



Congrès du CNCH 2022

Nouveautés dans l'Insuffisance Cardiaque à Fonction VG préservée

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Avec le soutien institutionnel d'AstraZeneca

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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, Organon, Sanofi, Servier, Vifor.

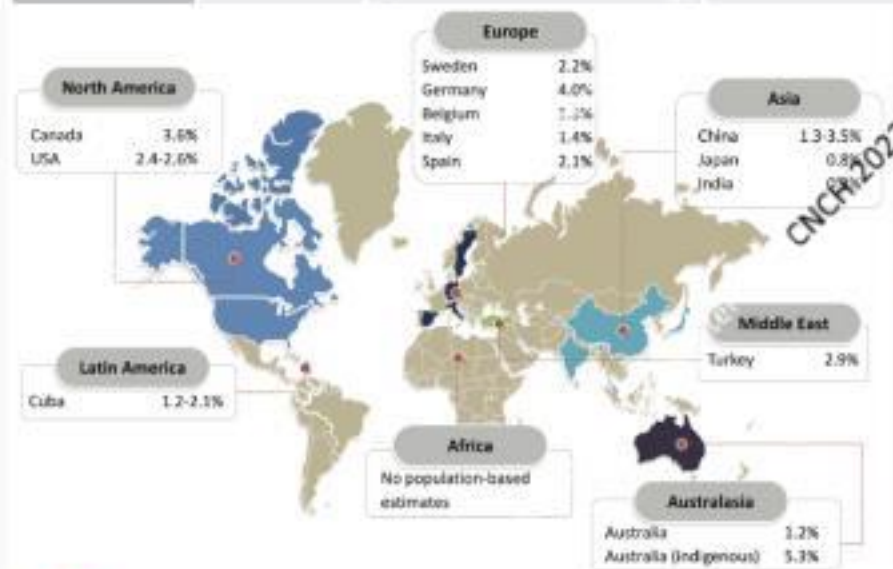
2- Au cours des 3 années précédentes mon équipe de recherche a reçu des financements des sociétés suivantes :

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
LVEF ≤40%	LVEF 41–49% ^b	LVEF ≥50%
–	–	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

Drugs	HFrEF	HFmrEF	HFpEF
SGLT2 ^d	IA		
ACE / ARNI	IA IB	IIb C	
MRA	IA	IIb C	
Betablocker	IA	IIb C	
Diuretic	C	C	C

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

Eligibility Criteria

- Age \geq 40 years
- NYHA class II-IV
- LVEF $>$ 40% (including prior LVEF \leq 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)

Double-blind
Treatment period

Dapagliflozin 10mg once daily

Event Driven (1117 estimated events)

Placebo

Solomon et al. Eur J Heart Fail 2021

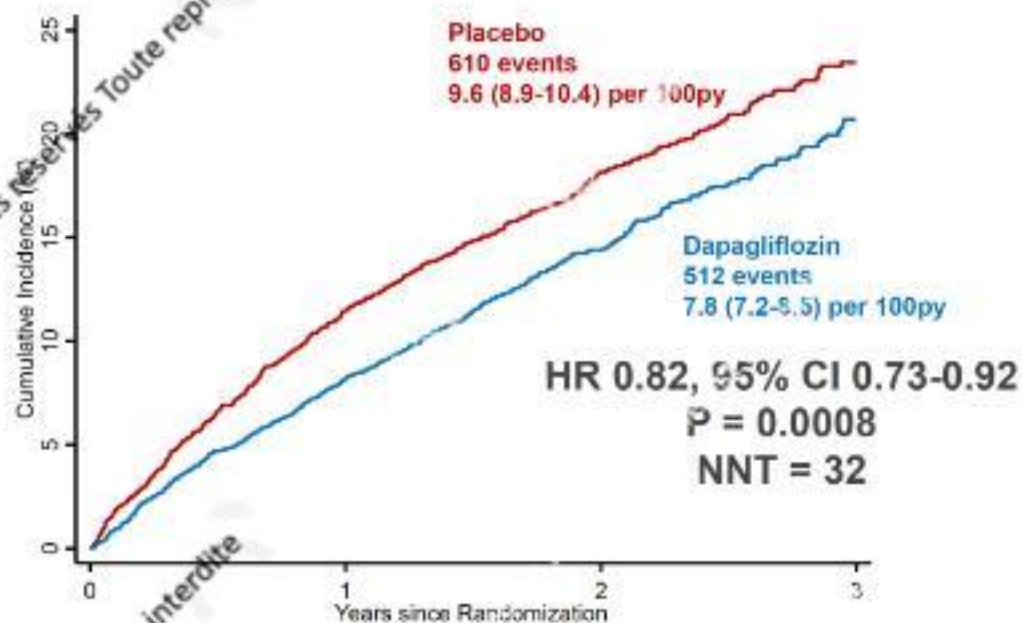
Caractéristiques des patients à l'inclusion

