@AtulPathak31

Insuffisance cardiaque : quoi de neuf ?

Professor Atul PATHAK MD, PhD.

Cardiovascular Medicine. *Hopital Princesse Grace*
MONACO

Hypertension and Heart failure: Molecular and Clinical Investigations. *CNRS 5288, TOULOUSE,*
FRANCE

University Pennsylvania , PHILADELPHIA,
USA

CENTRE SCIENTIFIQUE DE MONACO

cnrs

GRACE-PENN MEDICINE

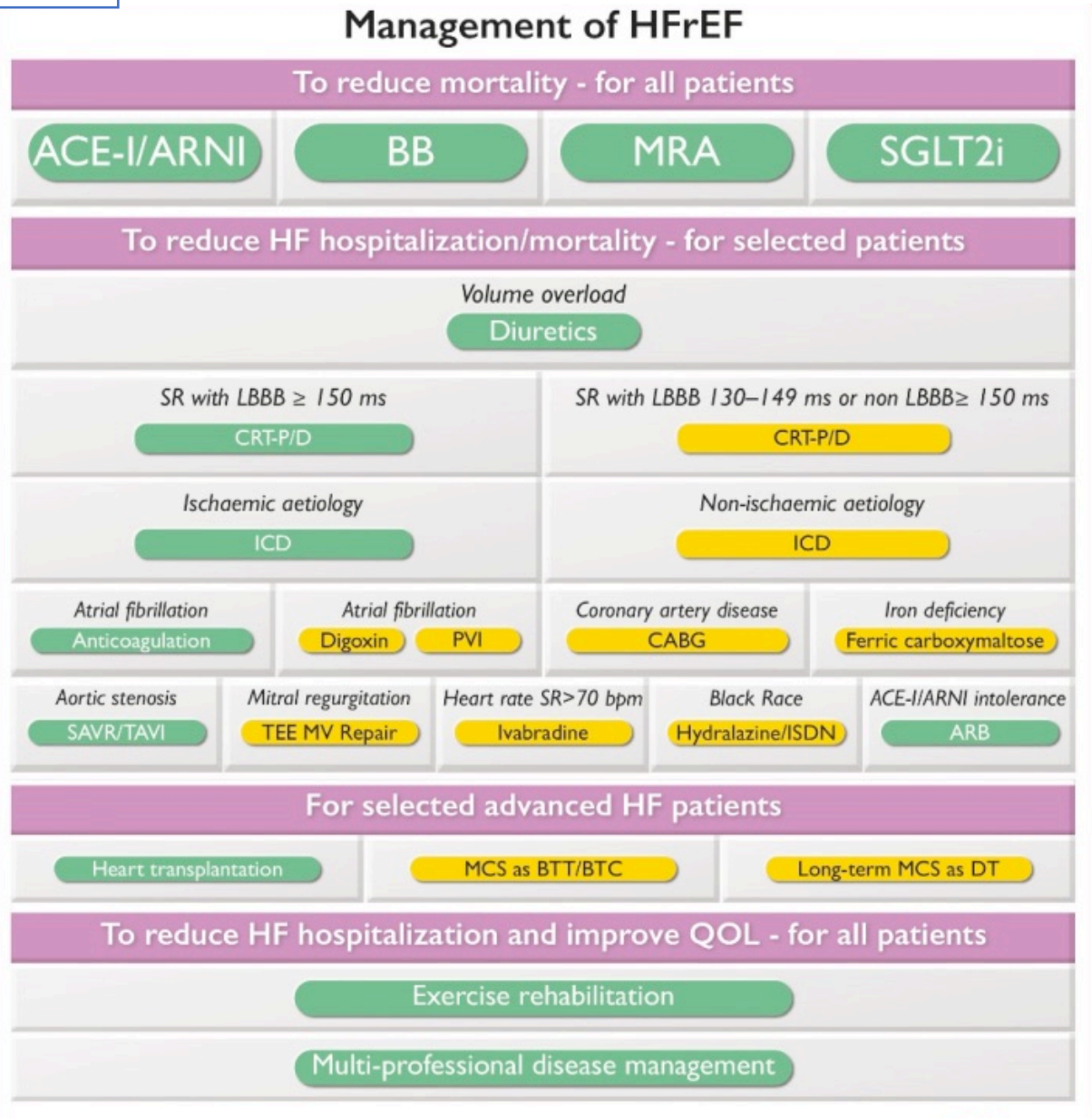
ESH

European Hypertension Excellence Center Princess Grace Hospital Monaco

Ce que nous savions

Qui ? Tout patient IC à FE reduite

Quand ? Dès le diagnostic.



www.escardio.org/guidelines

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab368)

Ce que nous avons appris

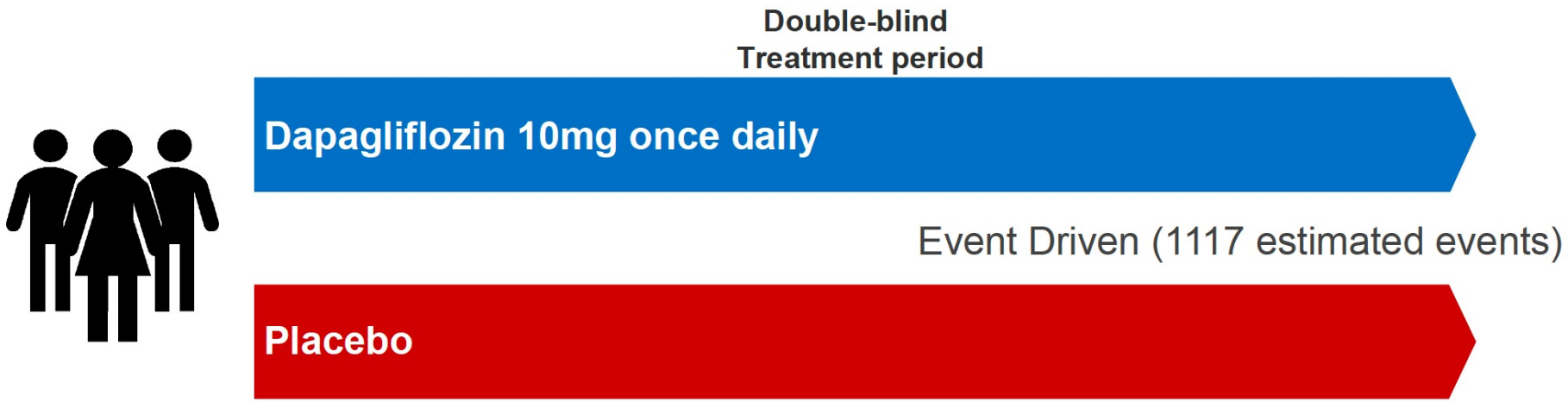
DELIVER Study Design

Randomized, double-blind, placebo-controlled trial testing the hypothesis that dapagliflozin would reduce cardiovascular death or worsening heart failure in patients with heart failure and mildly reduced or preserved ejection fraction

DELIVER

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



Solomon et al. Eur J Heart Fail 2021

Endpoints and Analysis Plan

Dual Primary Endpoints – Full Population and Patients with LVEF < 60%

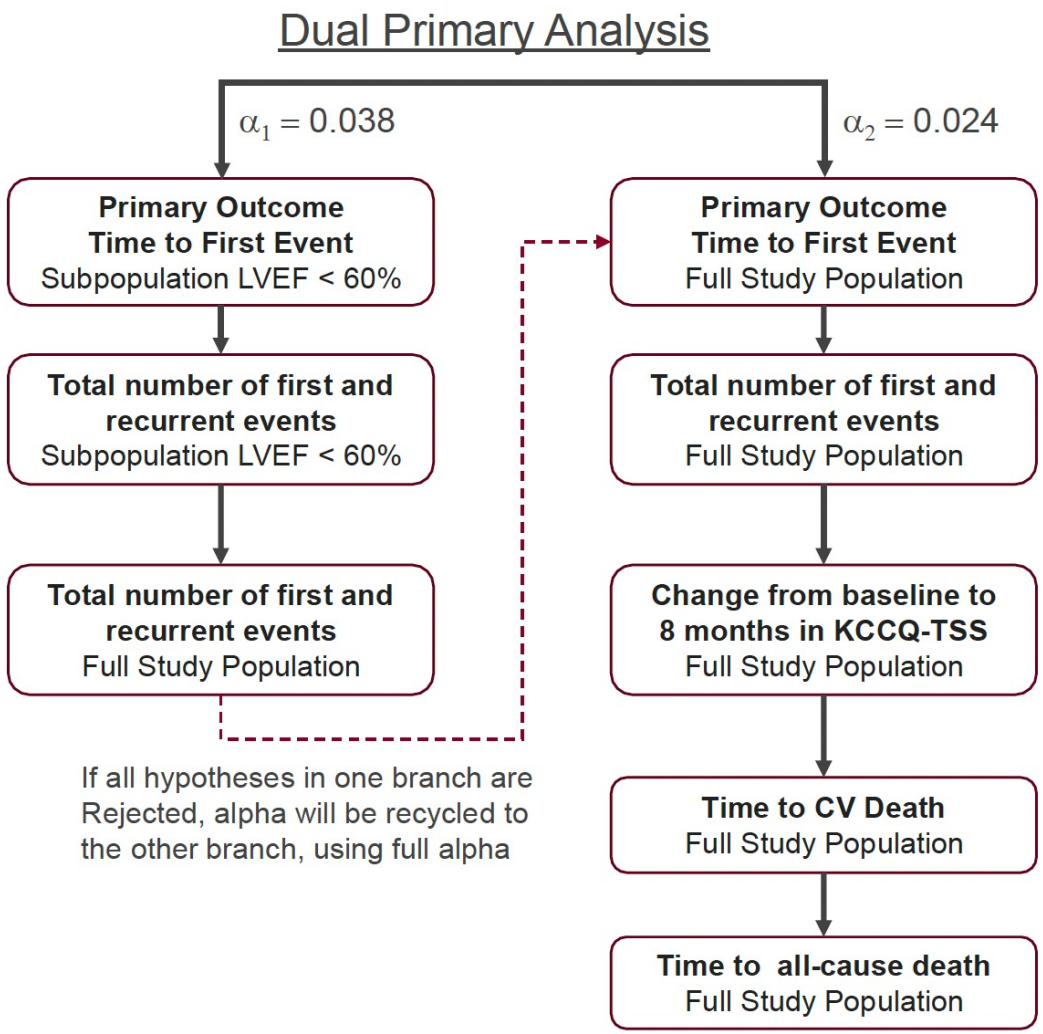
Primary Endpoint

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)



