0.73–0.87)	0.68 (0.56–0.83)	0.76 (0.63–0.91)	0.97 (0.77–1.22)	0.87 (0.77–0.98)	0.13
Cardiovascular death	0.80 (0.71–0.89)	0.62 (0.48–0.80)	0.76 (0.61–0.96)	0.86 (0.65–1.15)	0.92 (0.77–1.09)	0.09
HF hospitalization	0.80 (0.71–0.89)	0.85 (0.65–1.12)	0.73 (0.57–0.93)	0.88 (0.65–1.20)	0.79 (0.67–0.94)	0.78
All-cause mortality	0.84 (0.76–0.93)	0.68 (0.55–0.85)	0.77 (0.63–0.95)	0.91 (0.69–1.18)	0.97 (0.83–1.14)	0.06
Significant worsening in KCCQ clinical score (≥5) at 8 mo†	0.83(0.76–0.92)‡	0.73 (0.60–0.89)‡	0.86 (0.71–1.04)‡	0.93 (0.71–1.21)‡	0.86 (0.74–1.01)‡	0.14

# Effect of sacubitril/valsartan versus enalapril on glycaemic control in patients with heart failure and diabetes: a post-hoc analysis from the PARADIGM-HF trial

le traitement par sacubitril/valsartan a été associé à amélioration du MB glucidique chez les DT2.



**Diminution des taux d'HbA<sub>1c</sub>**



**Initiation d'une insulinothérapie moindre**

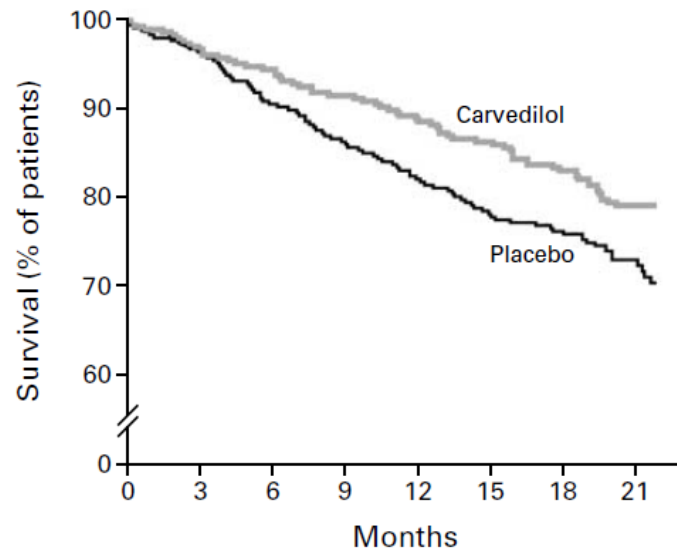


**(COPERNICUS) trial**

**Les Bêtabloquants**

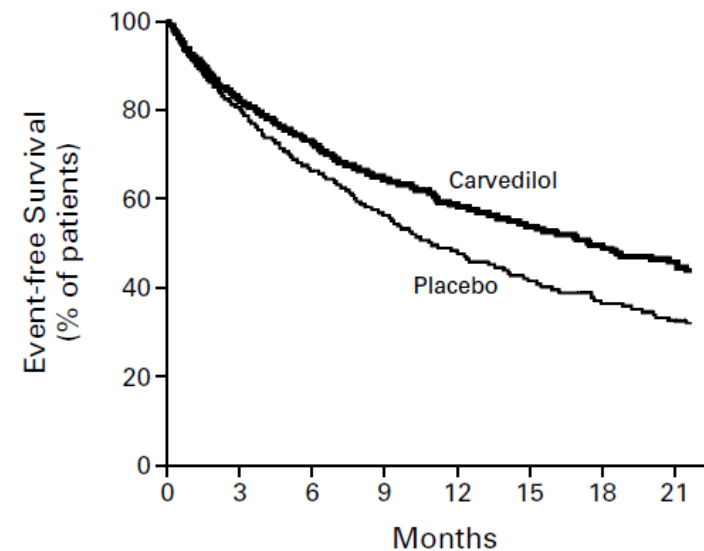
EFFECT OF CARVEDILOL ON SURVIVAL IN SEVERE CHRONIC HEART FAILURE

les bêtabloquants réduisent la mortalité et la morbidité chez les patients souffrant d'ICFER qui reçoivent déjà des inhibiteurs de l'ECA et des diurétiques.



NO. OF PATIENTS AT RISK

Placebo	1133	937	703	580	446	286	183	114
Carvedilol	1156	947	733	620	479	321	208	142



NO. OF PATIENTS AT RISK

Placebo	1133	767	513	377	262	154	88	55
Carvedilol	1156	789	559	431	318	208	122	81

# Survival and Hospitalization in Heart Failure Patients With or Without Diabetes Treated With $\beta$ -Blockers

Le bénéfice des bêtabloquants est retrouvé que le patients soit diabétique ou non

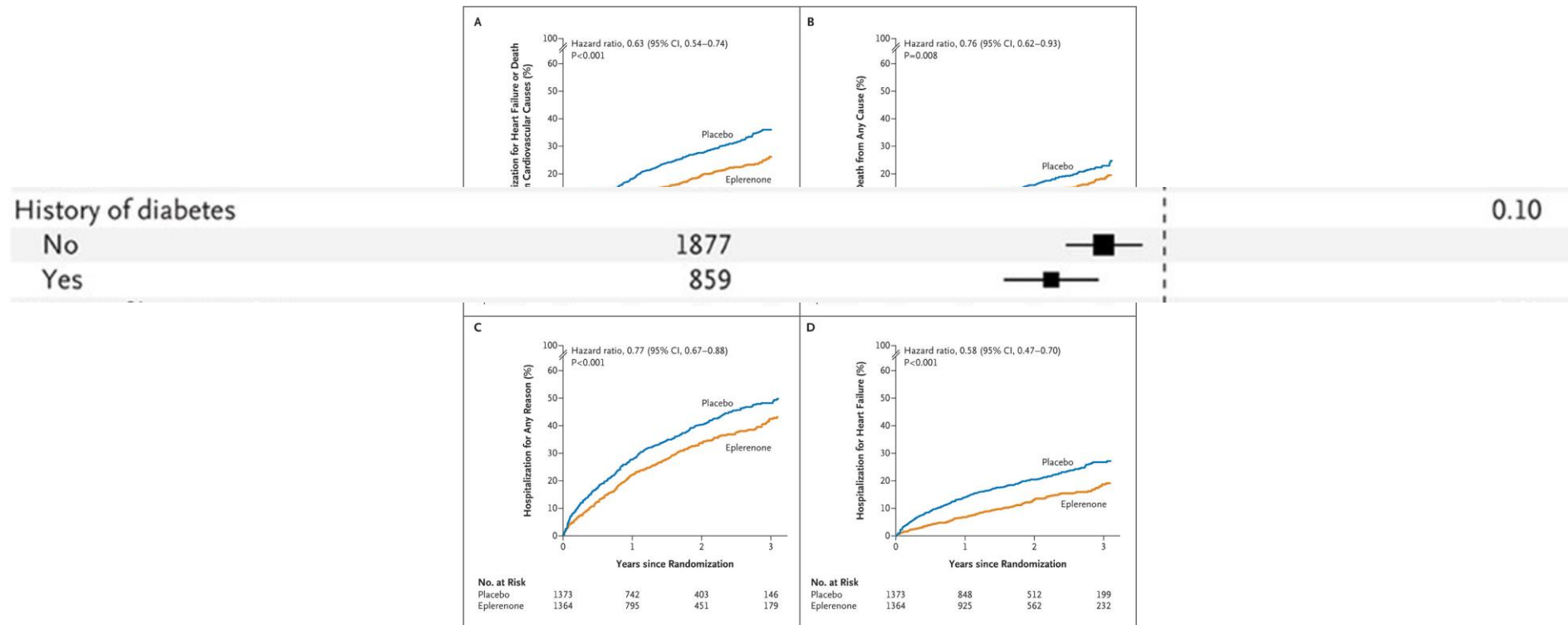
**Table 5.** Relative Risk of Mortality or Hospitalization in Diabetic and Nondiabetic Patients According to the Use of  $\beta$ -Blockers

	Total	$\beta$ -Blockers	No $\beta$ -Blockers	RR (95% CI)
<b>Mortality</b>				
Total population	2843	125 (7.9%)	216 (17.1%)	0.46 (0.38–0.57)
Nondiabetics	2222	89 (7.1%)	154 (16.0%)	0.44 (0.35–0.57)
Diabetics	621	36 (11.2%)	62 (20.8%)	0.54 (0.37–0.78)
<b>Hospitalization</b>				
Total population	2586	334 (22.8%)	326 (29.1%)	0.78 (0.69–0.89)
Nondiabetics	2031	249 (21.3%)	239 (27.8%)	0.76 (0.66–0.89)
Diabetics	555	85 (29.0%)	87 (33.2%)	0.87 (0.68–1.10)
<b>Mortality or hospitalization</b>				
Total population	2781	423 (27.5%)	478 (38.5%)	0.71 (0.64–0.79)
Nondiabetics	2173	310 (25.3%)	345 (36.4%)	0.69 (0.61–0.79)
Diabetics	608	113 (36.0%)	133 (45.2%)	0.80 (0.65–0.97)

Eplerenone in Patients with Systolic Heart Failure  
and Mild Symptoms

the EMPHASIS-HF Study

Réduction de la mortalité et les hospitalisations dues à l'insuffisance cardiaque chez les patients avec et sans diabète.



# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

NOVEMBER 21, 2019

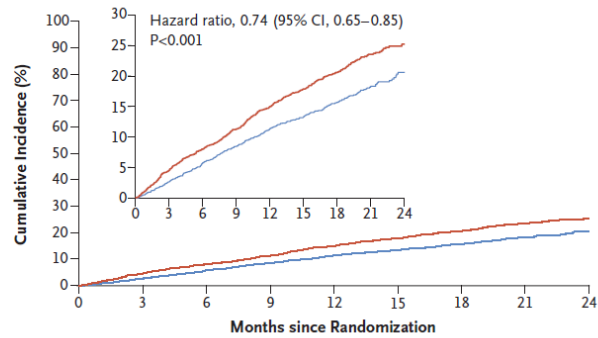
VOL. 381 NO. 21

## Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

## Les iSGLT2

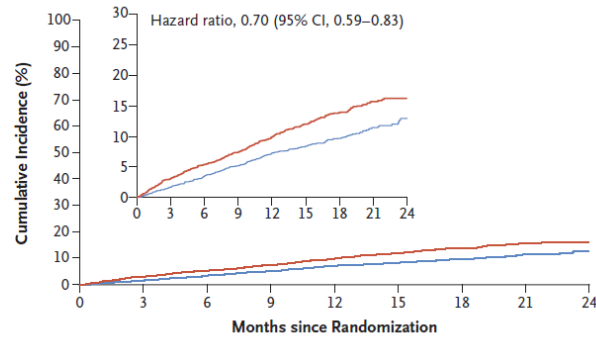
### the DAPA-HF Trial

A Primary Outcome



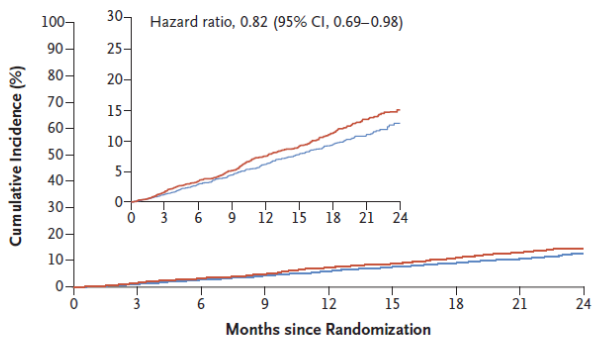
No. at Risk	0	3	6	9	12	15	18	21	24
Placebo	2371	2258	2163	2075	1917	1478	1096	593	210
Dapagliflozin	2373	2305	2221	2147	2002	1560	1146	612	210

B Hospitalization for Heart Failure



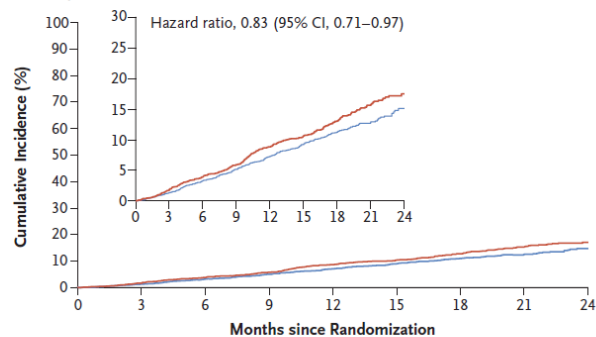
No. at Risk	0	3	6	9	12	15	18	21	24
Placebo	2371	2264	2168	2082	1924	1483	1101	596	212
Dapagliflozin	2373	2306	2223	2153	2007	1563	1147	613	210

C Death from Cardiovascular Causes



No. at Risk	0	3	6	9	12	15	18	21	24
Placebo	2371	2330	2279	2230	2091	1636	1219	664	234
Dapagliflozin	2373	2339	2293	2248	2127	1664	1242	671	232

D Death from Any Cause



No. at Risk	0	3	6	9	12	15	18	21	24
Placebo	2371	2330	2279	2231	2092	1638	1221	665	235
Dapagliflozin	2373	2342	2296	2251	2130	1666	1243	672	233

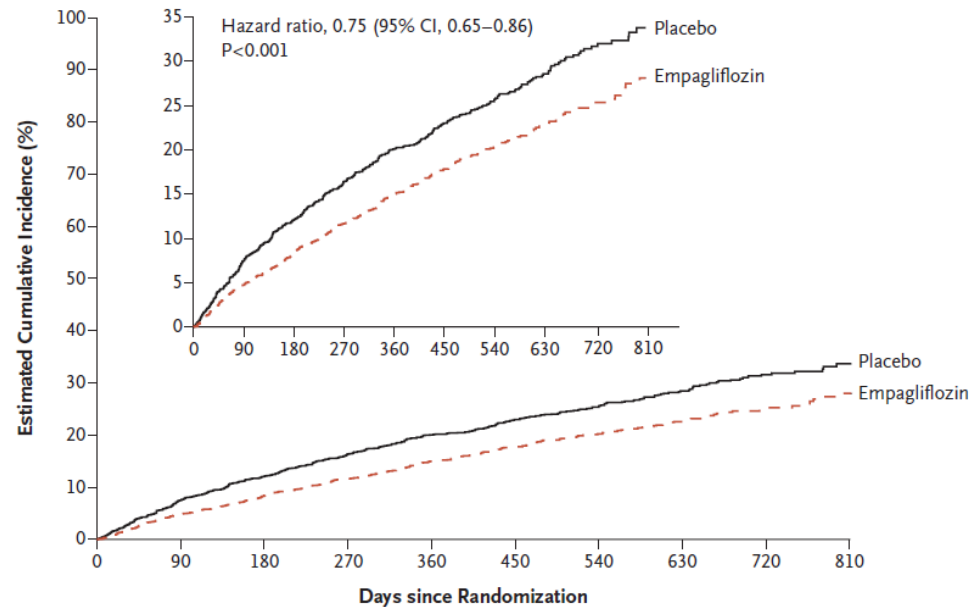
- FEVG ≤ 40%; TMO; DFG ≥ 30ml/mn/1,73<sup>2</sup>
- Réduction de 26 % du critère d'évaluation principal:
  - Aggravation de l'IC
  - Et un décès d'origine CV.
- Réduction de 17% de la mortalité totale.
- Bénéfices observés chez les patients avec et sans diabète.
- Indépendants du traitement antidiabétique

## Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure

# Les iSGLT2

the EMPEROR-Reduced Trial

A Primary Outcome



No. at Risk

Placebo	1867	1715	1612	1345	1108	854	611	410	224	109
Empagliflozin	1863	1763	1677	1424	1172	909	645	423	231	101

- FEVG  $\leq$  40%; TMO; DFG  $\geq$  20ml/mn/1,73<sup>2</sup>
- Réduction de 25 % du critère d'évaluation principal:
  - Décès d'origine CV
  - Et hospitalisations dues à une IC+++.
- Bénéfices observés chez les patients avec et sans diabète.



ESC

European Society  
of Cardiology

European Heart Journal (2021) 42, 3599–3726

doi:10.1093/eurheartj/ehab368

ESC GUIDELINES

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

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

# Autres classes thérapeutiques

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<b>Loop diuretics</b>		
Diuretics are recommended in patients with HFrEF with signs and/or symptoms of congestion to alleviate HF symptoms, improve exercise capacity, and reduce HF hospitalizations. <sup>137</sup>	<b>I</b>	<b>C</b>
<b>ARB</b>		
An ARB <sup>c</sup> is recommended to reduce the risk of HF hospitalization and CV death in symptomatic patients unable to tolerate an ACE-I or ARNI (patients should also receive a beta-blocker and an MRA). <sup>138</sup>	<b>I</b>	<b>B</b>

# GESTION ET OPTIMISATION DU TRAITEMENT DE L'ICFER



# Safety, tolerability, and efficacy of up-titration of guideline-directed medical therapies for acute heart failure (STRONG-HF): a multinational, open-label, randomised, trial

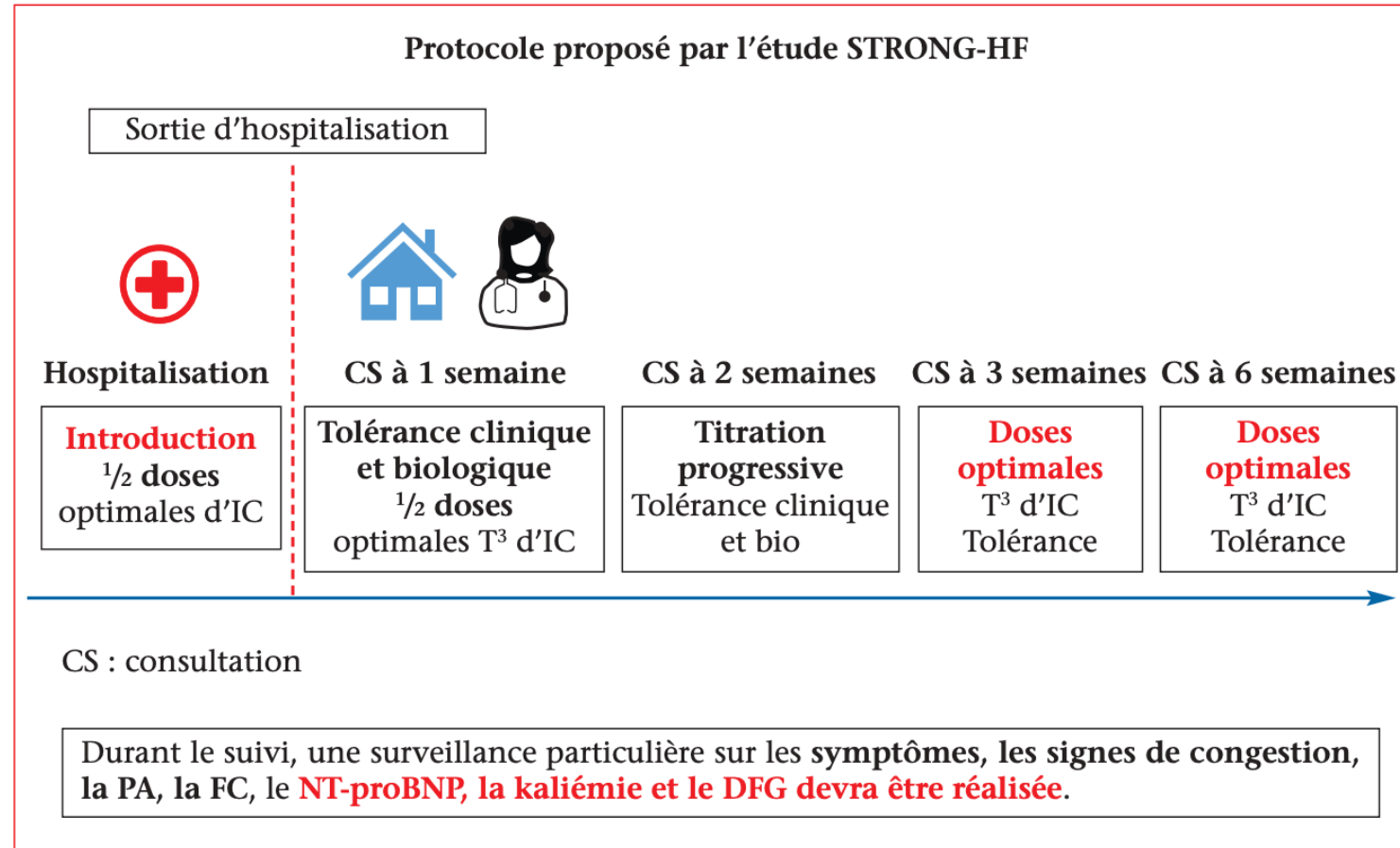
La prescription des 4 classes thérapeutiques avant la sortie de l'hôpital et une titration rapide des doses, étaient sûrs et associés à un risque réduit de décès ou de réadmission pour IC à 180 jours.

