Collège National des Cardiologues des Hôpitaux

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Nouveautés dans l'Insuffisance Cardiaque à Fonction VG préservée

Pr Angoulvant Denis
CHRU & Université de Tours

@AngoulvantD

Avec le soutien institutionnel d'AstraZeneca

Collège
National des
Cardiologues des
Hôpitaux

Liens d’intérêt 2022 - Pr D Angoulvant

1- Au cours des 3 années précédentes j’ai été rémunéré pour des actions de communication et/ou d’expertise par les sociétés suivantes :

Amgen, Alnylam, Astra-Zeneca, Bayer, BMS, Boehringer, Bouchara Recordati, Pfizer, Lilly, Novartis, Novo Nordisk, Sanofi, Servier, Vifor.

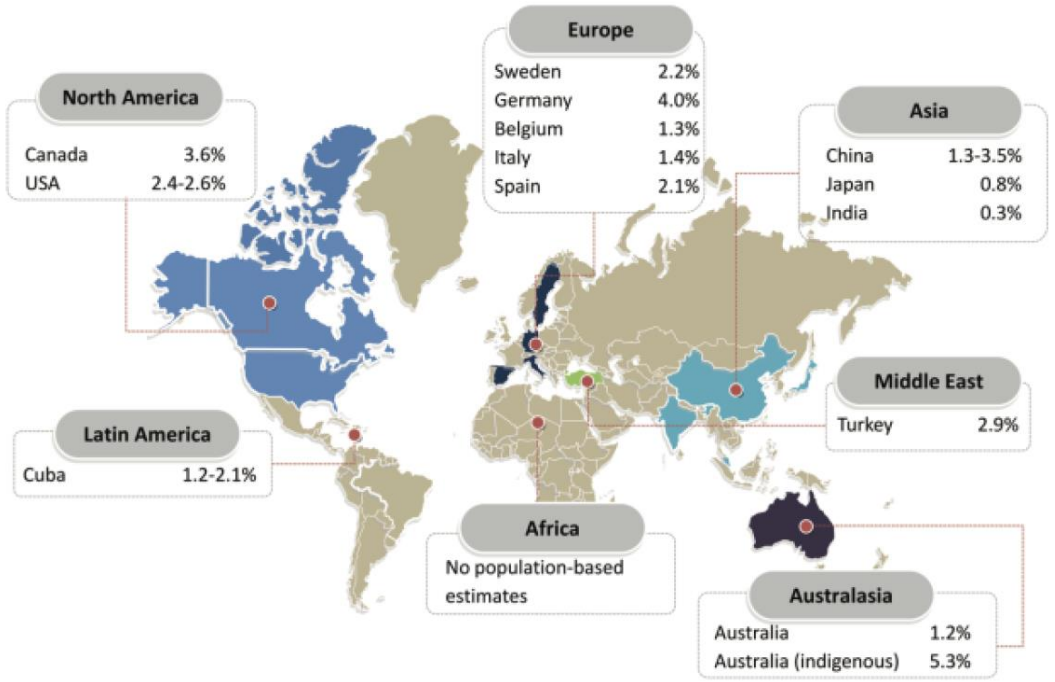
2- Au cours des 3 année précédentes mon équipe de recherche a reçu des financements des sociétés suivantes :

Abbott, Boston Scientific, Medtronic

Les définitions de l'ESC en 2021

Table 3 Definition of heart failure with reduced ejection fraction, mildly reduced ejection fraction and preserved ejection fraction

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF ≤40%	LVEF 41–49%[b]	LVEF ≥50%
	3	–	–	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides[c]



T A. McDonagh et al. Eur Heart J 2021

An estimated 64.3 Million People are Living with Heart Failure Worldwide

Nearly half of patients with HF have an EF>40%

Groenewegen et al. Eur J Heart Fail 2020

Les reco de l'ESC en 2021 concernant le traitement pharmacologique de l'HFpEF

	HFrEF	HFmrEF	HFpEF
	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
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Drugs	HFrEF	HFmrEF	HFpEF
SGLT2i	IA		
ACE / ARNI	IA IB	IIb C	
MRA	IA	IIb C	
Betablocker	IA	IIb C	
Diuretic	C	C	C