DELIVER Baseline Characteristics

Well Balanced Between Treatment Groups

	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%
Race		
White	70.7%	71.0%
Black	2.6%	2.5%
Asian	20.1%	20.6%
Other	6.6%	5.9%
Geographic Region		
Europe and Saudi Arabia	47.7%	48.2%
Asia	19.4%	19.8%
Latin America	19.2%	18.5%
North America	13.7%	13.5%
NYHA Class at Baseline		
II	73.9%	76.6%
III/IV	26.1%	23.4%
KCCQ Total Symptom Score	70 ± 23	70 ± 22

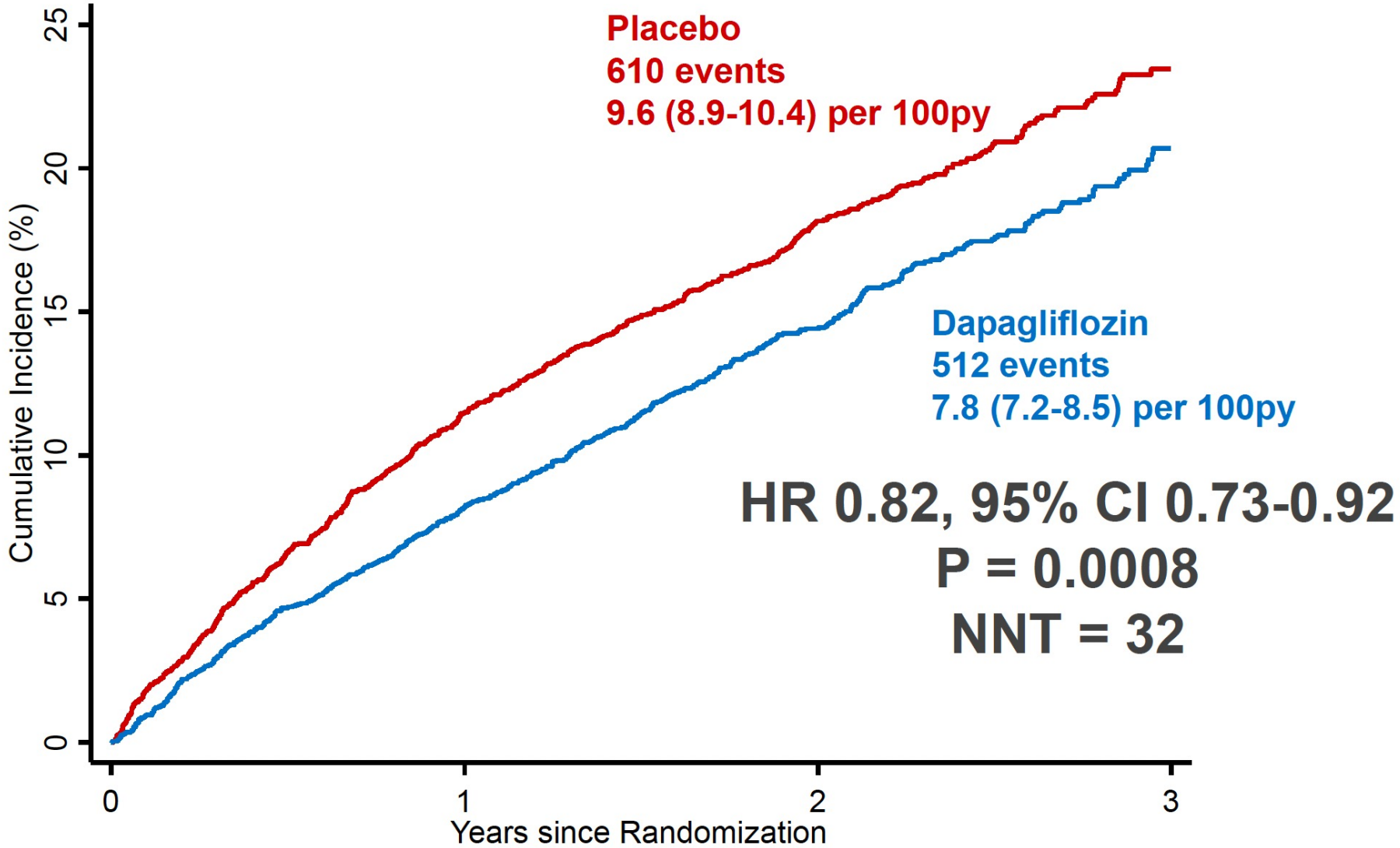
DELIVER Baseline Characteristics (2)

Well Balanced Between Treatment Groups

	Dapagliflozin N=3131	Placebo N=3132
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/1.73m^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%