	High-intensity care group (n=542)	Usual care group (n=536)	Adjusted treatment effect (95% CI)	Adjusted risk ratio (95% CI)	p value
<b>Primary endpoint</b>					
All-cause death or heart failure readmission by day 180*	74/506 (15.2%)	109/502 (23.3%)	8.1 (2.9 to 13.2)	0.66 (0.50 to 0.86)	0.0021
<b>Secondary endpoints</b>					
Change from baseline to day 90 in EQ-5D VAS†	10.72 (0.88)	7.22 (0.90)	3.49 (1.74 to 5.24)	NA	<0.0001
All-cause death by day 180*	39/506 (8.5%)	48/502 (10.0%)	1.6 (-2.3 to 5.4)	0.84 (0.56 to 1.26)	0.42
All-cause death or heart failure readmission by day 90*	55 (10.4%)	72 (13.8%)	3.4 (-0.4 to 7.3)	0.73 (0.53 to 1.02)	0.081

# 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Recommendation	Class <sup>a</sup>	Level <sup>b</sup>
An intensive strategy of initiation and rapid up-titration of evidence-based treatment before discharge and during frequent and careful follow-up visits in the first 6 weeks following a HF hospitalization is recommended to reduce the risk of HF rehospitalization or death. <sup>c,d,e 16</sup>	<b>I</b>	<b>B</b>

# Titration et optimisation du traitement de l'IC dans l'étude STRONG-HF



Traitement de l'insuffisance  
cardiaque à FE modérément  
réduite et à FE préservée

# Études portant sur l'IC à FE > 40% (HFmEF et HFpEF)

Trial	Intervention	Major inclusion criteria	Mean follow-up	Primary endpoints	Drug effect on symptoms
Aldo-DHF <sup>71</sup>	Spirolactone vs. placebo	LVEF ≥50%, NYHA II–III, peak VO <sub>2</sub> ≤25 mL/min/kg, diastolic dysfunction on echocardiography or AF, age ≥50 y	1.0 y	Reduction in E/e' by -1.5 (P<0.001) No change in peak VO <sub>2</sub> (P = 0.81)	Spirolactone – no improvement in symptoms or QOL
TOPCAT <sup>72</sup>	Spirolactone vs. placebo	LVEF≥45%, ≥1 HF sign, ≥1 HF symptom, HF hospitalization within recent 12 months, or BNP ≥100 pg/mL or NT-proBNP ≥360 pg/mL, age ≥50 y	3.3 y	No difference in combined CV death, aborted cardiac arrest, or HF hospitalization (19% vs. 20%, P = 0.14)	Spirolactone – not reported
DIG-PEF <sup>73</sup>	Digoxin vs. placebo	HF with LVEF >45%, SR	3.1 y	No difference in combined HF mortality or HF hospitalization (21% vs. 24%, P = 0.14)	Digoxin – not reported
PARAMOUNT <sup>74</sup>	Sac/Val vs. valsartan	HF with LVEF ≥45%, NYHA II–III, NT-proBNP >400 pg/mL	12 weeks	Reduction in NT proBNP: ratio of change Sac/Val 0.77, 95% CI, 0.64–0.92 (P = 0.005)	Sac/Val – improvement in QOL-KCCQ
RELAX <sup>75</sup>	Sildenafil vs. placebo	HF with LVEF ≥45%, NYHA II–IV, peak VO <sub>2</sub> <60% of reference values, NT-proBNP >400 pg/mL or high LV filling pressures	24 weeks	No change in peak VO <sub>2</sub> (P = 0.90)	Sildanefil – no improvement
PARAGON-HF <sup>76</sup>	Sac/Val vs. valsartan	HF with LVEF ≥45%, NYHA II–IV, left atrial enlargement OR LVH AND elevated BNP ≥300 pg/mL or NT-proBNP ≥900 pg/mL OR HF hospitalization in the last 9 months	35 months median	Trend towards a reduction in total HF hospitalizations or CV death by 13%, 95% CI, 0.75–1.01, P=0.056)	Sac/Val – no improvement in QOL-KCCQ

**Pas de réduction significative du critère d'évaluation principal**

Trial	Intervention	Major inclusion criteria	Mean follow-up	Primary endpoints	Drug effect on symptoms
PEP-CHF <sup>68</sup>	Perindopril vs. placebo	LV wall motion index ≥1.4 (corresponding to LVEF ≥40%), symptomatic HF treated with diuretic, diastolic dysfunction in echocardiography, age ≥70 y	2.1 y	No difference in combined all-cause mortality or CV hospitalization (36% vs. 37%, P = 0.35)	Perindopril – improvement in functional class and 6MWT
I-PRESERVE <sup>69</sup>	Irbesartan vs. placebo	LVEF ≥45%, NYHA III–IV with corroborative evidence, or NYHA II with HF hospitalization in recent 6 months, age ≥60 y	4.1 y	No difference in combined all-cause mortality or HF hospitalization (24% vs. 25%, P = 0.54)	Irbesartan – no improvement in MLHFQ
CHARM-Preserved <sup>70</sup>	Candesartan vs. placebo	LVEF >40%, NYHA II–IV, history of cardiac hospitalization	3.0 y	Trend towards a reduction in combined CV mortality or HF hospitalization by 11% (22% vs. 24%, unadjusted P = 0.12, adjusted P = 0.051)	Candesartan – not reported

# Les données rétrospectives et les analyses de sous-groupes des ECR dans l'HFmEF

Clinical characteristics	LVEF	Symptoms	Hospitalization for HF <sup>a</sup>	CV death or HF hospitalization <sup>a</sup>	CV mortality	All-cause mortality	Comment
Diuretics							No relevant trials
ACE-I		(Improved)		<b>0.38 (0.19–0.75)<sup>b</sup></b>			PEP-CHF <sup>c</sup>
Candesartan		(Improved)	<b>0.72 (0.55–0.95)<sup>d</sup></b>	<b>0.76 (0.61–0.96)</b>	0.81 (0.60–1.11)	0.79 (0.60–1.04)	CHARM-Preserved <sup>c</sup>
Irbesartan				0.98 (0.85–1.12)			I-PRESERVE <sup>c</sup>
ARNI (Sac/Val)		Improved	NYR	<b>0.78 (0.64–0.95)</b>	NYR	NYR	PARAGON-HF <sup>c</sup> (compared to valsartan)
MRA			0.76 (0.46–1.27)	0.72 (0.50–1.05)	0.69 (0.43–1.12)	0.73 (0.49–1.10)	TOPCAT <sup>c</sup>
Beta-blocker (SR)	Improved		0.95 (0.68–1.32)	0.83 (0.60–1.13)	<b>0.48 (0.24–0.97)</b>	0.59 (0.34–1.03)	IPD Meta-analysis
Beta-blocker (AF)	Improved		1.15 (0.57–2.32)	1.06 (0.58–1.94)	0.86 (0.36–2.03)	1.30 (0.63–2.67)	IPD Meta-analysis
Digoxin			0.80 (0.63–1.03)	0.96 (0.79–1.17)	1.24 (0.94–1.64)	1.08 (0.85–1.37)	DIG <sup>67</sup>

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

### Insuffisance cardiaque à FE modérément réduite (HFmrEF)

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Diuretics are recommended in patients with congestion and HFmrEF in order to alleviate symptoms and signs. <sup>137</sup>	<b>I</b>	<b>C</b>
An ACE-I may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. <sup>11</sup>	<b>IIb</b>	<b>C</b>
An ARB may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. <sup>245</sup>	<b>IIb</b>	<b>C</b>
A beta-blocker may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. <sup>12,119</sup>	<b>IIb</b>	<b>C</b>
An MRA may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. <sup>246</sup>	<b>IIb</b>	<b>C</b>
Sacubitril/valsartan may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. <sup>13,247</sup>	<b>IIb</b>	<b>C</b>

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### Insuffisance cardiaque à FE préservée (HFpEF)