	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 ± 8.0	54.3 ± 8.9
LVEF < 60%	70.3%	69.3%
HF with Improved EF (Prior LVEF ≤ 40%)	10.3%	10.5%
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	40.8%	40.5%
Atrial Fibrillation/Flutter at Enrollment	42.4%	42.1%
Type 2 Diabetes	44.7%	44.9%
eGFR (mL/min/1.73m ²)	61.2 ± 19.0	60.9 ± 19.3
eGFR < 60 mL/min/1.73m ²	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:
décès CV ou aggravation de l'IC



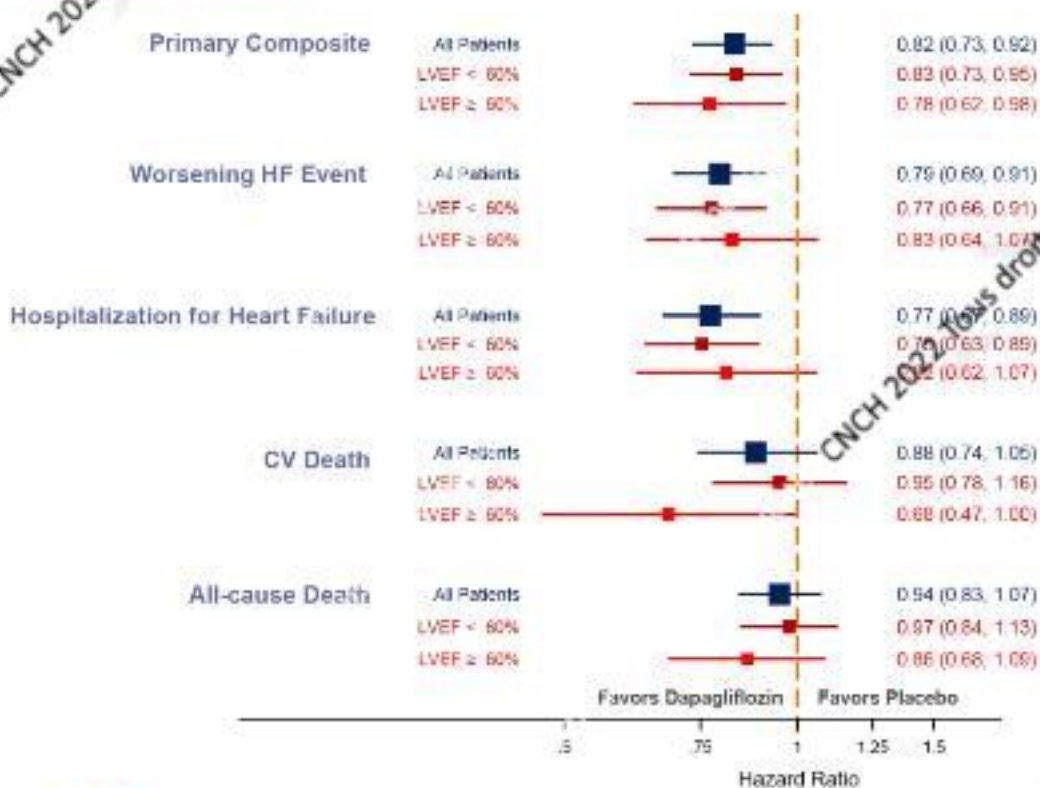
Bénéfice sur le critère IC y compris si FEVG ≥ 60%