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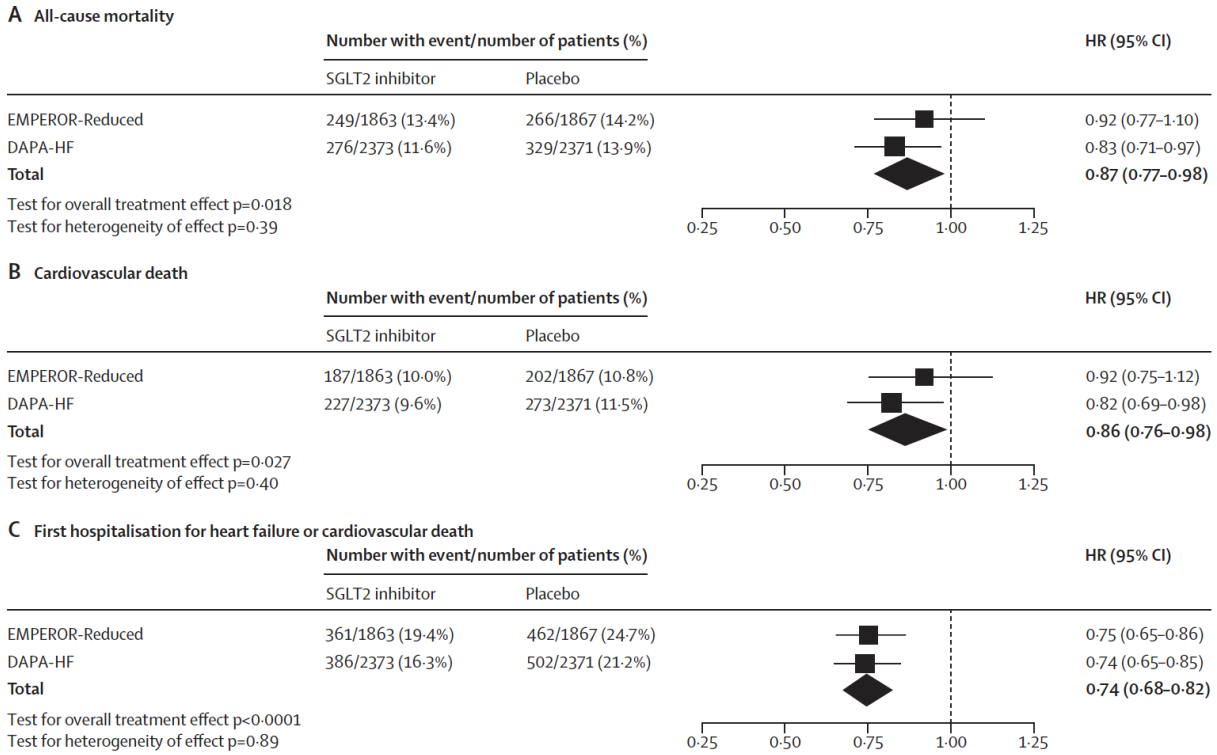
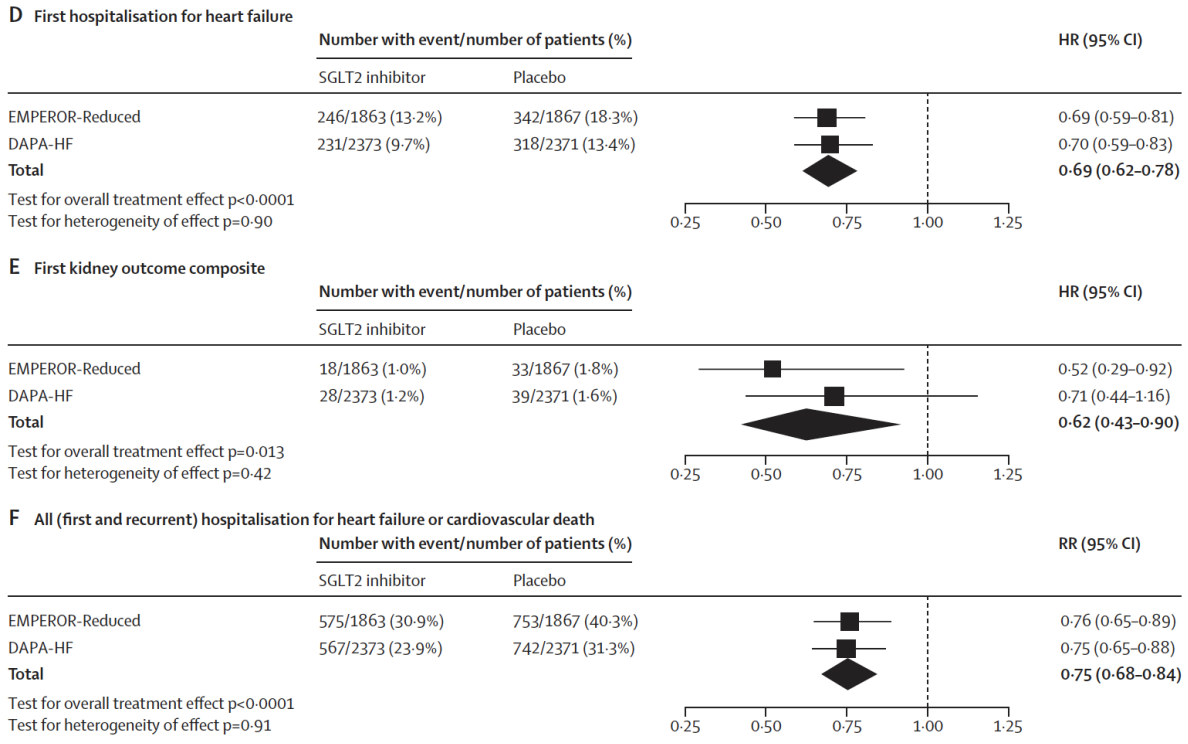
Nouveautés dans l'HFpEF

T A. McDonagh et al. Eur Heart J 2021

Efficacité des gliflozines chez les patients insuffisants cardiaques à FEVG altérée