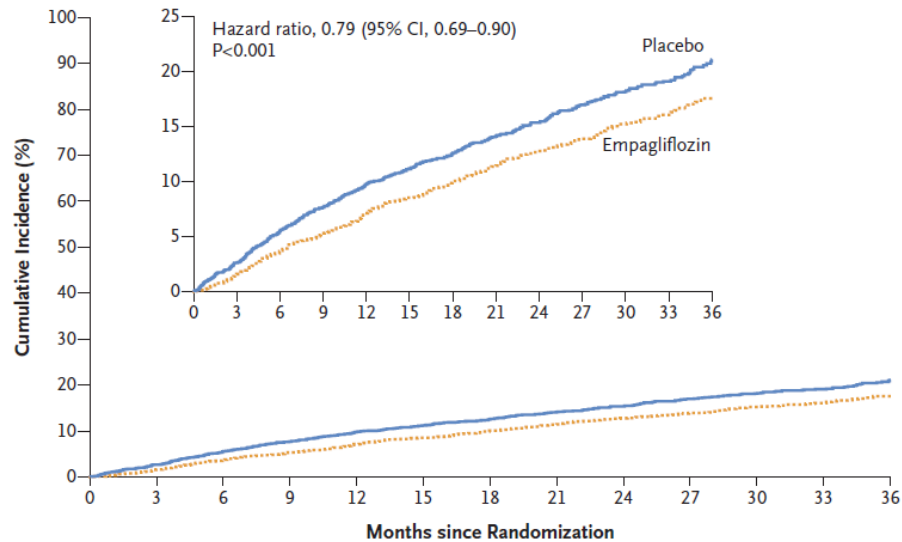
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Screening for, and treatment of, aetiologies, and cardiovascular and non-cardiovascular comorbidities is recommended in patients with HFpEF (see relevant sections of this document).	<b>I</b>	<b>C</b>
Diuretics are recommended in congested patients with HFpEF in order to alleviate symptoms and signs. <sup>137</sup>	<b>I</b>	<b>C</b>

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# iSGLT2 dans l'IC avec FE > 40%

Réduction significative du critère d'évaluation principal : décès cardiovasculaires ou hospitalisations dues à une insuffisance cardiaque.

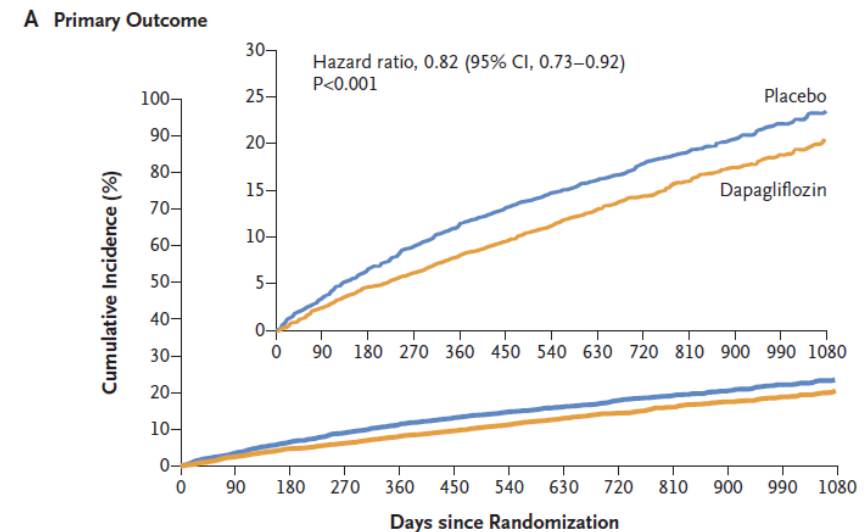
## The EMPEROR-Preserved (Empaglifozine)



No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36
Placebo	2991	2888	2786	2706	2627	2424	2066	1821	1534	1278	961	681	400
Empagliflozin	2997	2928	2843	2780	2708	2491	2134	1858	1578	1332	1005	709	402

N Engl J Med 2021;385:1451-61.

## The DELIVER Trial (Dapaglifozine)



No. at Risk	0	90	180	270	360	450	540	630	720	810	900	990	1080
Placebo	3132	3007	2896	2799	2710	2608	2318	2080	1923	1554	1140	772	383
Dapagliflozin	3131	3040	2949	2885	2807	2716	2401	2147	1982	1603	1181	801	389

N Engl J Med 2022;387:1089-98.

# SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials



## Cardiovascular death or heart failure hospitalisation

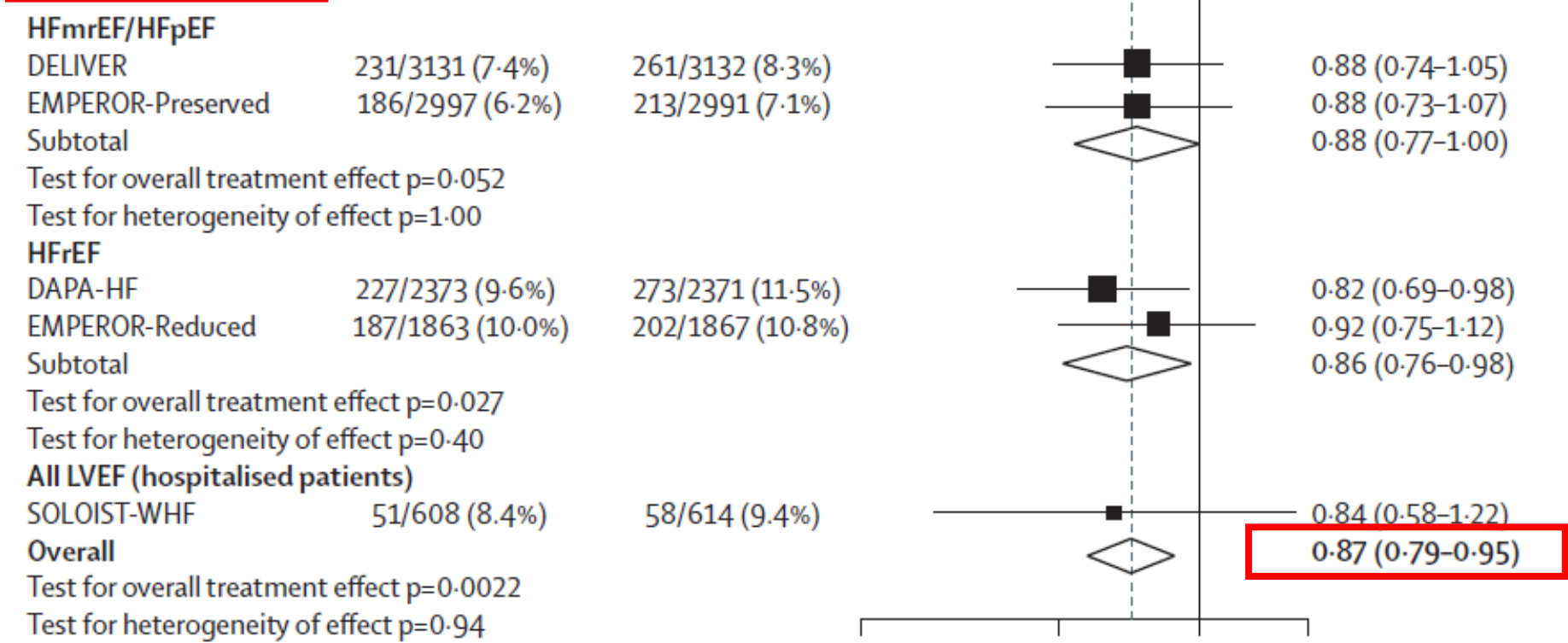
	Number with event/ number of patients (%)			Hazard ratio (95% CI)
	SGLT2 inhibitors	Placebo		
<b>HFmrEF/HFpEF</b>				
DELIVER	475/3131 (15.2%)	577/3132 (18.4%)		0.80 (0.71–0.91)
EMPEROR-Preserved	415/2997 (13.8%)	511/2991 (17.1%)		0.79 (0.69–0.90)
Subtotal				0.80 (0.73–0.87)
Test for overall treatment effect	p<0.0001			
Test for heterogeneity of effect	p=0.89			
<b>HFrEF</b>				
DAPA-HF	382/2373 (16.1%)	495/2371 (20.9%)		0.75 (0.65–0.85)
EMPEROR-Reduced	361/1863 (19.4%)	462/1867 (24.7%)		0.75 (0.65–0.86)
Subtotal				0.75 (0.68–0.83)
Test for overall treatment effect	p<0.0001			
Test for heterogeneity of effect	p=1.00			
<b>All LVEF (hospitalised patients)</b>				
SOLOIST-WHF				0.71 (0.56–0.89)
<b>Overall</b>				<b>0.77 (0.72–0.82)</b>
Test for overall treatment effect	p<0.0001			
Test for heterogeneity of effect	p=0.87			

**RRR  
33%**

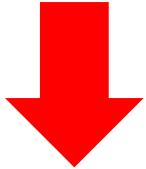
# SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials



## Cardiovascular death



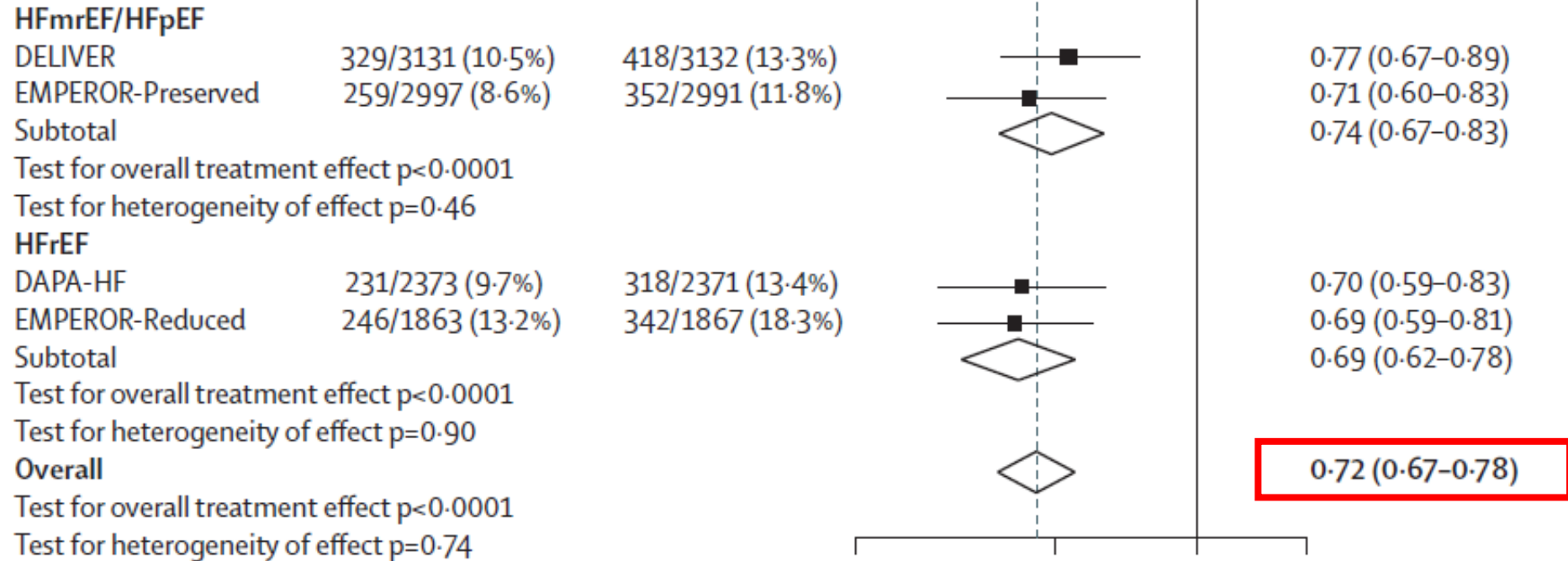
**RRR  
13%**



# SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials



## Heart failure hospitalisation

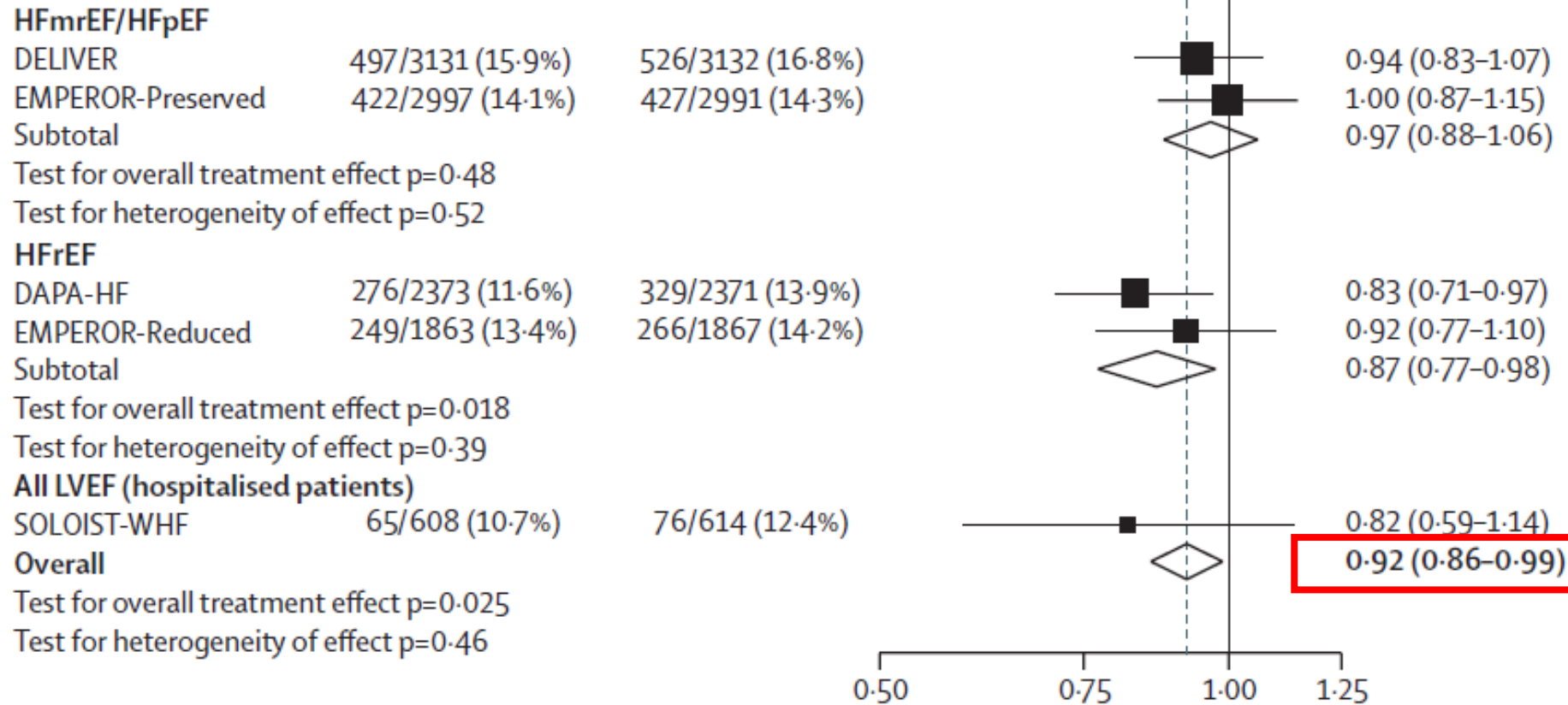


**RRR  
28%**

# SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials

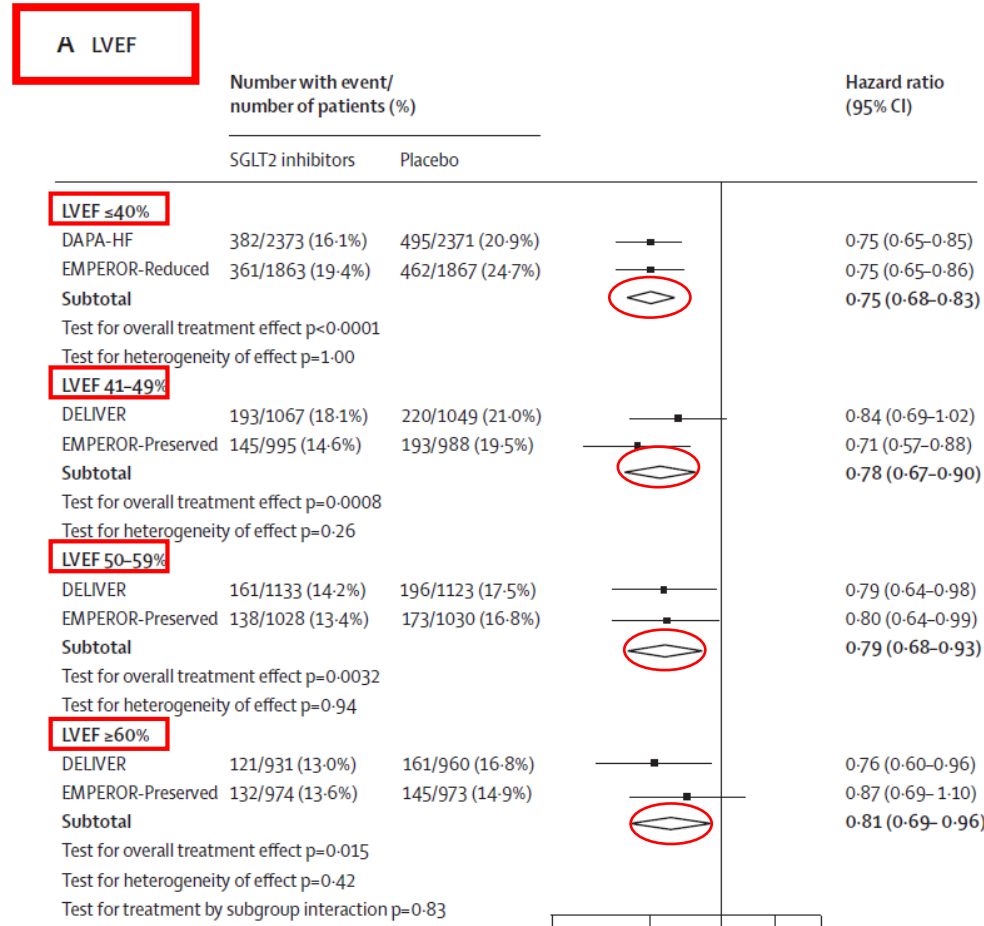


## All-cause death

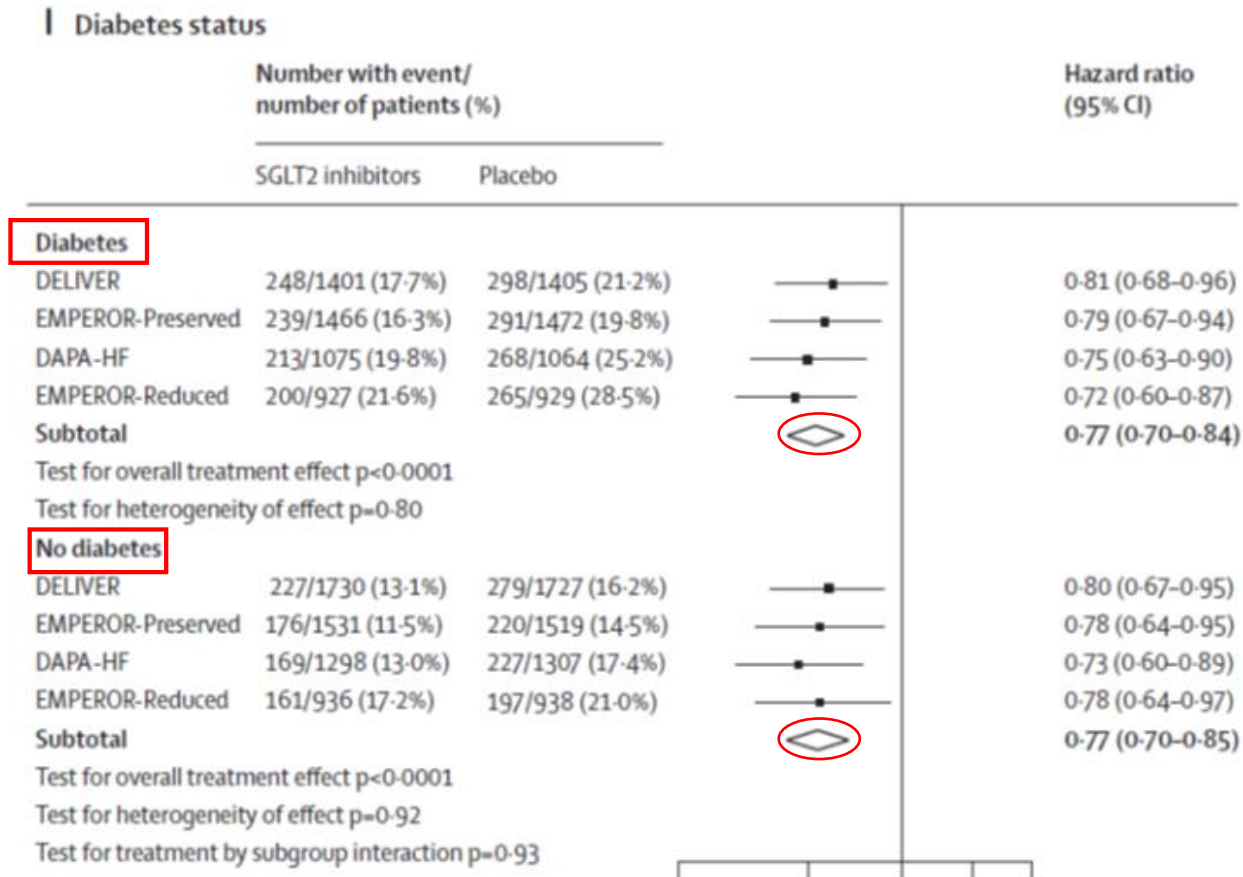


**RRR  
08%**

# SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials

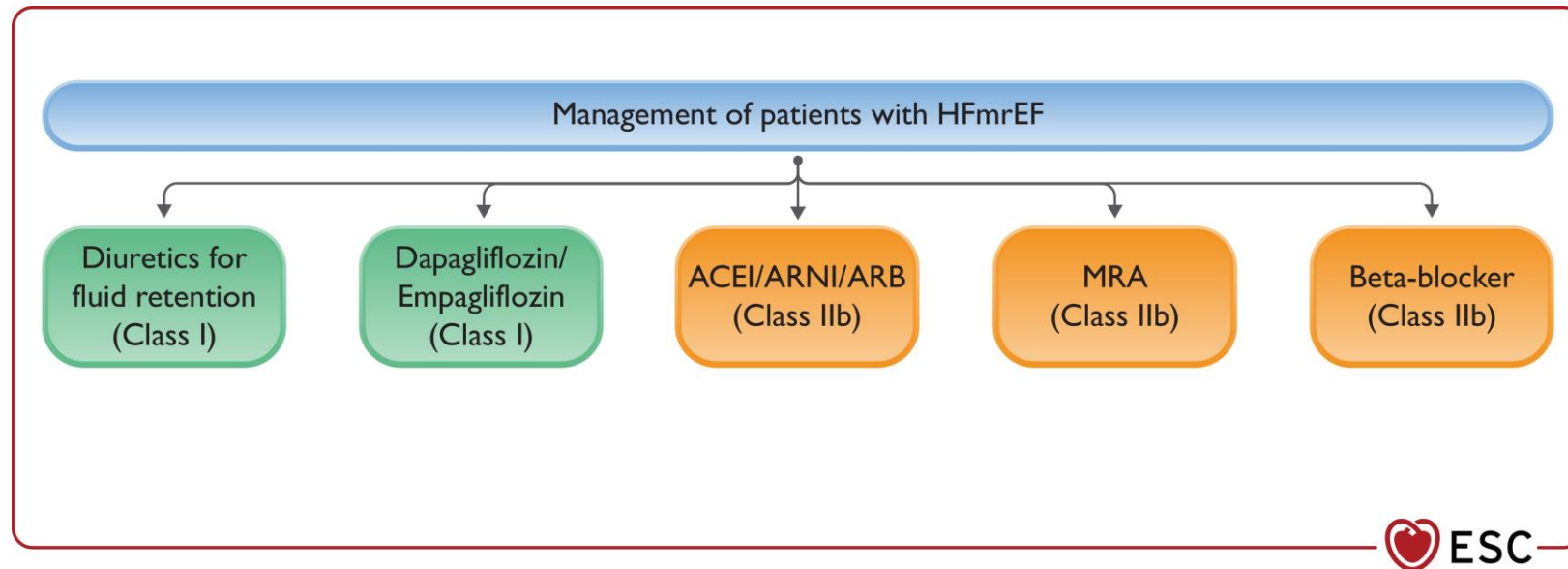


# SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials



## 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

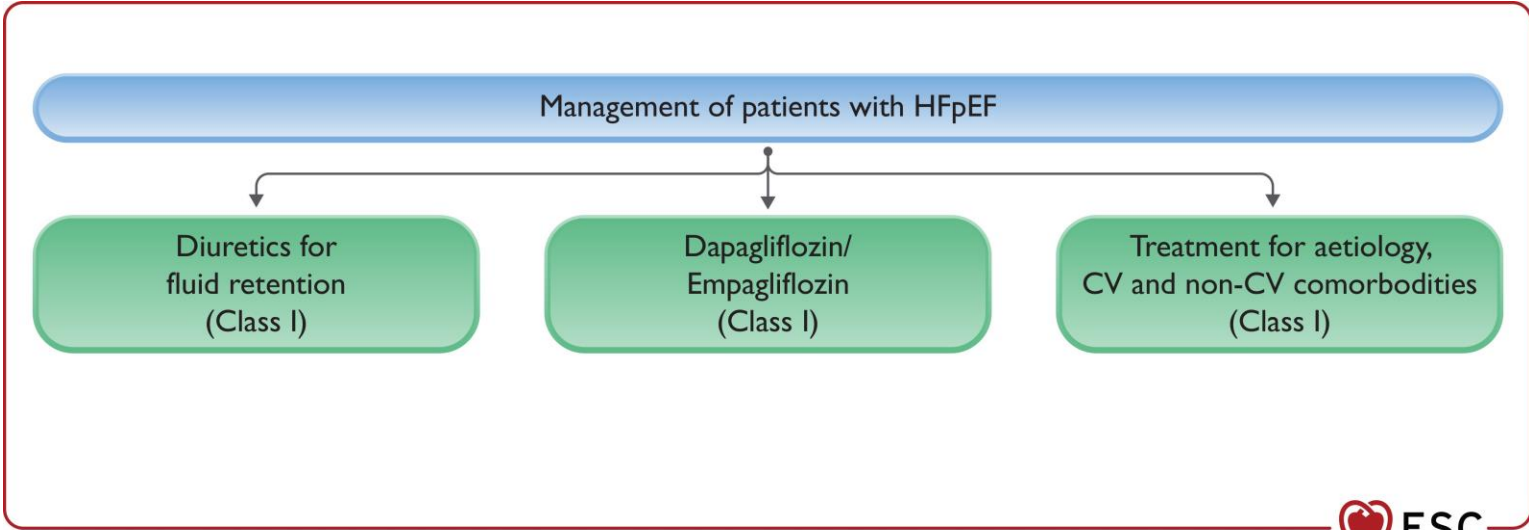
# IC à FE modérément réduite (HFmrEF)



Recommendation	Class <sup>a</sup>	Level <sup>b</sup>
An SGLT2 inhibitor (dapagliflozin or empagliflozin) is recommended in patients with HFmrEF to reduce the risk of HF hospitalization or CV death. <sup>c 6,8</sup>	I	A

## 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

# IC à FE préservée (HFpEF)



Recommendation	Class <sup>a</sup>	Level <sup>b</sup>
An SGLT2 inhibitor (dapagliflozin or empagliflozin) is recommended in patients with HFpEF to reduce the risk of HF hospitalization or CV death. <sup>c 6,8</sup>	I	A

© ESC 2023

# IC + DT2 + Comorbidités

1. La carence martiale
2. L'insuffisance rénale

# 1. La carence martiale

- Prévalence de 30% à 50% dans l'ICC; passe à 70-80% dans l'ICA<sup>1</sup>
- Dans 2/3 des cas, elle existe sans anémie<sup>2</sup>
- Facteur de mauvais pronostic dans l'IC<sup>3</sup>:
  - Réduit la capacité physique à l'exercice
  - Augmente la risque d'hospitalisations récurrentes
  - Facteur indépendant de mortalité
- Dépistage<sup>4</sup>: Recommandation IC
  - Carence martiale absolue: ferritinémie < 100 mcg/l
  - Carence martiale fonctionnelle: ferritinémie 100-300 mcg/l et CS < 20%