Aucun signal de sécurité

All Patients N = 6233

LVEF < 60% N = 4372 (70%)

LVEF ≥ 60% N = 1891 (30%)

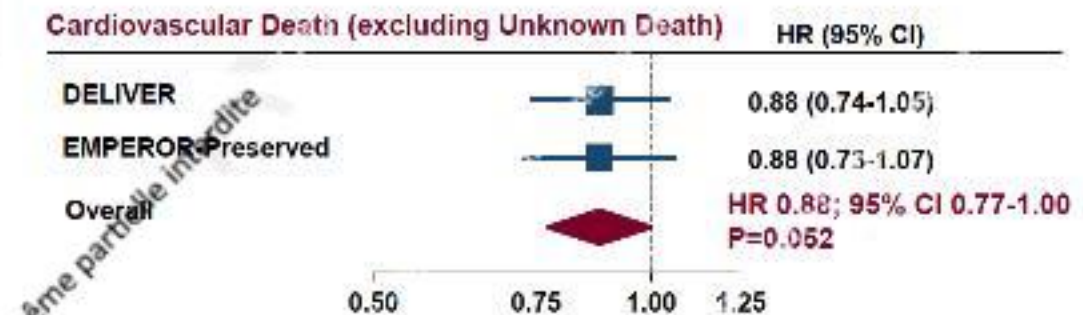
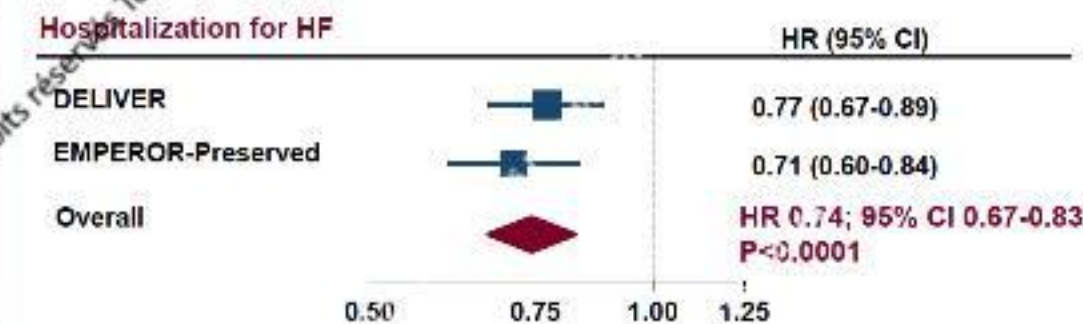
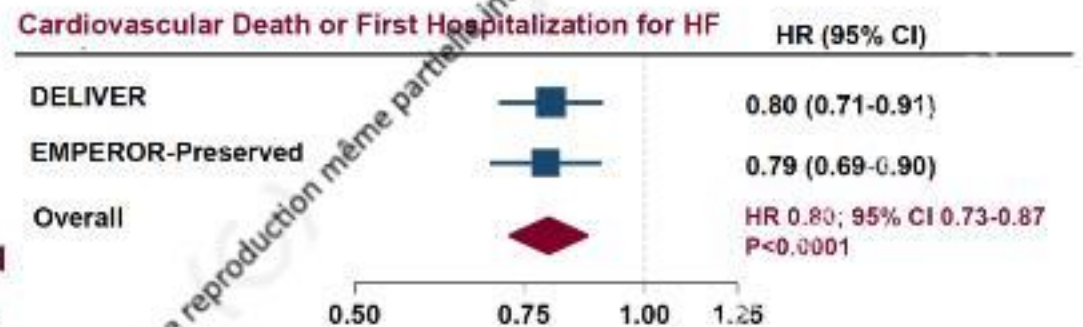


	Dapagliflozin ^a n=3126	Placebo ^a n=3127
Any SAE (including death)	1361 (43.5%)	1423 (45.5%)
Any AE leading to treatment discontinuation	102 (5.8%)	181 (5.8%)
Any AE leading to treatment interruption	436 (13.9%)	494 (15.8%)
Any amputation	19 (0.6%)	25 (0.8%)
Any definite or probable diabetic ketoacidosis	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%)