Primary Endpoint: CV Death or Worsening HF

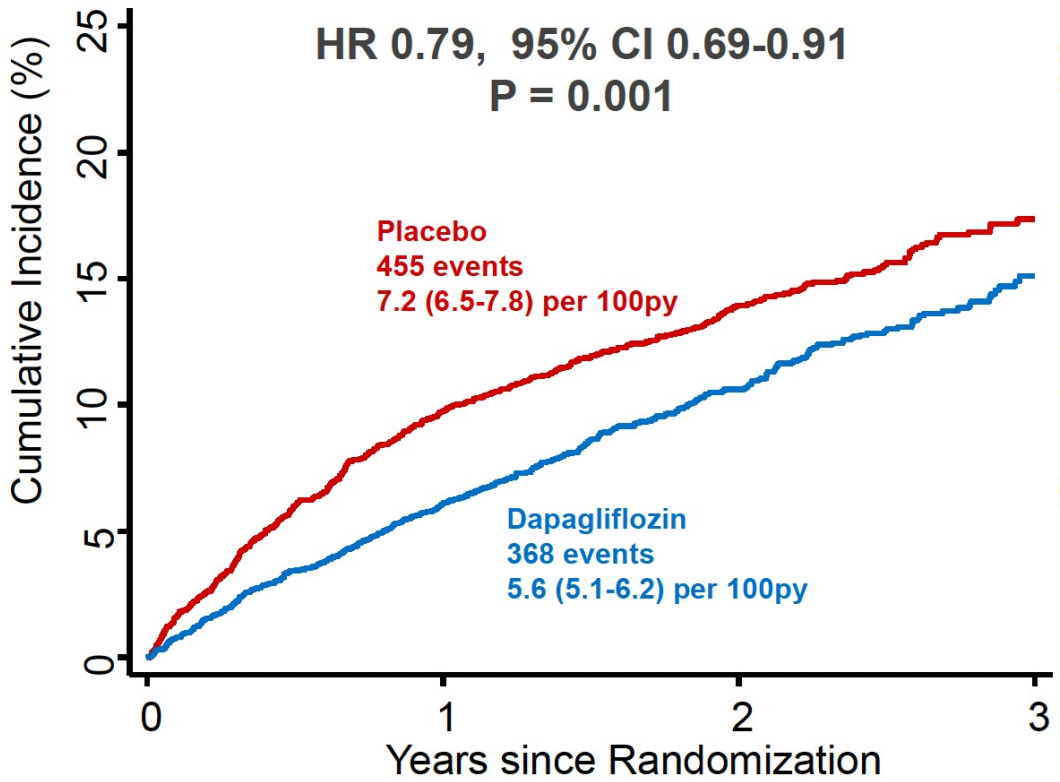
Full Population



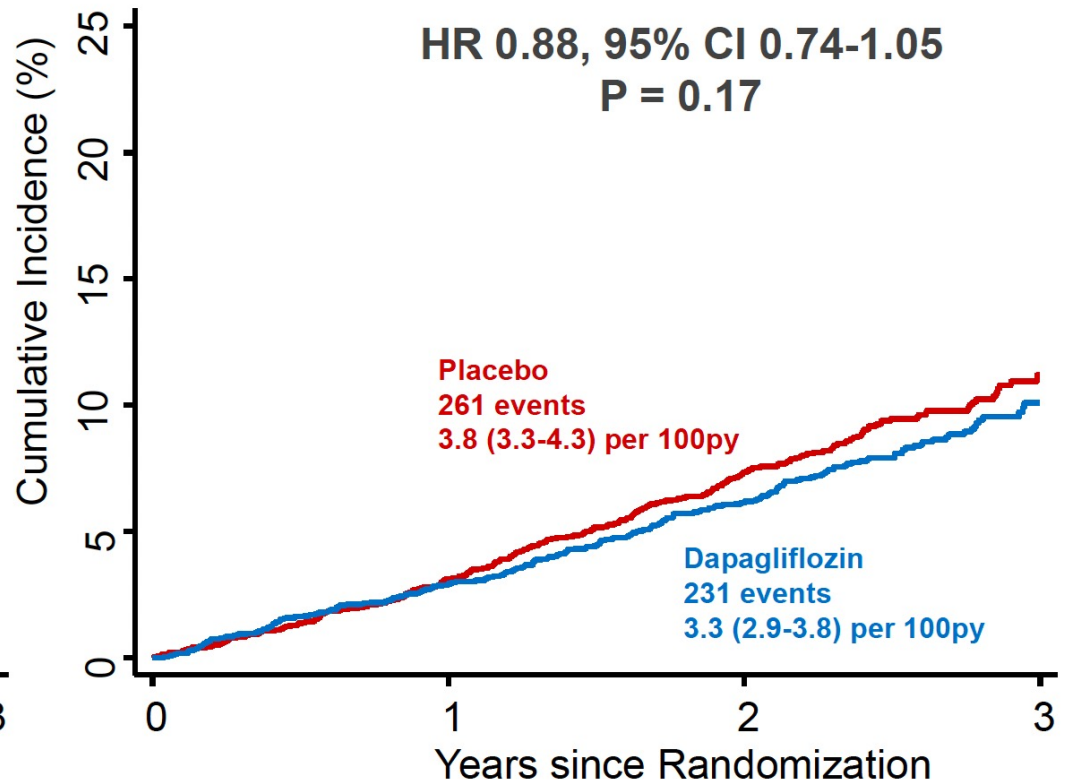
Components of Primary Endpoint

Full Population

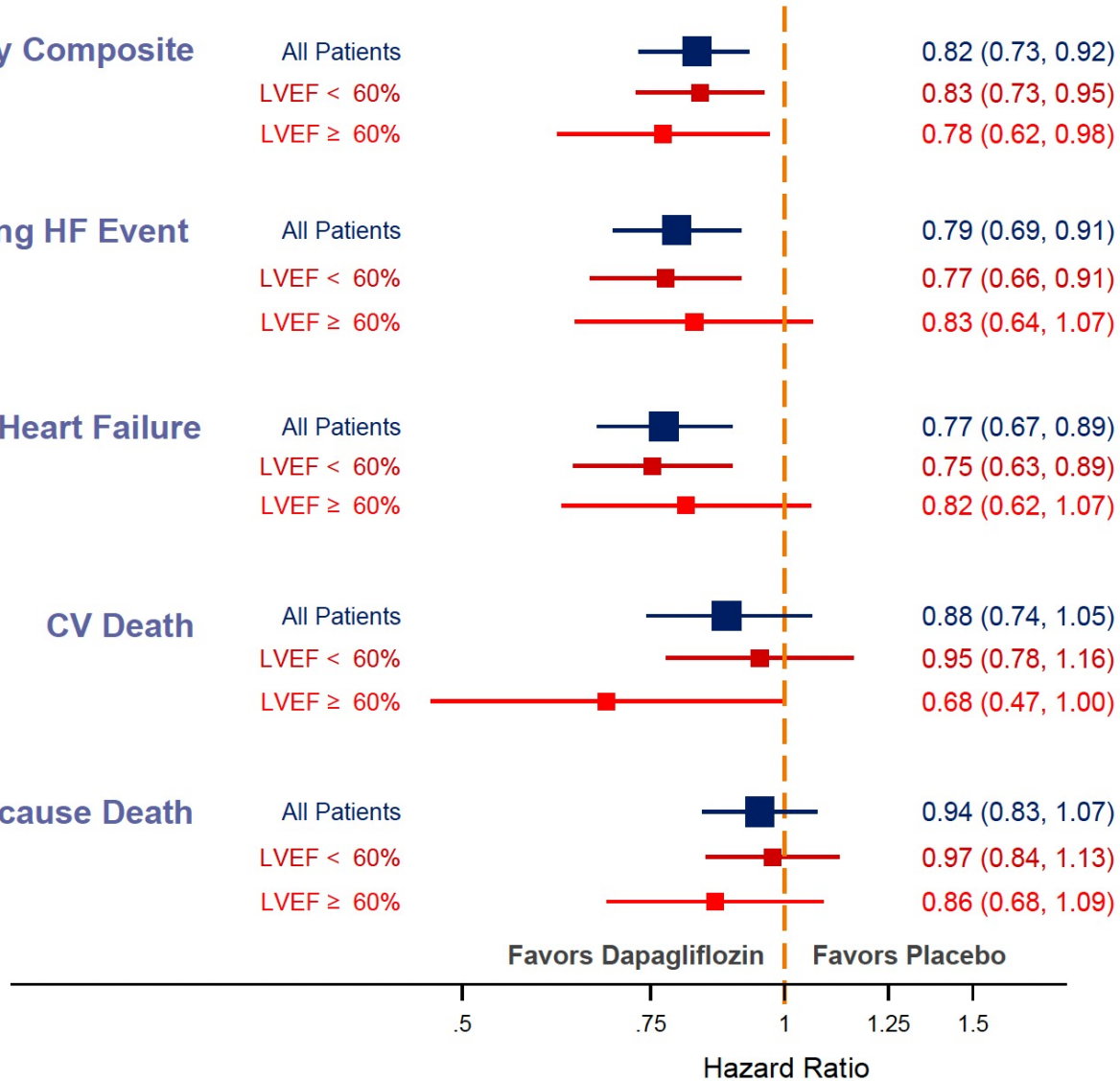
Worsening Heart Failure (HF Hospitalization + Urgent HF Visit)



Cardiovascular Death



Outcomes by LVEF < 60% or LVEF ≥ 60%

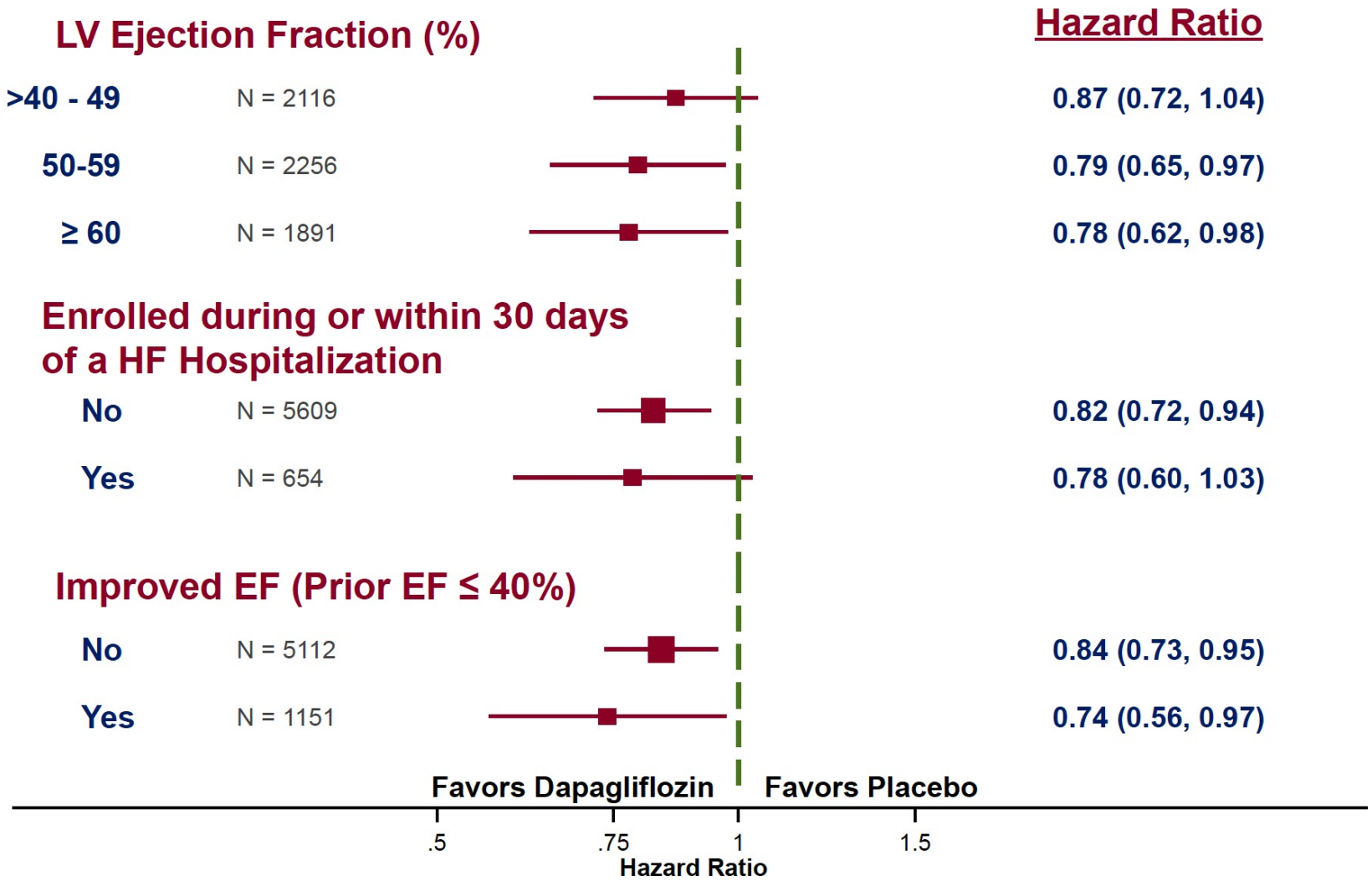


All Patients N = 6263

LVEF < 60% N = 4372 (70%)

LVEF ≥ 60% N = 1891 (30%)

Primary Endpoint in Prespecified Subgroups



60% is the new 40% or not ….

Peu importe la FE …

Adverse Events*

AE data collection of Serious Adverse Events, Adverse Events leading to treatment discontinuation and other selected adverse events

	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%)

*On treatment (in patients receiving at least one dose and up to 30 days following last dose of IP)