1. JACC, 71, . N° 7, 2018: 782 – 93

2. Am Heart J 2013; 165: 575-582

3. International journal of cardiology. 2018.03.039

4. European Heart Journal (2021) 42, 35993726

# Supplémentation IV Carboxymaltose ferrique (CMF) améliore les symptômes et la capacité physique à l'effort

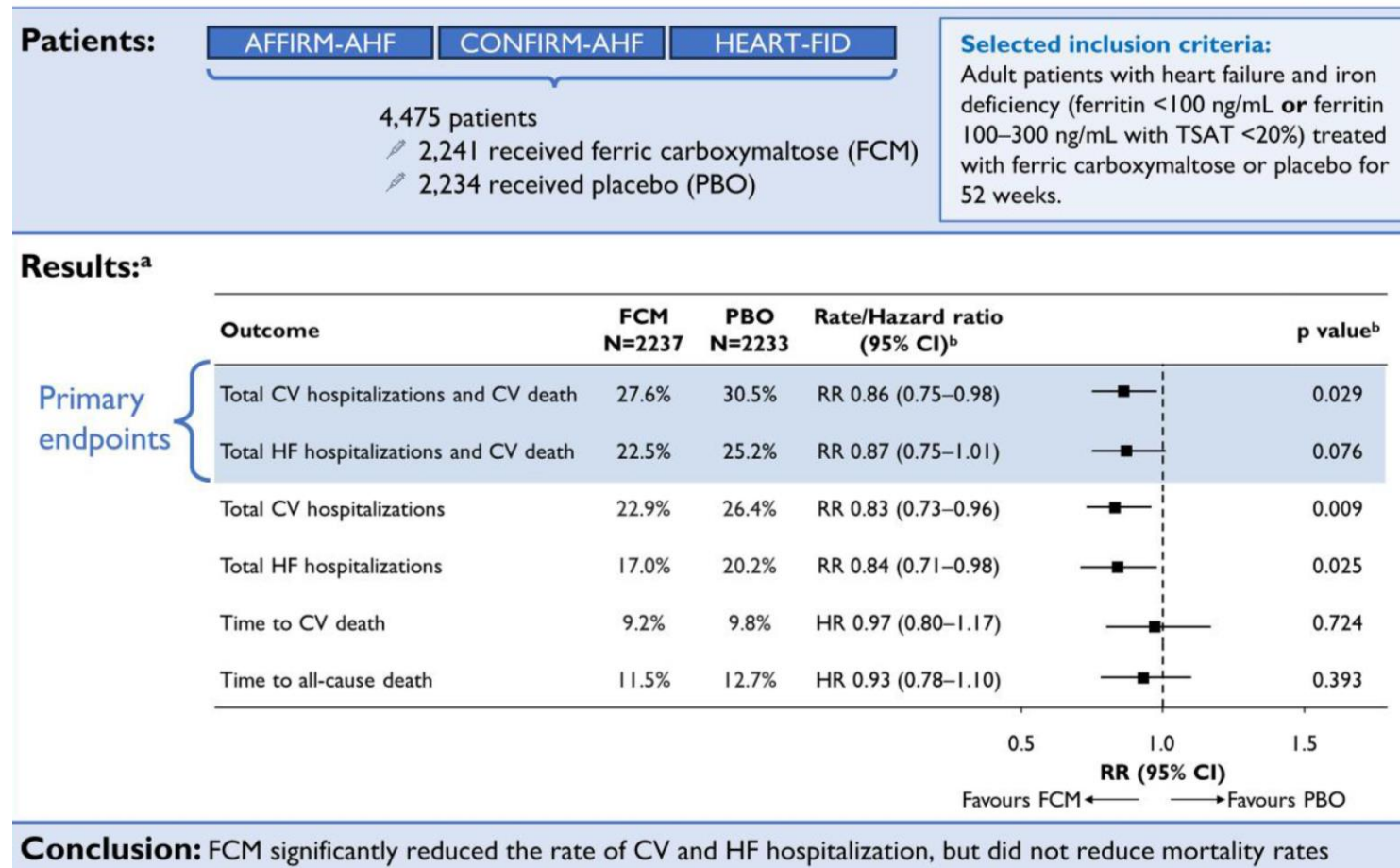
	FAIR-HF <sup>1</sup>	CONFIRM-HF <sup>2</sup>	EFFECT-HF <sup>3</sup>
Type d'insuffisance (I) cardiaque	NYHA2 et FEVG < 40% ou NYHA3 et FEVG < 45%	NYHA2 ou 3, FEVG < 45%	NYHA2 ou 3, FEVG < 45 %
Définition de la CM	Ferritinémie <100 ng/mL ou 100–299 ng/mL avec CST < 20 %		
Type d'étude	Carboxymaltose ferrique versus placebo		versus traitement standard
Nombre de patients	304 / 155	152 / 152	86 / 86
Durée de l'étude	24 semaines	52 semaines	24 semaines
Critère principal de jugement et résultats	Auto-évaluation : OR 2,51 pour amélioration.  Variation de NYHA : OR 2,40 pour amélioration de NYHA 1 classe.	Variation du test de marche de 6min : amélioration de 33 +11 m (p = 0.002).	Variation du pic de VO2 : -0.16 versus -1.19 mL/min/kg (p = 0.020).

1. N Engl J Med. 2009;361:2436–2448.

2. Eur Heart J. 2015;36:657–668.

3. Circulation. 2017;136:1374–1383.

# Supplémentation IV Carboxymaltose ferrique (CMF) Méta-analyse : impact sur les hospitalisations et décès



# Que disent les recommandations?



ESC

European Society  
of Cardiology

European Heart Journal (2021) 42, 3599–3726  
doi:10.1093/eurheartj/ehab368

ESC GUIDELINES

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

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
It is recommended that all patients with HF be periodically screened for anaemia and iron deficiency with a full blood count, serum ferritin concentration, and TSAT.	I	C



ESC

European Society  
of Cardiology

European Heart Journal (2023) 00, 1–13  
https://doi.org/10.1093/eurheartj/ehad195

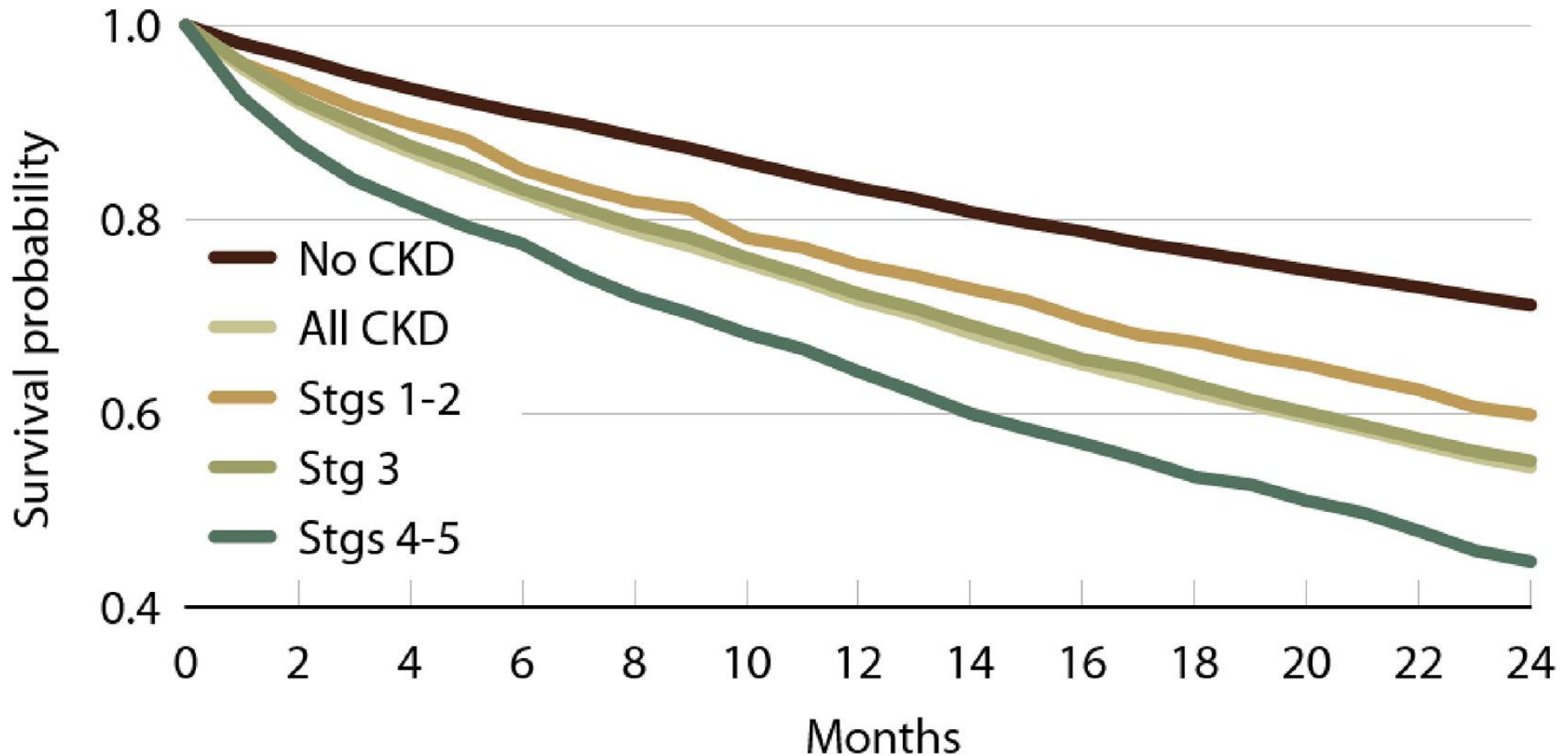
ESC GUIDELINES

## 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Intravenous iron supplementation is recommended in symptomatic patients with HFrEF and HFmrEF, and iron deficiency, to alleviate HF symptoms and improve quality of life. <sup>c 12,41,47–49</sup>	I	A
Intravenous iron supplementation with ferric carboxymaltose or ferric derisomaltose should be considered in symptomatic patients with HFrEF and HFmrEF, and iron deficiency, to reduce the risk of HF hospitalization. <sup>c 12,41,43–46</sup>	IIa	A