Analyse poolée des patients des études DELIVER et EMPEROR Preserved

Key Eligibility Criteria in DELIVER and EMPEROR-Preserved

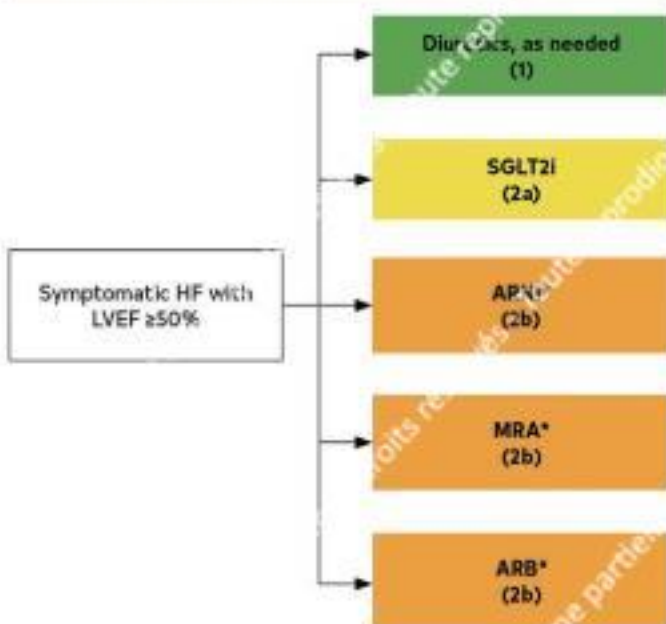
Key Inclusion Criteria	DELIVER	EMPEROR-Preserved
Symptomatic HF	NYHA class II-IV	NYHA class II-IV
Cardiac Structure and Function	LVEF > 40% and evidence of structural heart disease	LVEF > 40% and either evidence of structural heart disease or history of HF hospitalization within 12mo
Prior LVEF ≤ 40% with improved LVEF to > 40%	Included	Excluded
Elevated NT-proBNP	<ul style="list-style-type: none"> ≥ 300 pg/mL (without AF) or ≥ 600 pg/mL (with AF) 	<ul style="list-style-type: none"> > 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 included
Diuretics	At least intermittent need for diuretics	Stable oral diuretics for ≥ 1 week
Body mass index	≤ 50 kg/m ²	< 45 kg/m ²
Estimated glomerular filtration rate	≥ 25 mL/min/1.73 m ²	≥ 20 mL/min/1.73 m ²



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

Treatment of HFpEF



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

	HFrEF	HFmrEF	HFpEF
	Symptoms ± Signs ^a	Symptoms ± Signs ^a	Symptoms ± Signs ^a
	LVEF <40%	LVEF 41–49% ^b	LVEF ≥50%
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Drugs	HFrEF	HFmrEF	HFpEF
SGLT2i	IA	I A (tbd)*	I A (tbd)*
ACEI/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.

P.A. Heidenreich et al. Circulation 2022

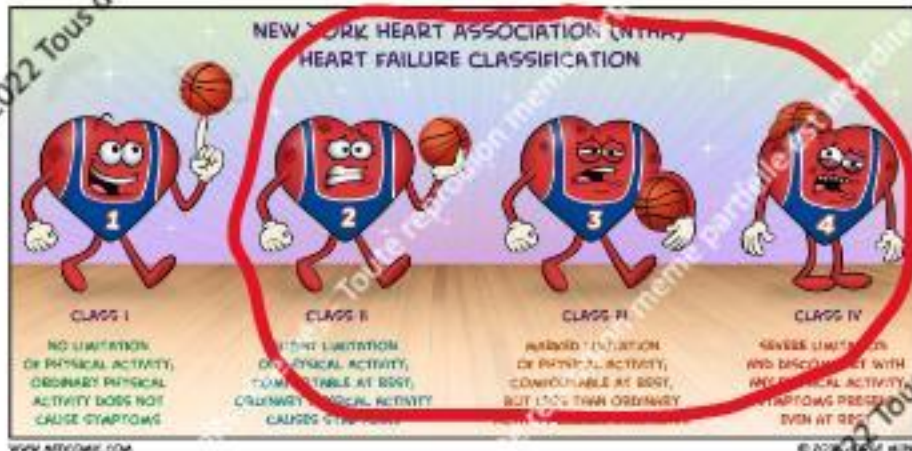
F Ruschitzka ESC congress 2022



Angoulvent Denis
Nouveautés dans l'HFpEF

Patient HFpEF (avec ou sans diabète)