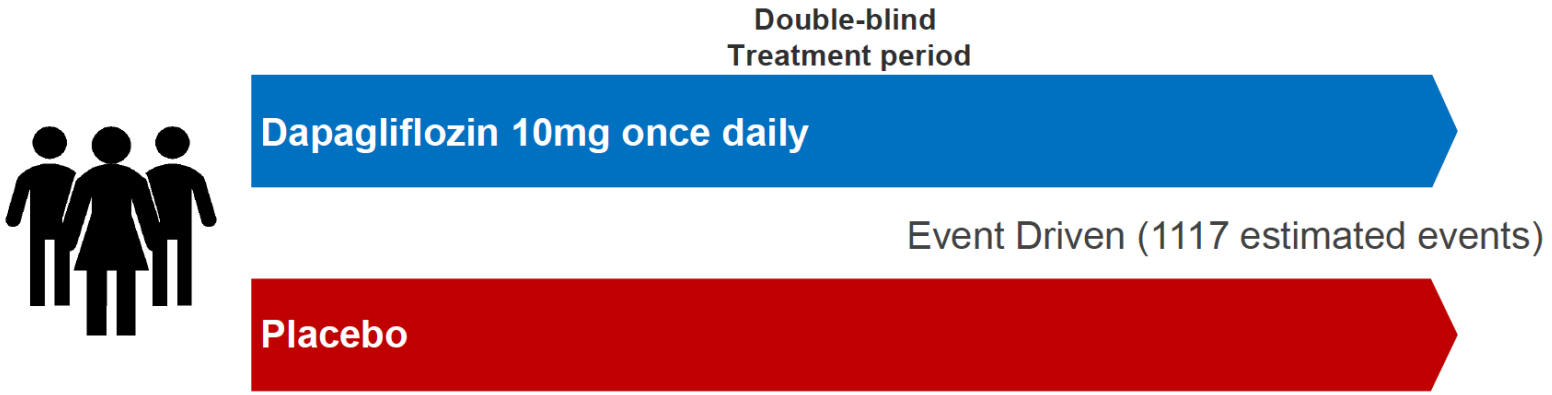
8474 patients inclus dans les deux études :
Réduction de la **mortalité totale** de 13% (HR 0,87; 0,77-0,98)
Réduction du critère **décès CV ou 1ère Hospitalisation pour IC de 26%** (HR 0,74; 0,68-0,83)
Réduction du critère **décès CV ou récidive d'hospitalisation pour IC de 25%** (HR 0,75; 0,68-0,84)
Réduction du critère **aggravation rénale de 38%** (HR 0,62; 0,43-0,9) (réduction du DFG > 50% ou insuffisance rénale terminale)

F Zanad et al. Lancet 2020

Etude DELIVER : La Dapagliflozine est-elle supérieure au placebo chez les patients HFpEF ?

Eligibility Criteria

- Age ≥ 40 years
- NYHA class II-IV
- LVEF > 40% (including prior LVEF ≤ 40%)
- Structural Heart Disease (LVH or LA Enlargement)
- Elevated Natriuretic Peptides (> 300 pg/ml or 600 pg/ml in AFF)
- Either Ambulatory or Hospitalized for Heart Failure



Primary Endpoint

Time to first Composite of

- CV death or
- Worsening Heart Failure (HF Hospitalization or Urgent HF Visit)

Secondary Endpoints

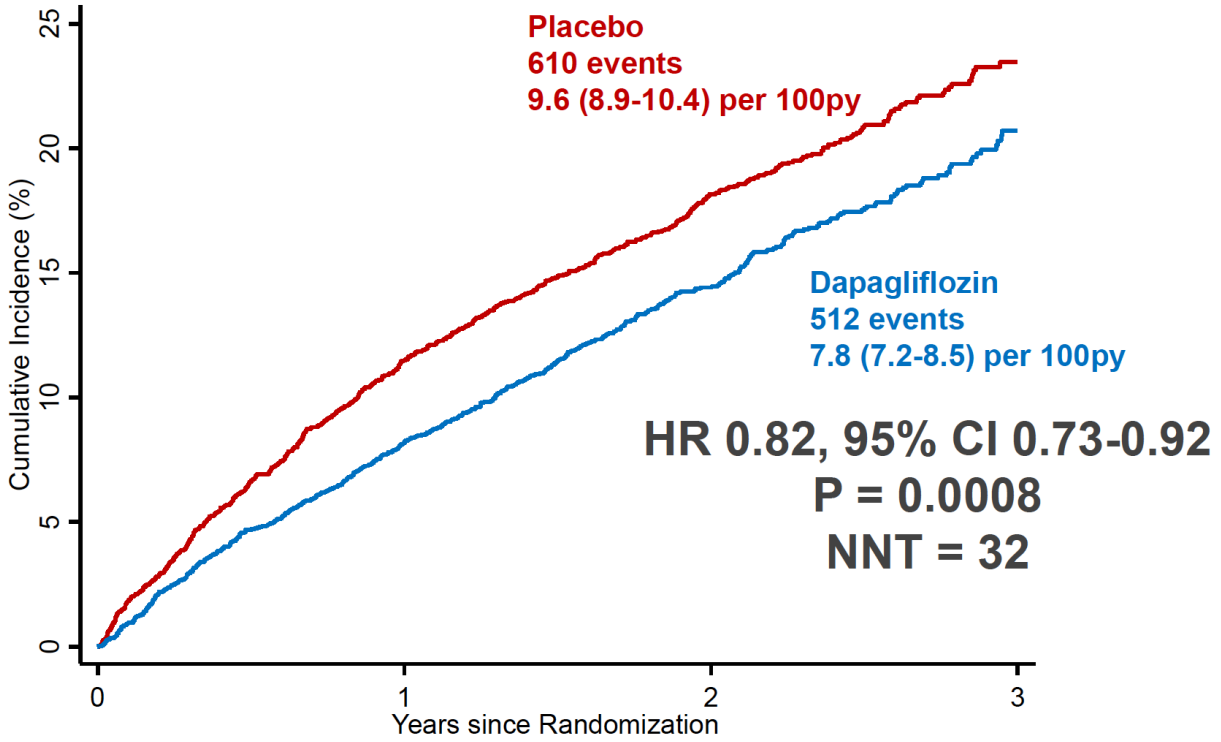
- Total HF Events + CV Death (both populations)
- Change in KCCQ TSS at 8 months (full)
- CV Death (full)
- All-Cause Death (full)

