Effectiveness of Empagliflozin in Patients with Heart Failure and COPD: Results From EMPEROR-Preserved and EMPEROR-Reduced

EMPEROR Heart failure studies

Stephan von Haehling,[1] Javed Butler,[2] Stefan D. Anker[3]

[1]University Medical Centre of Göttingen (UMG), Göttingen, Germany; [2]University of Mississippi Medical Center, Jackson, MI, USA; Baylor Scott and White Institute, Dallas, TX, USA; [3]Department of Cardiology (CVK) and Berlin Institute of Health Center for Regenerative Therapies (BCRT), German Centre for Cardiovascular Research (DZHK) Partner Site Berlin, Charité Universitätsmedizin Berlin, Berlin, Germany; Institute of Heart Diseases, Wrocław Medical University, Wrocław, Poland

BACKGROUND

- HF and COPD are chronic, progressive syndromes that share numerous risk factors and clinical symptoms.
- The SGLT2 inhibitor, empagliflozin, significantly reduced the risk of the composite primary outcome of CV death or HHF in EMPEROR-Reduced (HR 0.75 [95% CI 0.65, 0.86]; p<0.001) and EMPEROR-Preserved (HR 0.79 [95% CI 0.69, 0.90]; p<0.001).[1,2]

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OBJECTIVE

- To analyze the relationship between COPD status and outcomes in patients receiving empagliflozin or placebo in the EMPEROR-Preserved and EMPEROR-Reduced trials.

METHODS

- Patients with and without COPD were compared with respect to baseline characteristics and outcomes following treatment with empagliflozin.
- The primary endpoint was first HHF or CV death.
- Additional endpoints included HF hospitalizations, CV and all-cause mortality, quality of life using the KCCQ, and AEs.

RESULTS

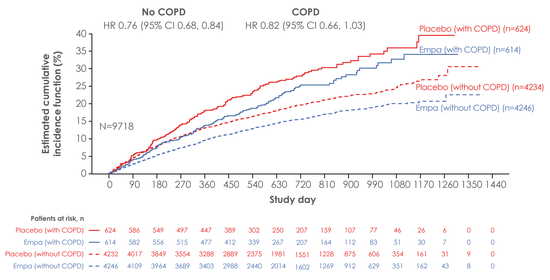
- Of 9718 patients from the EMPEROR trials, 1238 (12.7%) had COPD.
- Compared to patients without COPD, patients with COPD were more likely to be NYHA functional class III, male, have higher BMI, White, a smoker or ex-smoker, older, have a longer duration of HF, have higher hemoglobin and high-sensitivity troponin T values, and trend toward more advanced kidney dysfunction (**Table 1**).
- Patients with COPD exhibited a higher adjusted risk of reaching the primary endpoint of first HHF or CV death compared with those without COPD (adjusted HR 1.52 [95% CI 1.28, 1.80]; p<0.0001).
- The favorable impact of empagliflozin on the primary outcome remained consistent regardless of COPD status at baseline (no COPD: HR 0.76 [95% CI 0.68, 0.84]; COPD: HR 0.82 [95% CI 0.66, 1.03]; p for interaction 0.50) (**Figure 1**).

Table 1. Baseline characteristics

	No COPD (n=8480)	COPD (n=1238)	p-value
Female	3185 (37.6)	384 (31.0)	<0.0001
BMI, kg/m²	29.0±5.7	29.5±6.1	<0.0001
Age, years	69.6±10.5	72.1±8.7	<0.0001
Smoking status			
Never smoked	4376 (51.6)	332 (26.8)	<0.0001
Ex-smoker	3355 (39.6)	701 (56.6)	
Current smoker	634 (7.5)	189 (15.3)	
Race			
White	6137 (72.4)	1034 (83.5)	<0.0001
Black/African American	465 (5.5)	50 (4.0)	
Asian	1399 (16.5)	97 (7.8)	
Other	426 (5.0)	50 (4.0)	
NYHA class			
I	4 (<0.1)	0	<0.0001
II	6799 (80.2)	884 (71.4)	
III	1641 (19.4)	352 (28.4)	
IV	36 (0.4)	2 (0.2)	
Cause of HF			
Duration of HF, years	5.0±5.7	5.4±5.4	0.04
Ischemic	3485 (41.1)	561 (45.3)	0.005
Non-ischemic	4994 (58.9)	677 (54.7)	
LVEF, %	43.9±15.3	44.7±15.1	0.07
Hemodynamics			
Heart rate, bpm	70.6±11.8	71.2±11.8	0.10
Systolic BP, mmHg	128±16	128±16	0.97
Diastolic BP, mmHg	75±11	74±10	0.004
Hemoglobin, g/dL	13.45±1.60	13.58±1.65	0.006
HbA1c, % (n=4790)	7.32±1.55	7.24±1.40	
High-sensitivity troponin T, ng/L	25.6±32.8	28.5±26.7	<0.0001
NT-proBNP, pg/mL	2067±2892	2052±2513	0.11
eGFR, mL/min/1.73 m²	61.4±20.7	59.3±19.6	0.0006
Medical history			
Atrial fibrillation/flutter	3822 (45.1)	604 (48.8)	0.02
Diabetes mellitus	4152 (49.0)	642 (51.9)	0.06
Hypertension	7073 (83.4)	1049 (84.7)	0.24
Hypercholesterolemia	5430 (64.0)	864 (69.8)	<0.0001
Coronary artery disease	3249 (38.3)	555 (44.8)	<0.0001
Myocardial infarction	2953 (34.8)	450 (36.3)	0.29
CABG or PCI	2936 (34.6)	501 (40.5)	<0.0001
Valvular heart disease*	1313 (15.5)	215 (17.4)	0.09
Treatment			
ACEi/ARBs/ARNi	7131 (84.1)	994 (80.3)	0.53
Beta blockers	7628 (90.0)	1072 (86.6)	0.0003
Ivabradine	281 (3.3)	50 (4.0)	0.19
MRAs	4296 (50.7)	609 (49.2)	0.33
Loop diuretics	6210 (73.2)	994 (80.3)	<0.0001
Thiazides	1330 (15.7)	194 (15.7)	0.99
Pacemaker	469 (5.5)	80 (6.5)	0.18
CRT-D/CRT-P	389 (4.6)	77 (6.2)	0.01
ICD or CRT-D	1179 (13.9)	224 (18.1)	<0.0001