Pooled analysis of DAPA-HF and DELIVER

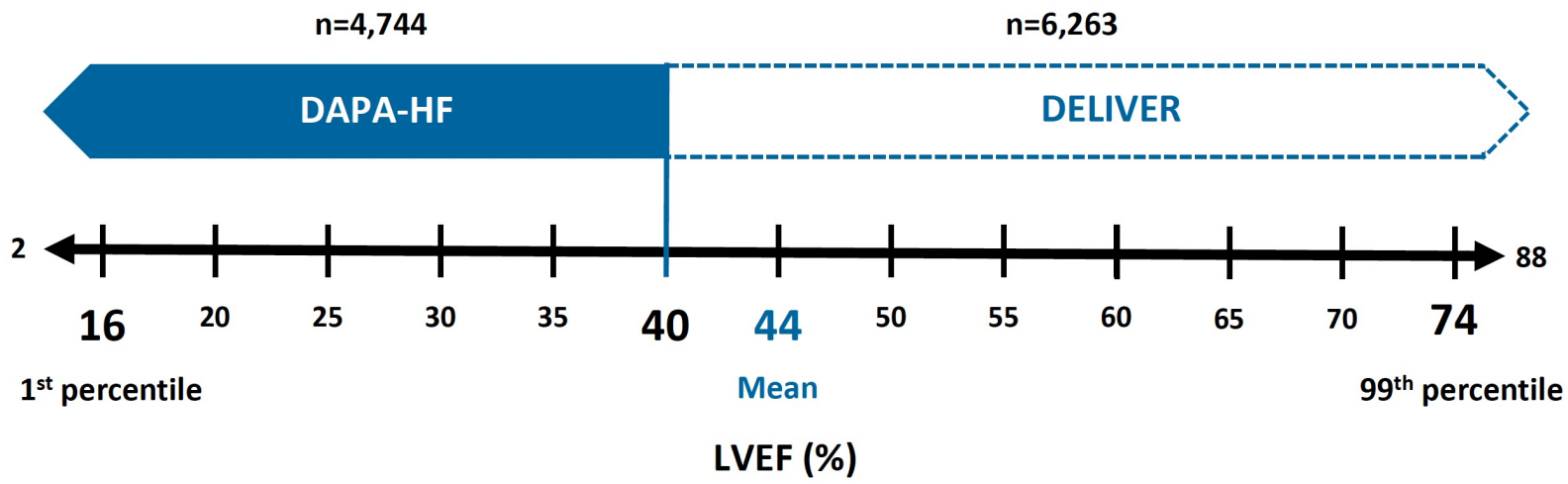
Pardeep S Jhund
BHF Glasgow Cardiovascular Research Centre, University of Glasgow
& Queen Elizabeth University Hospital, Glasgow

DAPA-HF and DELIVER pooled dataset

Dapagliflozin 10mg once daily vs placebo

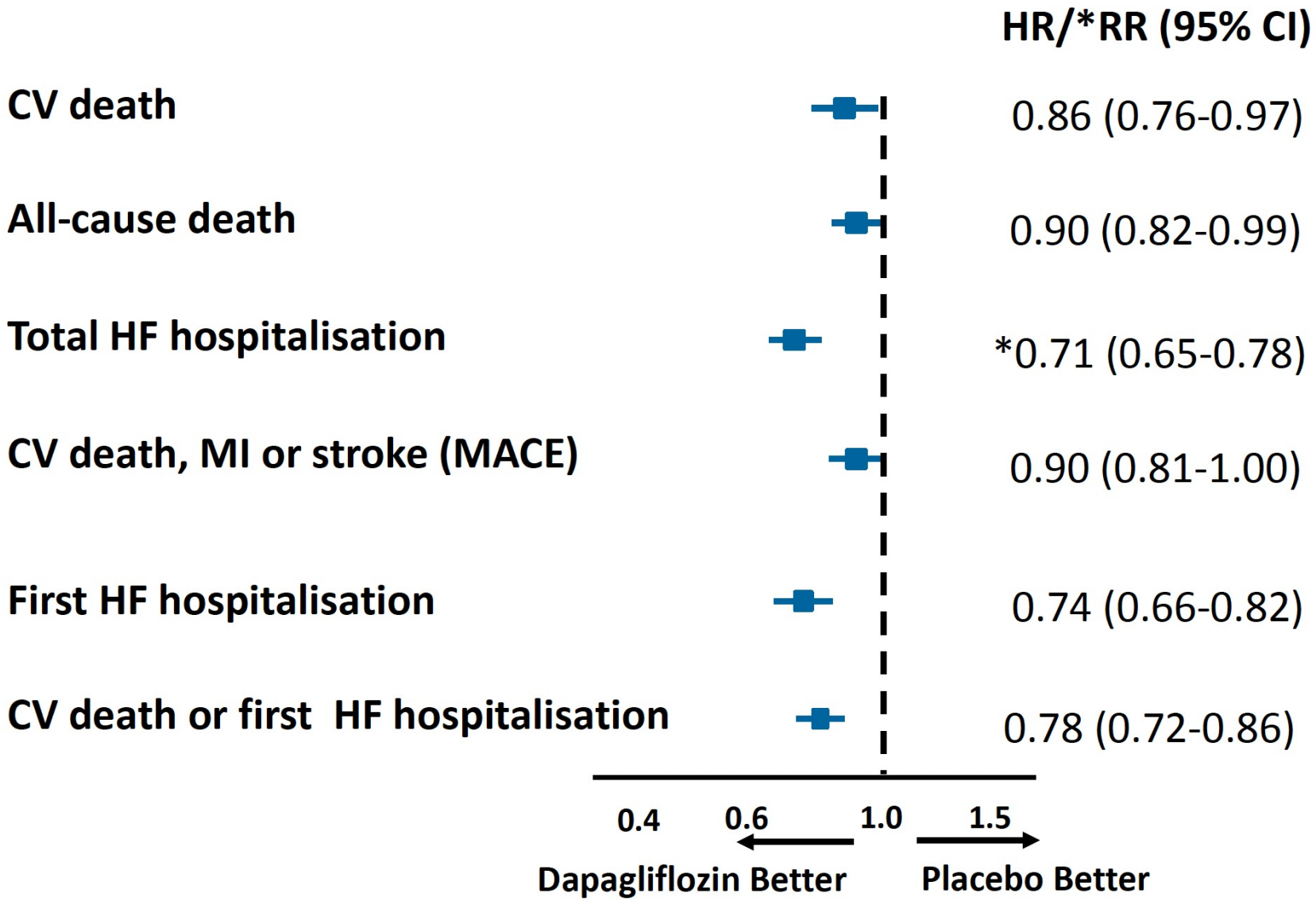
Median follow-up = 22 (IQR 17-30) months

Pooled dataset n=11,007

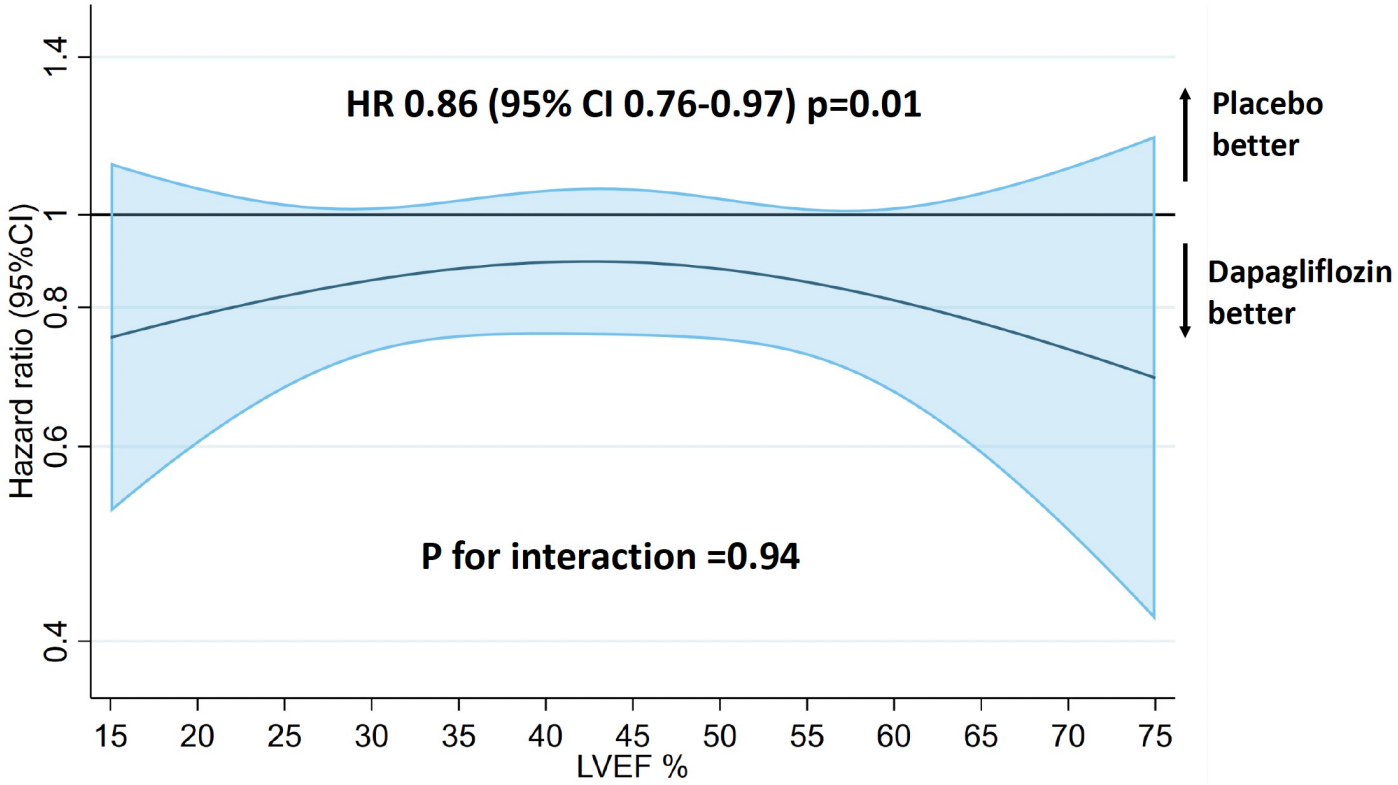


McMurray JJV et al Eur J Heart Fail. 2019;21:665-675 and Solomon SD et al Eur J Heart Fail 2021;23:1217-1225

DAPA-HF & DELIVER pooled: Outcome hierarchy



DAPA-HF & DELIVER pooled: Cardiovascular death



Ce que nous devrions faire

EMPEROR-Preserved trial #ESCCongress

Effect of empagliflozin on CV death and heart failure hospitalisations in patients with heart failure with a preserved ejection fraction, with and without diabetes

Conclusion

Empagliflozin reduces the risk of a composite of CV death or hospitalisation for heart failure (HF) in patients with HF and a preserved ejection fraction (HFpEF) with or without diabetes.

Background

The EMPEROR-Reduced trial previously showed that the SGLT2 inhibitor empagliflozin reduced the risk of CV death or hospitalisation for HF in patients with HF and a reduced ejection fraction.

Study objectives

EMPEROR-Preserved evaluated the effects of SGLT2 inhibition in HFpEF patients with and without diabetes.

Who and what?