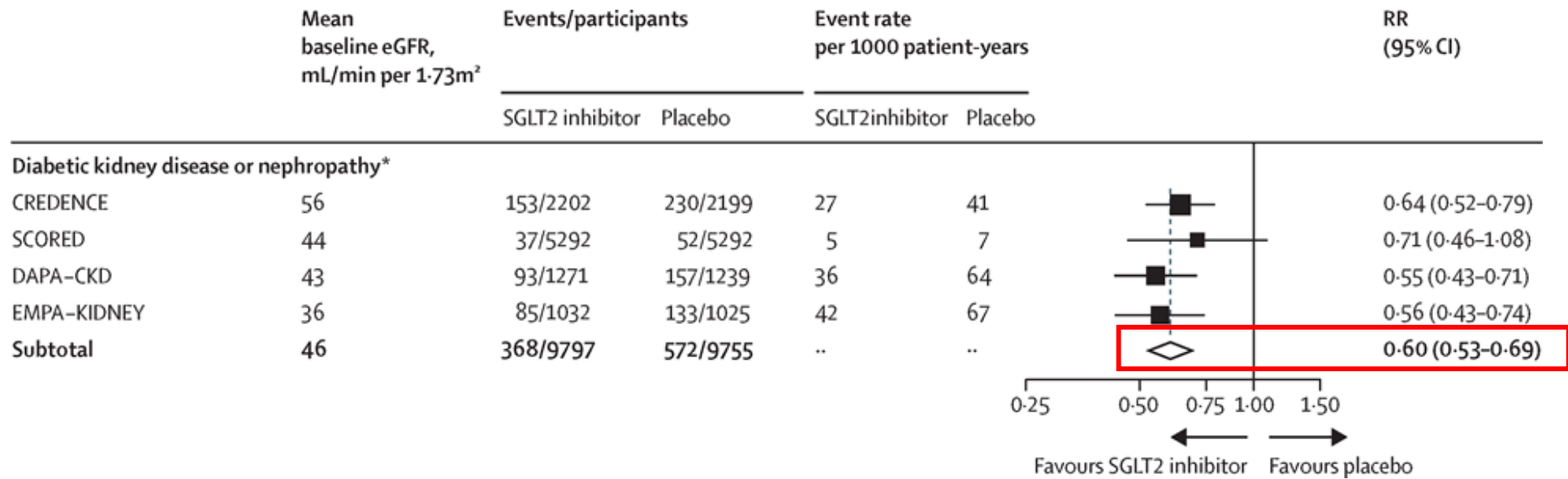
## 2. l'insuffisance rénale

DT2 + IRC + IC: impact pronostique majeur



# iSGLT2 et néphropathie diabétique « Méta-analyse »

**Chez les DT2 + atteinte rénale, les inhibiteurs du SGLT2 ont réduit le risque de progression de la maladie rénale de 40 % (0,60, 0,53–0,69)**



## Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes

### the FIDELIO-DKD

Outcome	Finerenone	Placebo	Finerenone	Placebo	Hazard Ratio (95% CI)	P Value
	(N=2833)	(N=2841)	(N=2833)	(N=2841)		
	no. of patients with event (%)		no. of patients with event per 100 patient-yr			
Primary composite outcome	504 (17.8)	600 (21.1)	7.59	9.08	0.82 (0.73–0.93)	0.001
Kidney failure	208 (7.3)	235 (8.3)	2.99	3.39	0.87 (0.72–1.05)	—
End-stage kidney disease	119 (4.2)	139 (4.9)	1.60	1.87	0.86 (0.67–1.10)	—
Sustained decrease in eGFR to <15 ml/min/1.73 m <sup>2</sup>	167 (5.9)	199 (7.0)	2.40	2.87	0.82 (0.67–1.01)	—
Sustained decrease of ≥40% in eGFR from baseline	479 (16.9)	577 (20.3)	7.21	8.73	0.81 (0.72–0.92)	—
Death from renal causes	2 (<0.1)	2 (<0.1)	—	—	—	—
Key secondary composite outcome	367 (13.0)	420 (14.8)	5.11	5.92	0.86 (0.75–0.99)	0.03
Death from cardiovascular causes	128 (4.5)	150 (5.3)	1.69	1.99	0.86 (0.68–1.08)	—
Nonfatal myocardial infarction	70 (2.5)	87 (3.1)	0.94	1.17	0.80 (0.58–1.09)	—
Nonfatal stroke	90 (3.2)	87 (3.1)	1.21	1.18	1.03 (0.76–1.38)	—
Hospitalization for heart failure	139 (4.9)	162 (5.7)	1.89	2.21	0.86 (0.68–1.08)	—
Death from any cause	219 (7.7)	244 (8.6)	2.90	3.23	0.90 (0.75–1.07)	—
Hospitalization for any cause	1263 (44.6)	1321 (46.5)	22.56	23.87	0.95 (0.88–1.02)	—
Secondary composite kidney outcome	252 (8.9)	326 (11.5)	3.64	4.74	0.76 (0.65–0.90)	—
Sustained decrease of ≥57% in eGFR from baseline	167 (5.9)	245 (8.6)	2.41	3.54	0.68 (0.55–0.82)	—

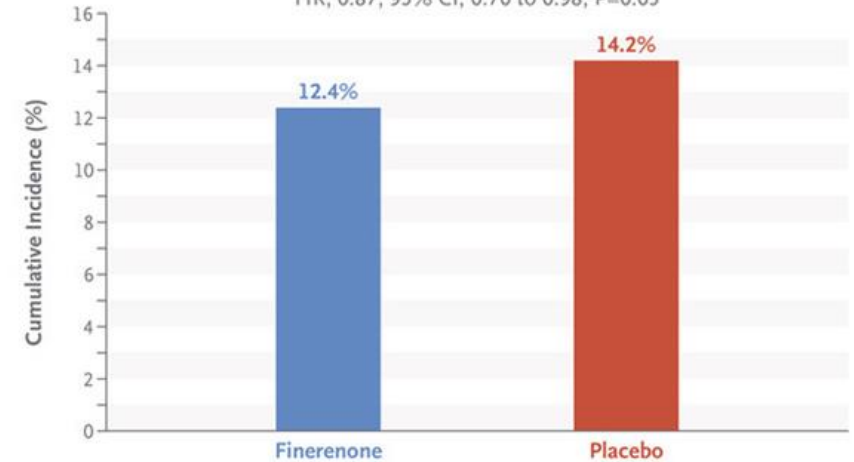
Finerenone réduit le risque d'IRT et d'évènements CV

N Engl J Med 2020;383:2219-29

## Cardiovascular Events with Finerenone in Kidney Disease and Type 2 Diabetes

### Death from Cardiovascular Causes, Nonfatal MI, Nonfatal Stroke, or Hospitalization for Heart Failure

HR, 0.87; 95% CI, 0.76 to 0.98; P=0.03



### the FIGARO-DKD

#### Hospitalization for Heart Failure

HR, 0.71; 95% CI, 0.56 to 0.90

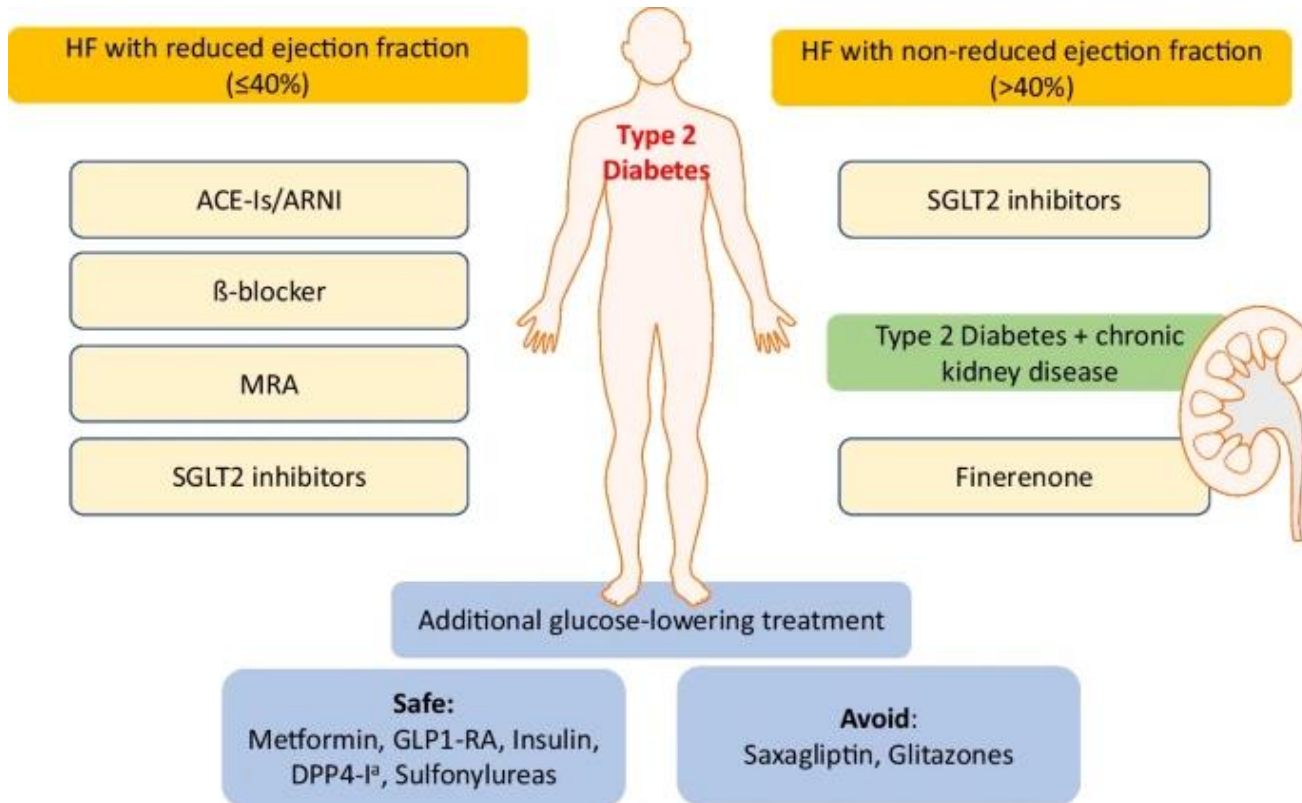


N Engl J Med 2021;385:2252-63.

# Hypoglycémifiants et Insuffisance cardiaque

- Insuline 😊
- Metformine 😊
- Sulfonylurées 😊
- Glitazones 😞 (augmentent le risque d'hospitalisation pour IC)
- Inhibiteurs de la DPP-4 😊 (saxagliptine 😞)
- Agonistes des récepteurs GLP-1 😊 (ICFEP+ obésité 😊 😊 😊)

# Conclusion



- DT2 + IC deux comorbidités fréquemment associées
- Dont les pronostics altérés se conjuguent.
- Approche multidisciplinaire fondée sur des données probantes
- Afin de réduire la morbimortalité