Solomon et al. Eur J Heart Fail 2021

Caractéristiques des patients à l'inclusion

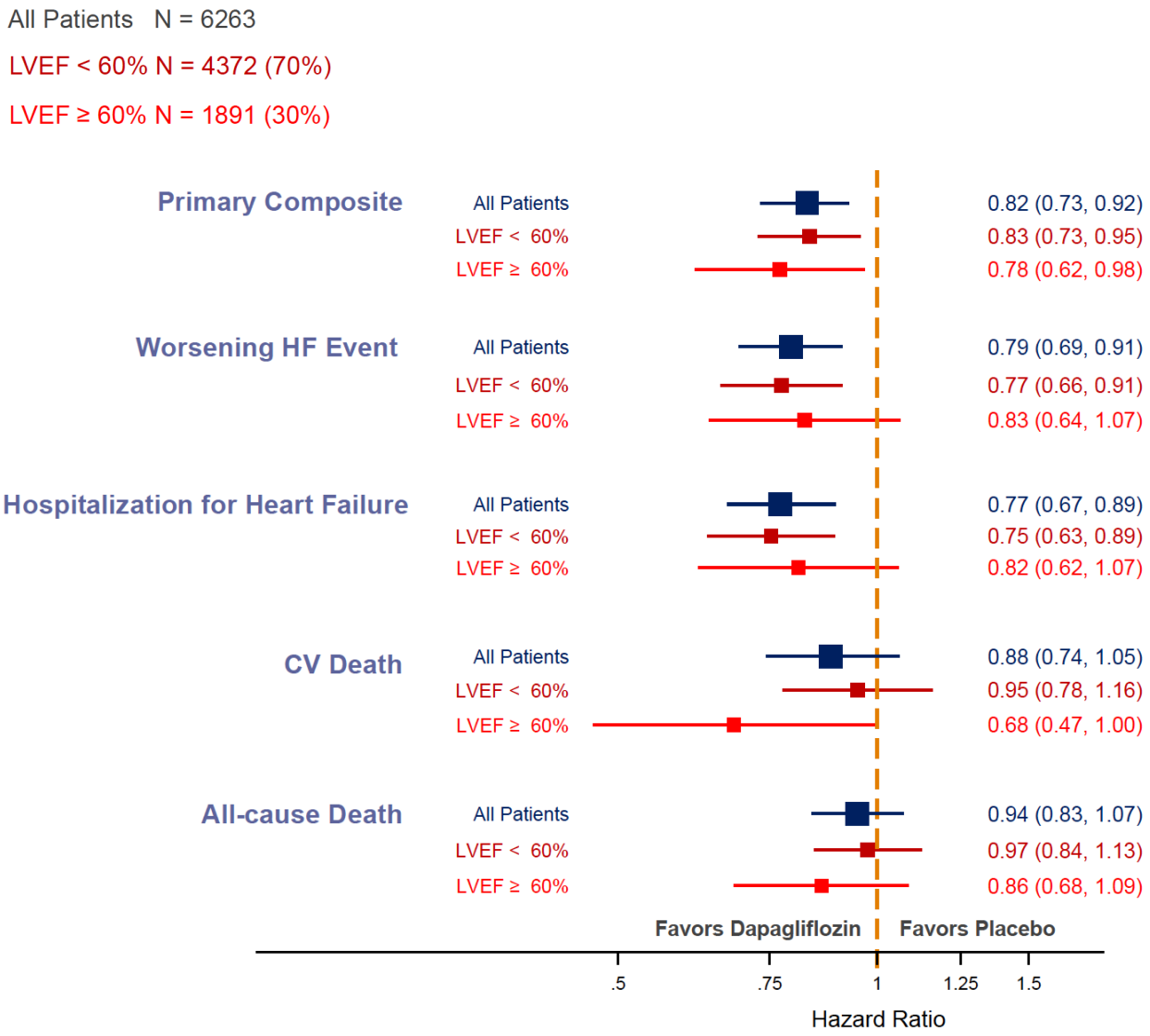
	Dapagliflozin N=3131	Placebo N=3132
Age (years)	71.8 ± 9.6	71.5 ± 9.5
Female Sex	43.6%	44.2%
Baseline LVEF (%)	54.0 ± 8.6	54.3 ± 8.9
LVEF < 60%	70.3%	69.3%
HF with Improved EF (Prior LVEF ≤ 40%)	18.3%	18.5%
NYHA Class at Baseline		
II	73.9%	76.6%
III/IV	26.1%	23.4%
KCCQ Total Symptom Score	70 ± 23	70 ± 22
NT-proBNP when no AFF (ECG) (pg/ml)	729 [472, 1299]	704 [467, 1265]
NT-proBNP in AFF (ECG) (pg/ml)	1408 [956, 2256]	1387 [966, 2180]
Prior HF Hospitalization	40.6%	40.5%
Atrial Fibrillation/Flutter at Enrollment	42.4%	42.1%
Type 2 Diabetes	44.7%	44.9%
eGFR (mL/min/1.73m²)	61.2 ± 19.0	60.9 ± 19.3
eGFR < 60 mL/min/1.73m²	48.4%	49.6%
Medications		
Loop diuretics	76.7%	76.9%
Angiotensin converting enzyme inhibitors (ACEi)	36.5%	36.7%
Angiotensin receptor blocker (ARB)	36.2%	36.4%
Sacubitril-valsartan	5.3%	4.3%
β-blocker	82.8%	82.5%
Mineralocorticoid receptor antagonist (MRA)	42.8%	42.4%