622 centres · 23 countries

5,988

symptomatic HFpEF patients
(left ventricular ejection fracion >40%)

randomised 1:1

Empagliflozin · Placebo

On top of all appropriate treatments
for HFpEF and co-morbidities

Primary endpoint

Median follow-up ▸ 26 months

Composite of CV death or
hospitalisation for HF

Empagliflozin 13.8%

Placebo 17.1%

6.9 vs 8.7 events per 100 patient-years

HR: 0.79; 95% CI: 0.69–0.90; *p=0.0003*)

Secondary outcomes

Hospitalisations for HF
(including first and recurrent events)

Empagliflozin < Placebo

HR: 0.73; 95% CI: 0.61–0.88; *p<0.001*)

Rate of decline in glomerular filtration
rate (eGFR) during study treatment

-1.25 Empagliflozin

-2.62 Placebo

ml/min/1.73 m²/year

p<0.0001

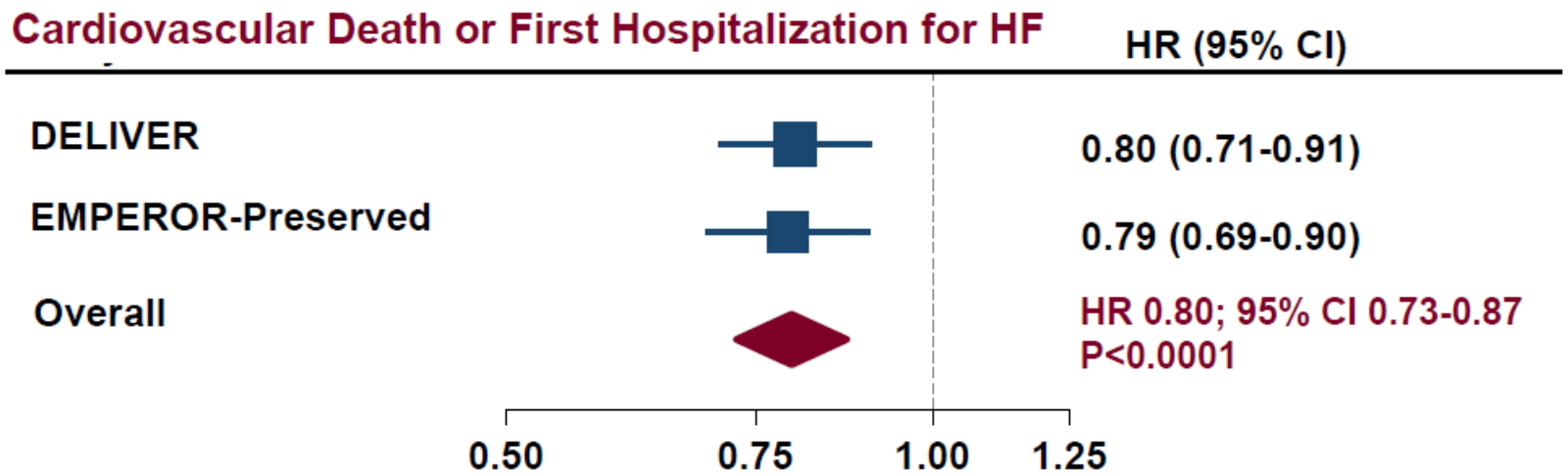
Serious adverse events

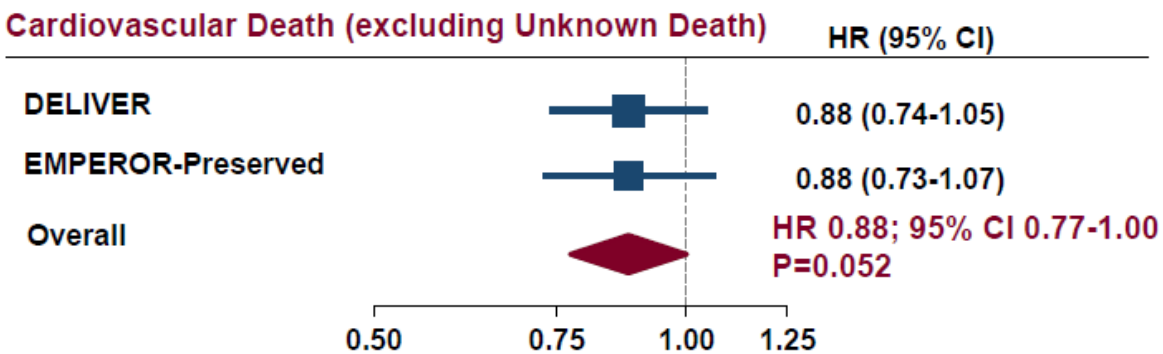
Empagliflozin 47.9%

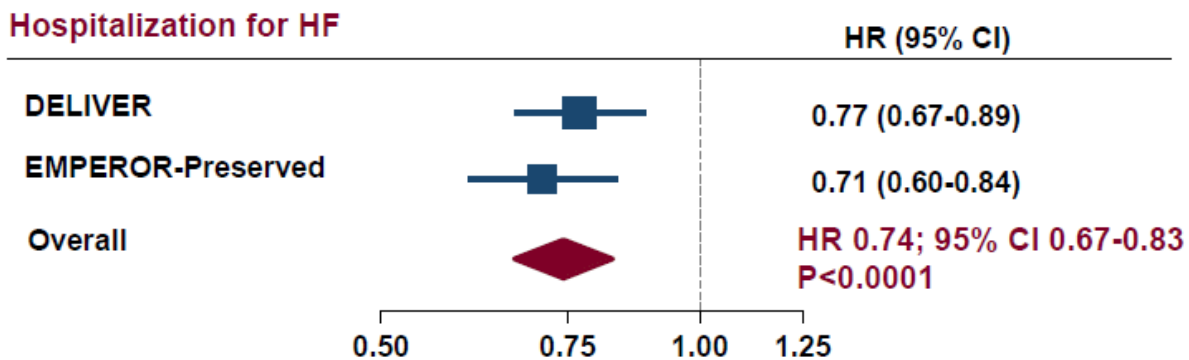
Placebo 51.6%

DELIVER and EMPEROR-Preserved Meta-Analysis:

↓ 20% (13-27%) Relative Risk Reduction of Primary Endpoint with Consistent Reductions in Both Components