Patient HFpEF vu en consultation, priorité à l'introduction de ISGLT2i (niveau de preuve le plus élevé)

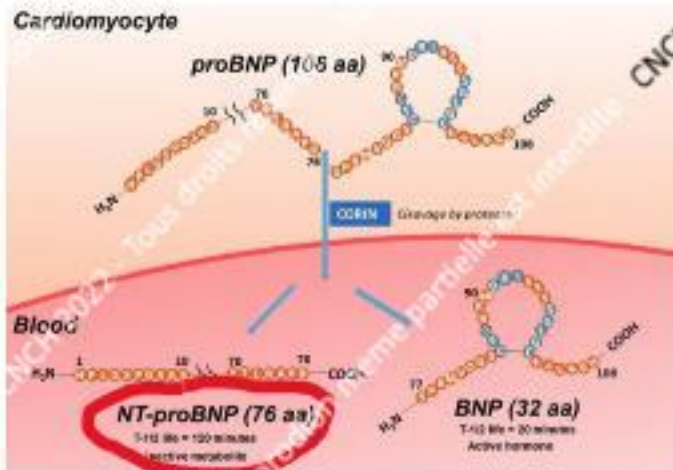


NYHA ≥ 2

NT-pro BNP
 > 300 pg/mL
 (> 900 si FA)
 et
 DFG > 20 mL/min

FEVG $> 40\%$
 et
 OG dilatée
 ou HVG

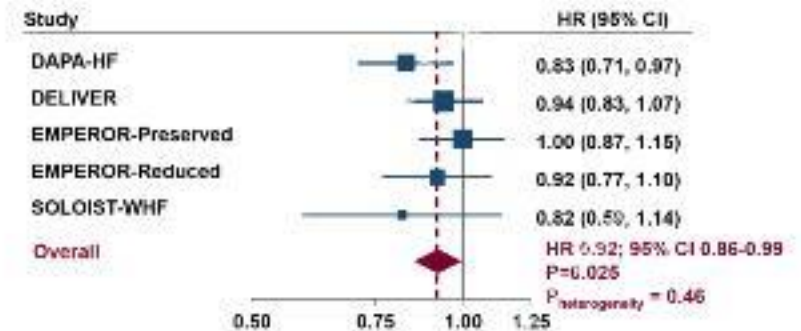
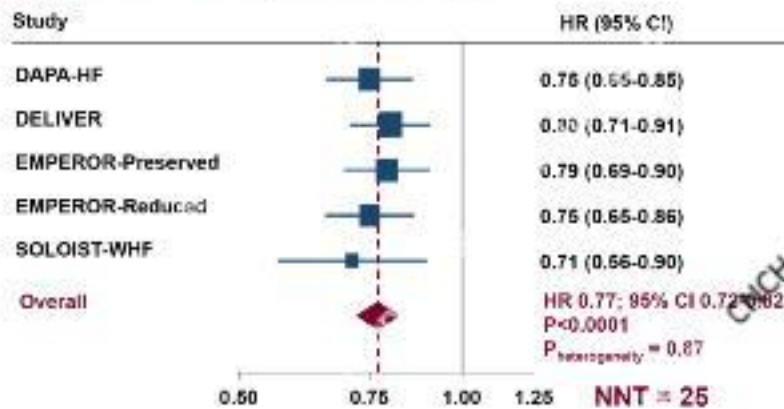
Ou Hospit
 pour
 IC ≥ 12 mois*



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



M Vaduganathan et al. Lancet 2022



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Hôpitaux

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