Réduction significative du critère majeur: décés CV ou aggravation de l'IC



Solomon et al. NEJM 2022

Bénéfice sur le critère IC y compris si FEVG ≥ 60%



Aucun signal de sécurité

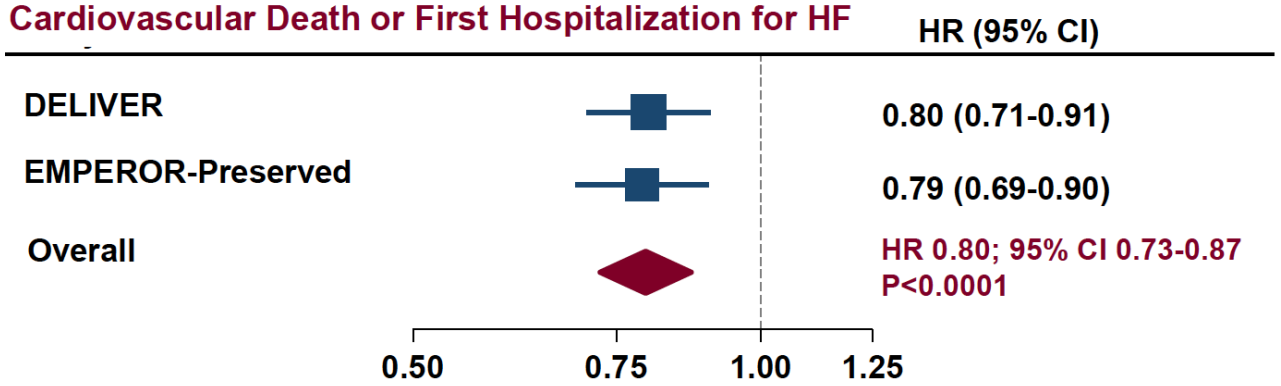
	Dapagliflozin* n=3126	Placebo* n=3127
Any SAE (including death)	1361 (43.5%)	1423 (45.5%)
Any AE leading to treatment discontinuation	182 (5.8%)	181 (5.8%)
Any AE leading to treatment interruption	436 (13.9%)	494 (15.8%)
Any amputation	19 (0.6%)	25 (0.8%)
Any definite or probable diabetic ketoacidosis	2 (0.1%)	0 (0.0%)
Any major hypoglycemic event	6 (0.2%)	7 (0.2%)
Events related to volume depletion	42 (1.3%)	32 (1.0%)
Renal Events	73 (2.3%)	79 (2.5%)