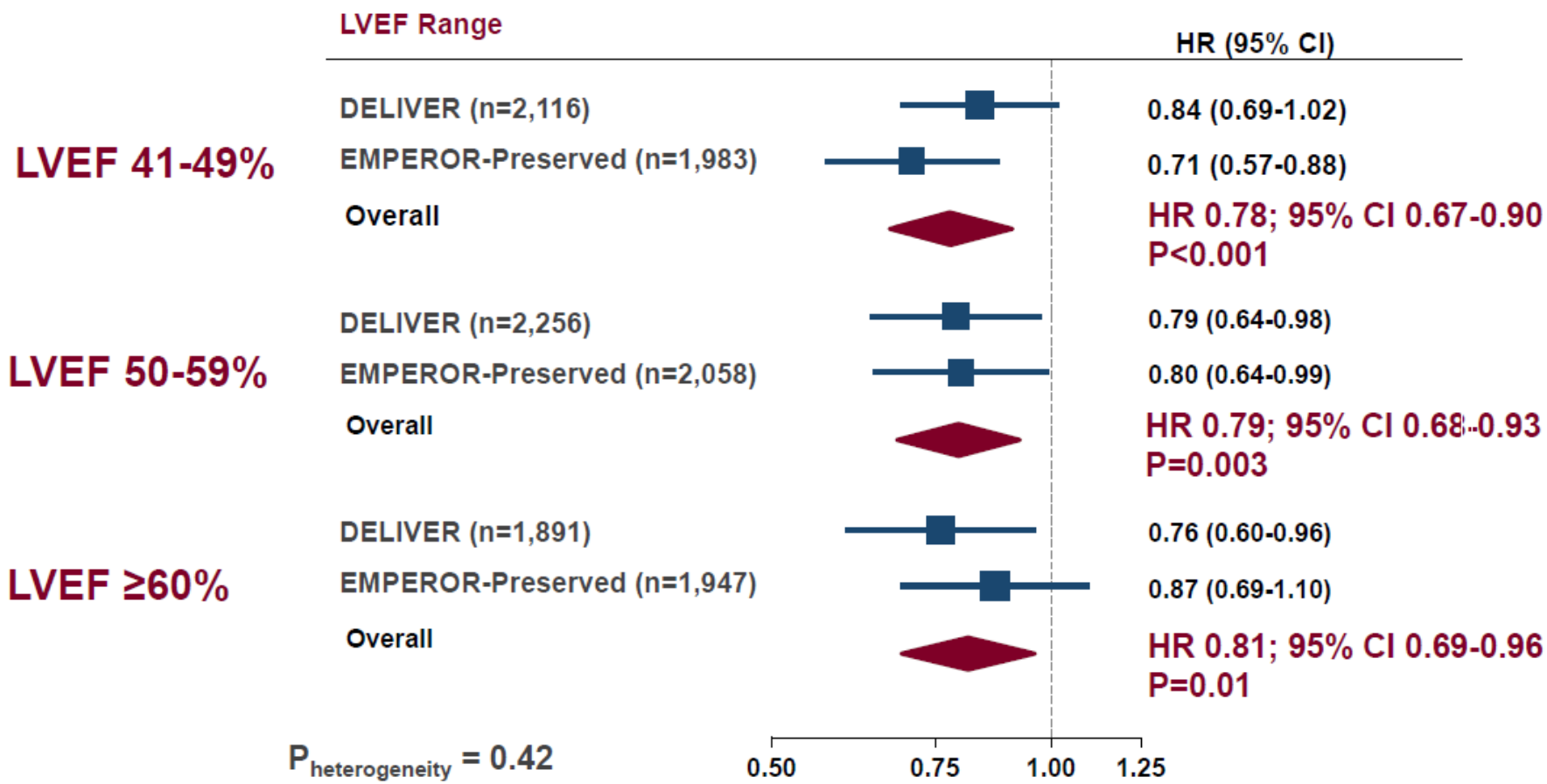






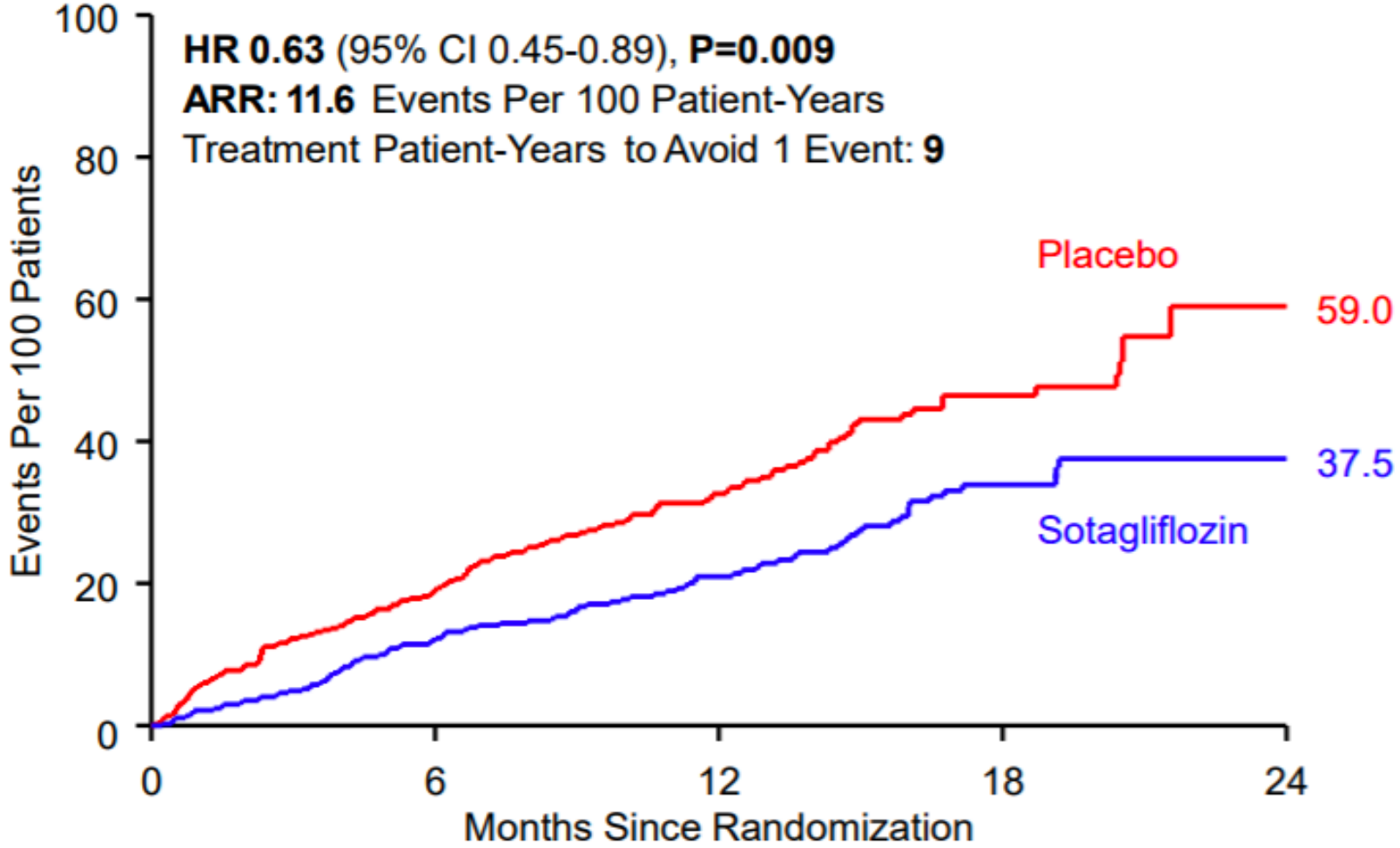
$P_{heterogeneity}$ >0.40 for all endpoints

DELIVER and EMPEROR-Preserved Meta-Analysis:
Consistent Reductions in Primary Endpoint across LVEF Range, including among LVEF ≥60%



Pooled Data: SOLOIST and SCORED Total CV Death, HHF, and Urgent HF Visit in 739 Patients with HFpEF (≥50%)

SOLOIST
SCORED



For this analysis, patients from SCORED needed to have a history of HF within 2 years.

Bhatt DL. ACC 2021, virtual.

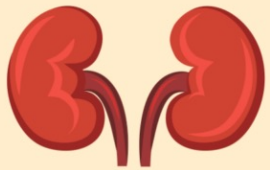
SOLOIST - WHF TRIAL

Bhatt DL et al. Sotagliflozin in Patients with Diabetes and Recent Worsening Heart Failure. N Engl J Med. 2021;384(2):117-128.

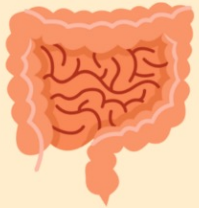
SOTAGLIFLOZIN

inhibits

SGLT-2 → increases urinary glucose excretion



SGLT-1 → delays intestinal glucose absorption



QUESTION

In patients with diabetes and recently worsening HF, does SOTAGLIFLOZIN:
↓ CV mortality?
↓ HF urgent visits?
↓ HF hospitalizations?

INCLUSION

18 - 85 yo patients with diabetes hospitalized for signs or symptoms of HF and treatment with IV diuretics

1222 patients

TOTAL NO. OF EVENTS (RATE PER 100 PATIENT YEARS)

	PRIMARY OUTCOME: HF urgent visits + HF hospitalizations + CV Death	SECONDARY OUTCOME: HF urgent visits + HF hospitalizations	SECONDARY OUTCOME: CV Death
Sotagliflozin n=608	245 (51)	194 (40)	51 (11)
	HR 0.67 95% CI 0.52-0.85 p<0.001	HR 0.64 95% CI 0.49-0.83 p<0.001	HR 0.84 95% CI 0.58-1.22 p=0.36
Placebo n=614	355 (76)	297 (64)	58 (13)