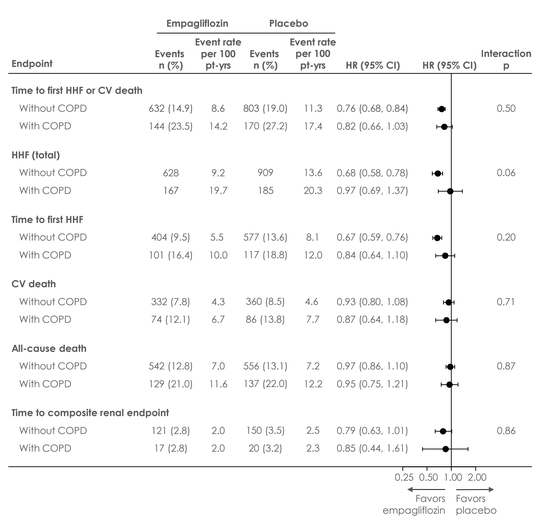
Data are n (%) or mean ± standard deviation. *Deemed clinically meaningful.

Figure 1. Primary composite endpoint: Time to first HHF or CV death



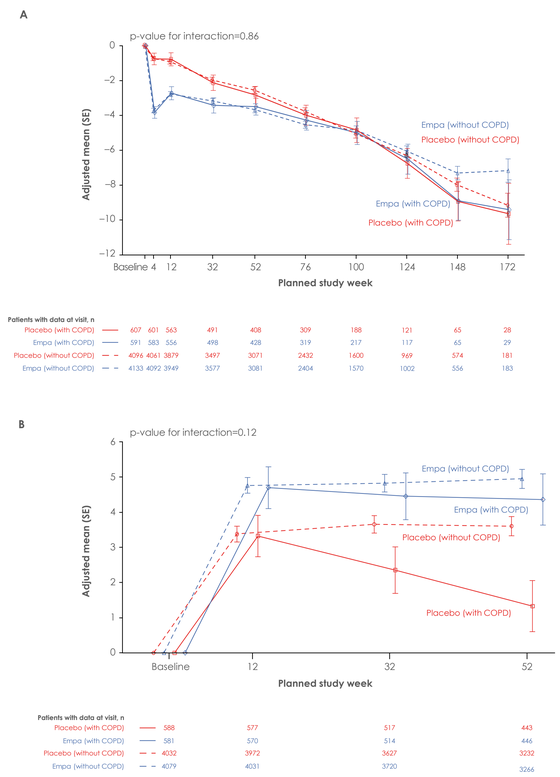
- The effect on HHF, CV, and all-cause mortality was not affected by COPD status (**Figure 2**).

Figure 2. Secondary endpoints



- The change in eGFR (**Figure 3A**) and KCCQ (**Figure 3B**) showed similar improvement in patients with or without COPD treated with empagliflozin.
- The distribution of AEs was comparable between patients receiving empagliflozin and those receiving placebo, irrespective of COPD status at baseline.

Figure 3. Changes in eGFR (A) and KCCQ (B) from baseline



CONCLUSIONS

- COPD is frequently encountered in patients with HF and is associated with worse outcomes.
- Patients with COPD were more often male, had higher BMI, were older, more likely to be White, more symptomatic, and had a higher comorbidity burden.
- The effectiveness of empagliflozin on the primary composite endpoint was sustained in patients with or without COPD, irrespective of the underlying type of HF.
- Among patients with COPD, treatment with empagliflozin is associated with as consistent an improvement in quality of life as in patients without COPD, irrespective of the underlying type of HF.
- Our results align with previous investigations from DELIVER and DAPA-HF.

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References
1. Packer M, et al. *N Engl J Med*. 2020;383:1413-24.
2. Anker S, et al. *N Engl J Med*. 2021;385:1451-61.

Abbreviations
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; AE, adverse event; ARNi, angiotensin receptor-neprilysin inhibitor; BP, blood pressure; BMI, body mass index; CABG, coronary artery bypass graft; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CRT-D/P, cardiac resynchronization therapy-device/pacemaker; CV, cardiovascular; eGFR, estimated glomerular filtration rate; Empa, empagliflozin; HbA1c, glycated hemoglobin; HF, heart failure; HHF, hospitalization for heart failure; HR, hazard ratio; ICD, implantable cardioverter defibrillator; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; pt-yrs, patient-years; SE, standard error; SGLT2, sodium-glucose co-transporter-2.

Disclosures
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