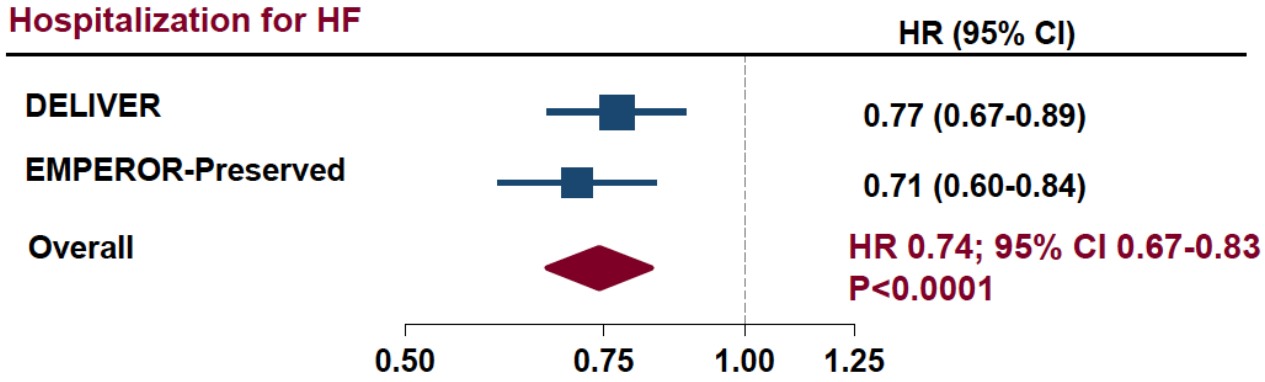
Solomon et al. NEJM 2022

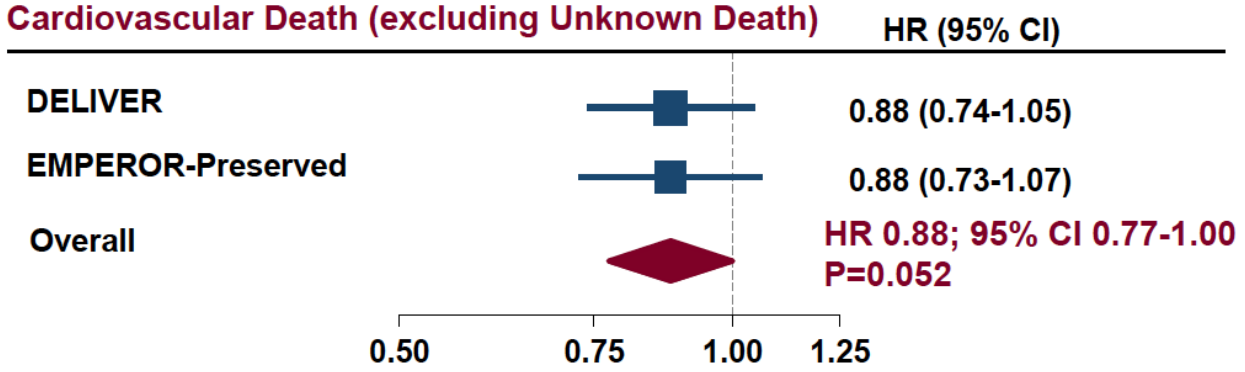
Analyse poolée des patients des études DELIVER et EMPEROR Preserved

Key Eligibility Criteria in DELIVER and EMPEROR-Preserved

Key Inclusion Criteria	DELIVER	EMPEROR-Preserved
Symptomatic HF	NYHA class II-IV	NYHA class II-IV
Cardiac Structure and Function	LVEF>40% and evidence of structural heart disease	LVEF>40% and either evidence of structural heart disease or history of HF hospitalization within 12mo
Prior LVEF≤40% with Improved LVEF to >40%	Included	Excluded
Elevated NT-proBNP	• ≥300 pg/mL (without AF) or • ≥600 pg/mL (with AF)	• >300 pg/mL (without AF) or • >900 pg/mL (with AF)
Setting of Enrollment	Ambulatory or hospitalized included as long as off intravenous HF therapies	Acute decompensated HF within 1 week of screening excluded
Diuretics	At least intermittent need for diuretics	Stable oral diuretics for ≥1 week
Body mass index	≤50kg/m^2	<45kg/m^2
Estimated glomerular filtration rate	≥25 mL/min/1.73 m^2	≥20 mL/min/1.73 m^2