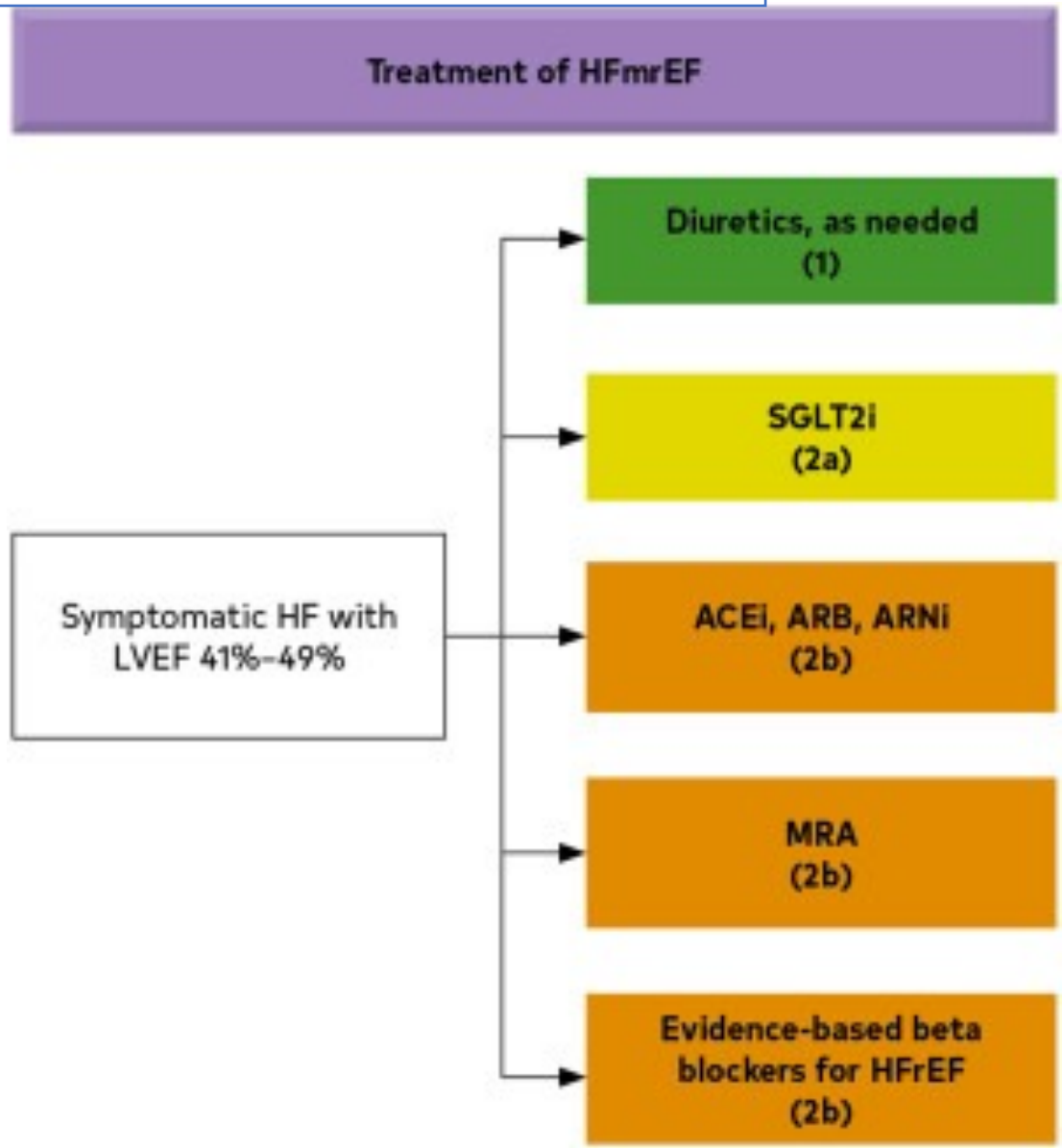
CONCLUSION

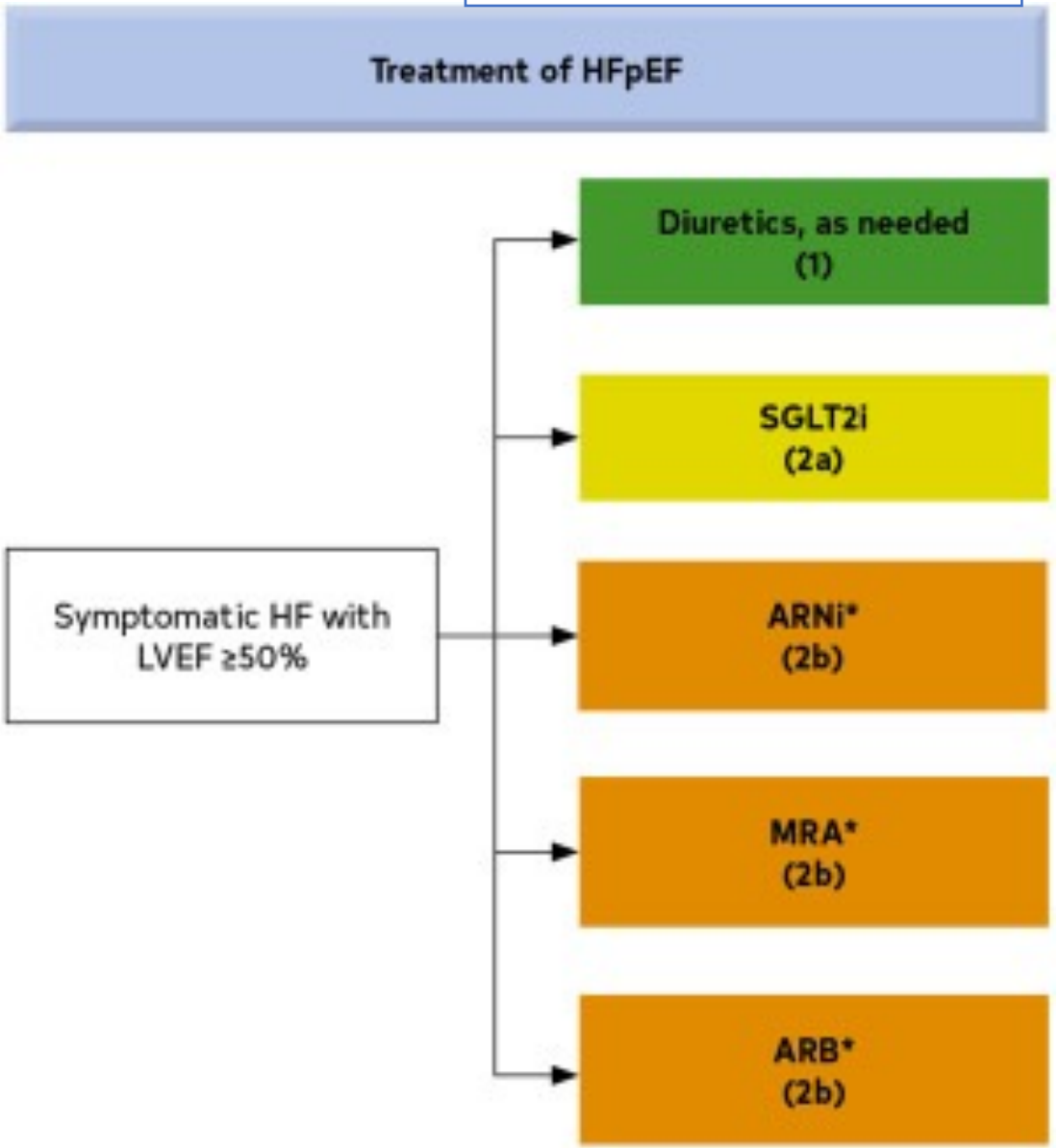
In patients with diabetes with worsening HF, sotagliflozin significantly decreased CV deaths, HF urgent visits, and HF hospitalizations

Created by @TDonisan | @CardioNerdsJC

Qui ? Tout patient IC, quelque soit sa FE.

Quand ? Dès le diagnostic.





2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

Conclusions

- SGLT2 i dans l’IC quelque soit la FE
- Le plus tot possible durant ou apres une decompensation
- Avec les traitements associés.

REVIVED-BCIS2 trial #ESCCongress

Percutaneous revascularisation for ischaemic ventricular dysfunction

Conclusion

Percutaneous coronary intervention (PCI) does not reduce all-cause mortality or heart failure hospitalisation in patients with severe left ventricular (LV) dysfunction and extensive coronary artery disease.

Impact on clinical practice

PCI should not be offered to stable patients with ischaemic LV dysfunction if the sole aim is to provide prognostic benefit. However, it is important to note that REVIVED-BCIS2 excluded patients with limiting angina or recent acute coronary syndromes, and PCI is still an option in these contexts.

Study objectives

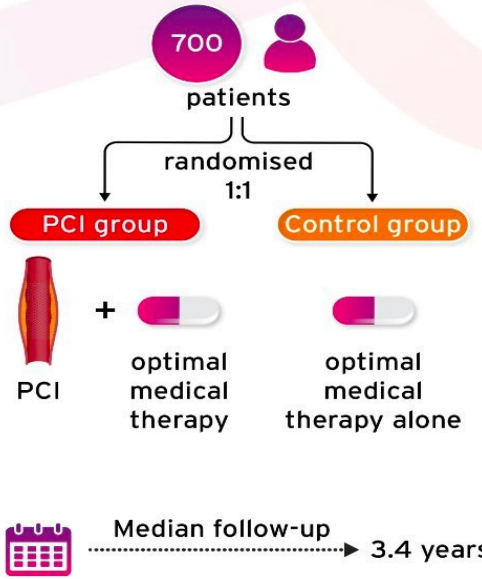
REVIVED-BCIS2 is the first adequately powered randomised trial to examine the efficacy and safety of PCI in patients with LV systolic dysfunction.

Who and what?

Population

Patients with

- severe LV dysfunction (ejection fraction ≤35%)
- extensive coronary disease
- demonstrable viability in at least 4 dysfunctional myocardial segments that could be revascularised by PCI



Primary endpoint

Composite of all-cause death or hospitalisation for heart failure

Secondary outcomes

LV ejection fraction at 6 and 12 months:

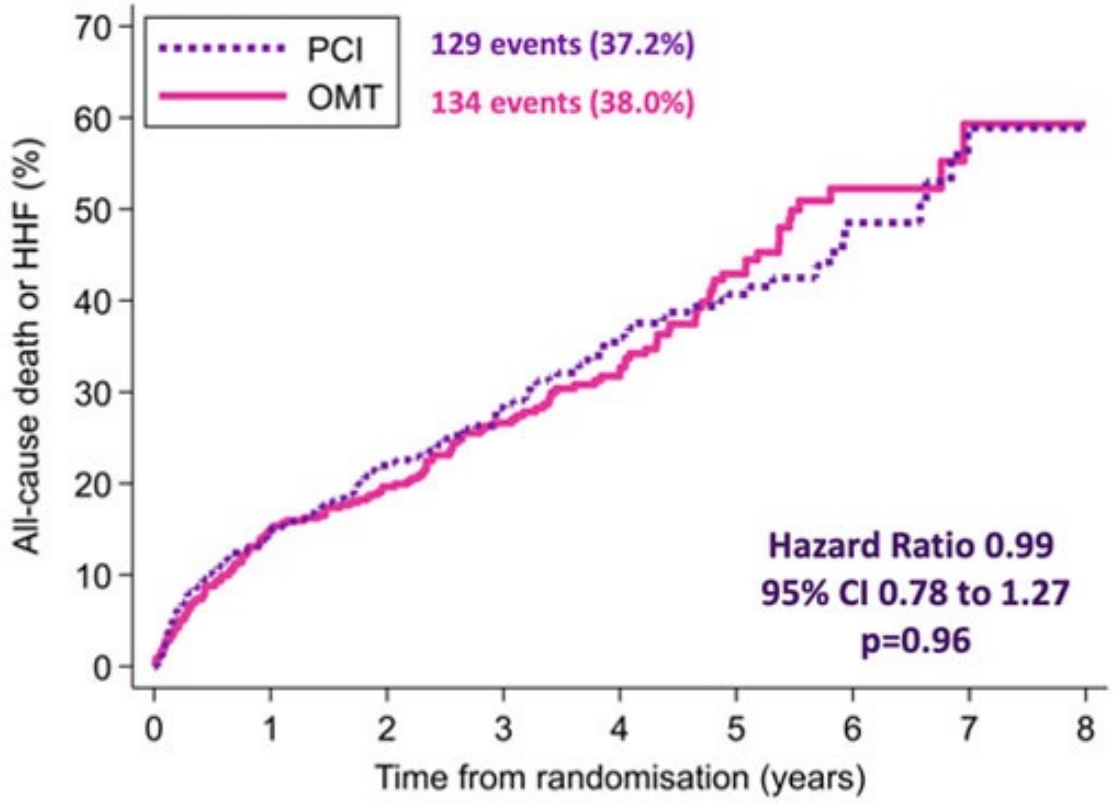
No differences between groups

Quality of life measures:

Favoured PCI at 6 and 12 months

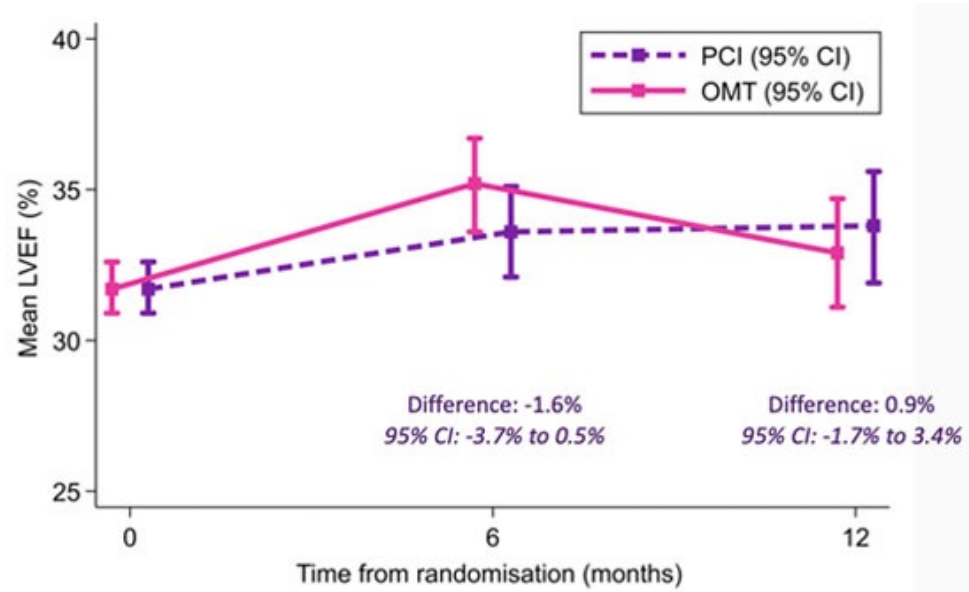
No difference between groups at 24 months

ESC



Number at risk

PCI	347	295	262	179	130	80	32	14	3
OMT	353	299	276	191	142	82	33	10	1



Number followed up

PCI	264	276	262
OMT	276	264	267

Acetazolamide in Decompensated Heart failure with Volume OveRload trial

ADVOR

N = 519

Double-blind, randomized

30 Hospitals in Belgium

Acute heart failure with volume overload

Maintenance loop diuretics for at least 1 month

NTproBNP > 1000 pg/ml

Stratified according to LVEF

High dose loop diuretics + Acetazolamide 500 mg IV

High dose loop diuretics + Matching placebo

Baseline characteristics: elderly heart failure population, well-treated, with a severe degree of volume overload.

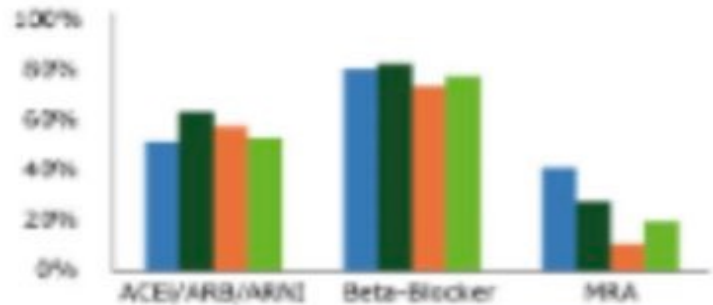
Mean age 78 years
63% men
57% LVEF > 40%

Significant degree of volume overload: 78% oedema up to knee or above

Median NT-proBNP 6173 pg/mL

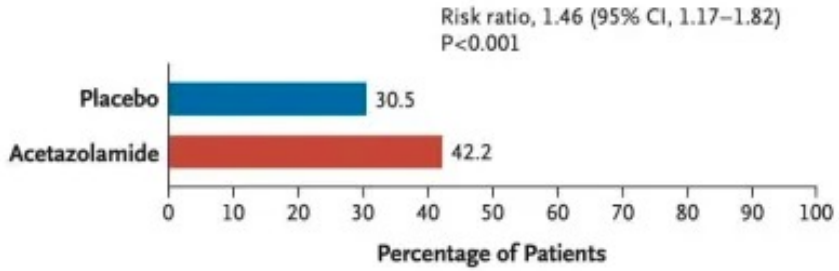
Overall high baseline heart failure medication prescription, comparable to other large diuretic trials in AHF

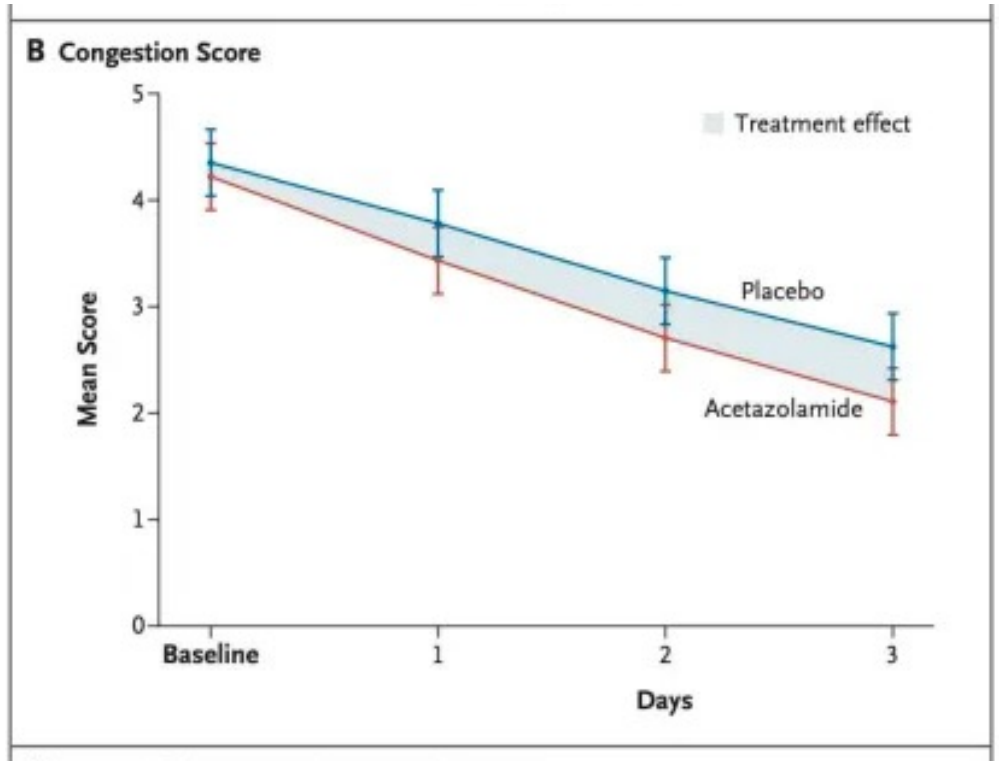
- ADVOR N = 519
- DOSE N = 308
- ATHENA N = 360
- CARRESS-HF N = 188



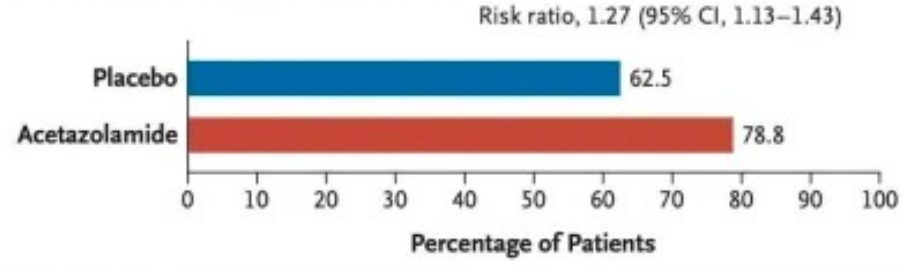
ADVOR is the largest diuretic trial in AHF with succesful decongestion as a primary endpoint.
The elderly enrolled population provides a good reflection of the real-world AHF patients in daily clinical practice.

A Successful Decongestion within 3 Days after Randomization





C Successful Decongestion at Discharge



Demain dans l’IC decompensée ? Le retour des diuretiques..

- LASILIX
- EMPA / DAPA en congestion
- ACETAZOLAMIDE

PERSPECTIVE trial #ESCCongress

Sacubitril/valsartan and cognitive function in HFmrEF and HFpEF

Conclusion

Sacubitril/valsartan does not change cognitive function, compared with valsartan, in patients with heart failure and mildly reduced or preserved ejection fraction (HFmrEF and HFpEF).

Impact on clinical practice

The absence of any negative effect on cognitive function is very important in removing a concern some doctors had about long-term treatment with sacubitril/valsartan.

Study objectives

PERSPECTIVE was the first randomised trial to prospectively evaluate the effect of long-term treatment with sacubitril/valsartan, compared with valsartan, on cognitive function in patients with HFmrEF and HFpEF.

Who and what?

Population

Adults aged ≥ 60 years with chronic symptomatic HF plus HF hospitalisation in the prior 12 months and/or NT-proBNP >200 pg/mL.

20 countries

137 centres

592 patients

randomised 1:1

- Sacubitril/valsartan
- Valsartan

Primary endpoint

Change in cognitive function from baseline to 3-year follow up evaluated using the CogState global cognition composite score (GCCS), which includes 7 tasks assessing attention, episodic memory, and executive function.

Sacubitril/valsartan — Valsartan

Difference in least-squares mean change in GCCS was -0.0180
95% CI -0.1230 to 0.0870; p=0.74

The change in GCCS from baseline to 3 years did not differ between patients treated with sacubitril/valsartan compared to those treated with valsartan.

Principal secondary outcome

Change from baseline to 3 years in amyloid β deposition in the brain measured using positron emission tomography in 491 patients.

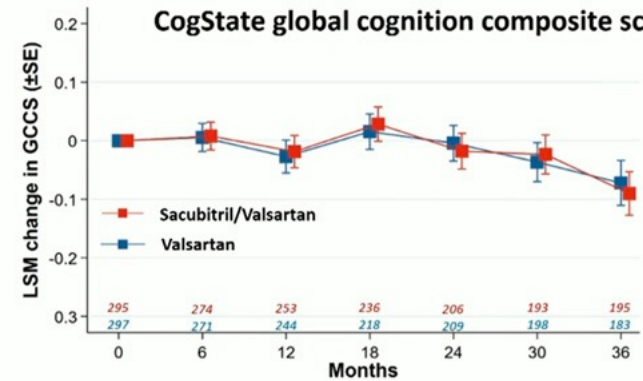
Sacubitril/valsartan — Valsartan

Difference in least-squares mean change in the standardised uptake value ratio was -0.0292
95% CI -0.0593 to 0.0010; p=0.058

Indicates amyloid β deposition in the brain tended to be less in patients treated with sacubitril/valsartan compared with valsartan.

ESC

PERSPECTIVE: Primary outcome



* LSM = least-squares mean; SE = standard error; GCCS = CogState global cognition composite score

Conclusions

- SGLT2 pour tous ?
- Plus de diuretiques ?
- Moins de revascularisation ?