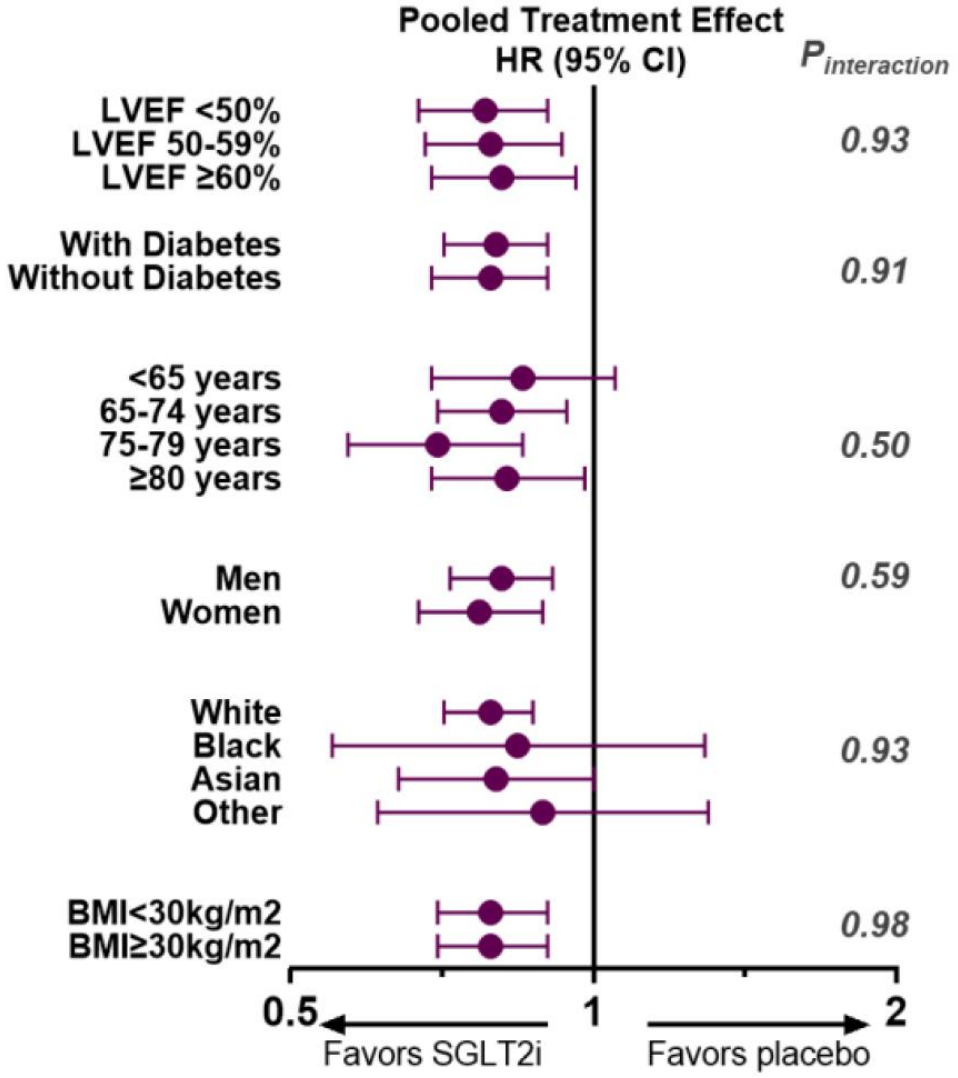


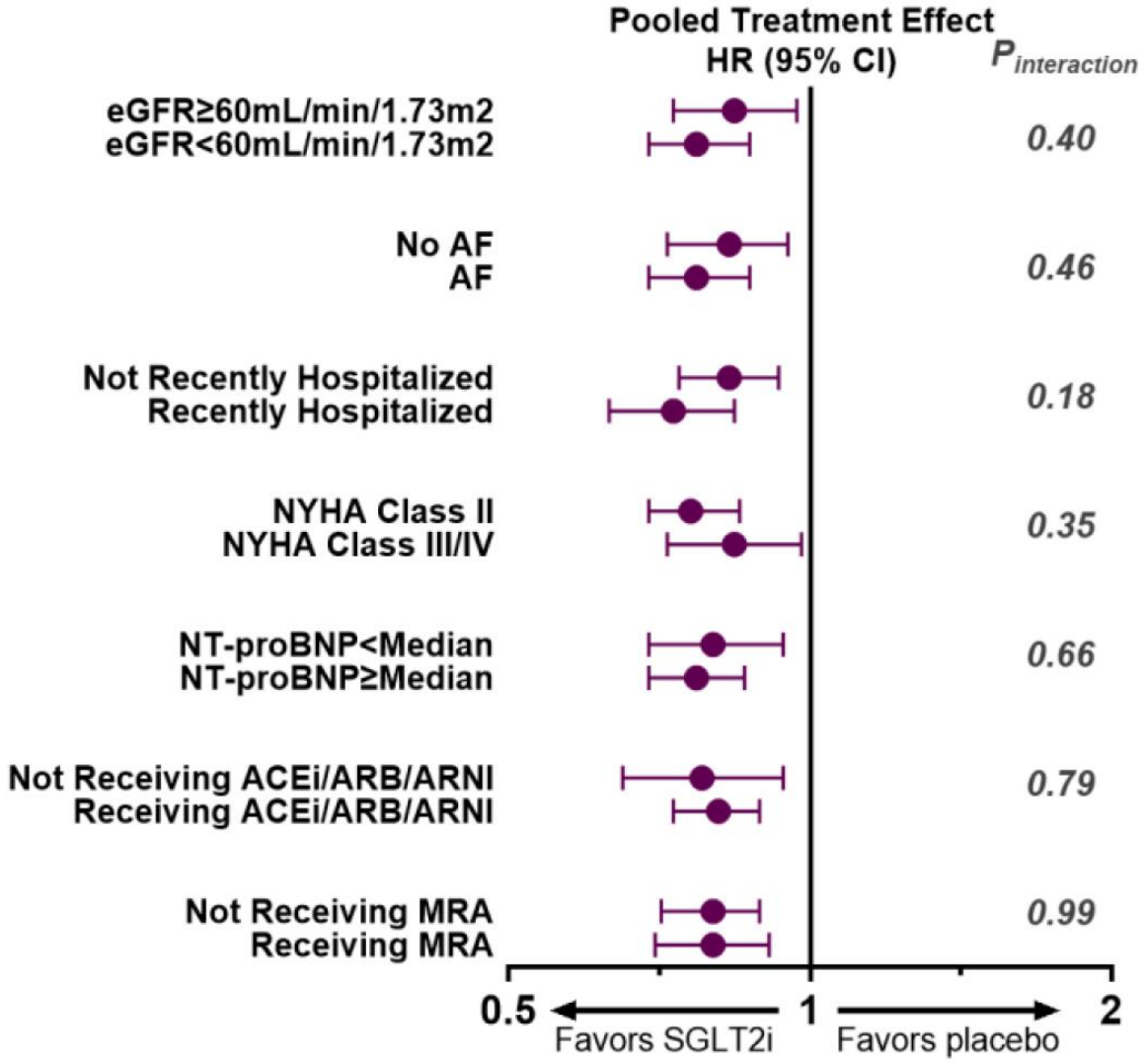




M Vaduganathan et al. Lancet 2022

Analyse poolée des patients des études DELIVER et EMPEROR Preserved

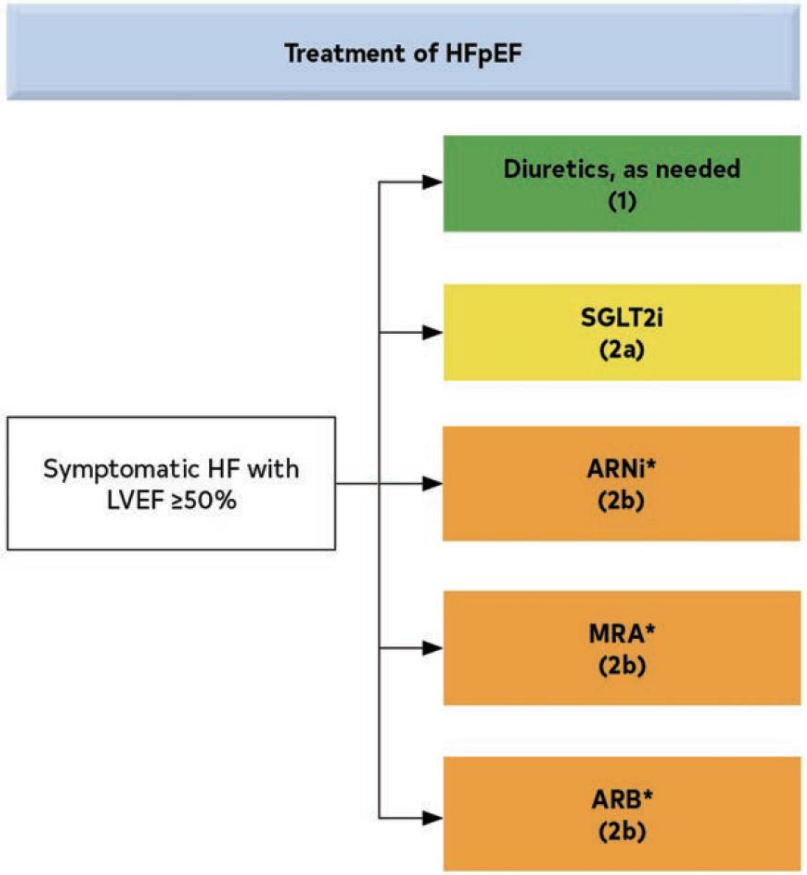




M Vaduganathan et al. Lancet 2022

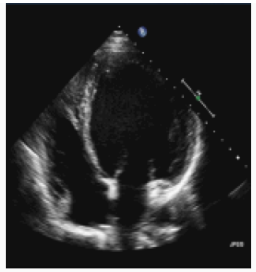
Nouvelle place des gliflozines dans les recommandations HFpEF

Les gliflozines font partie du traitement de première ligne recommandé aux USA chez les patients HFpEF en 2022



P.A. Heidenreich et al. Circulation 2022

Proposal for an Update of the Recommendations of the Pharmacological Treatment of Heart Failure



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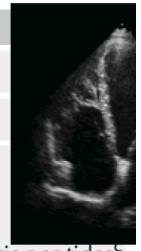


Drugs	HFrEF	HFmrEF	HFpEF
SGLT2i	IA	I A (tbd)*	I A (tbd)*
ACE / ARNI	IA	IIb C	
MRA	IA	IIb C	
Betablocker	IA	IIb C	
Diuretic	IA *	IA * *	IA * *

ESC CONGRESS 2022

* *Relieve from Congestion

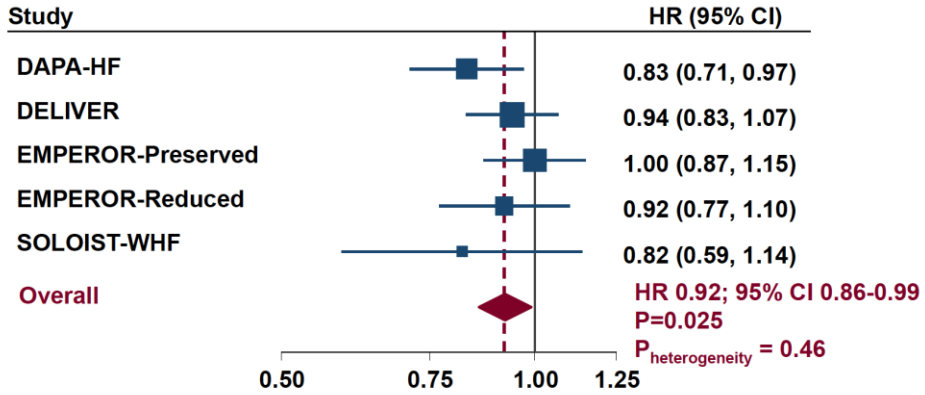
* Reductions of HF Hosp.

F Ruschitzka ESC congress 2022

Gliflozines pour tous ?

Meta-Analysis of 5 Large Placebo-Controlled Trials:
↓ 23% (18-28%) Relative Risk Reduction of Primary Endpoint (CV Death or HF Hospitalisation)

Meta-Analysis of 5 Large Placebo-Controlled Trials:
↓ 8% (1-14%) Relative Risk Reduction of All Cause Death



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