The effect of dapagliflozin in patients with HFrEF and COPD: a post-hoc analysis of DAPA-HF

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Background: Chronic obstructive pulmonary disease (COPD) is an important comorbidity in HFrEF, associated with worse outcomes and suboptimal treatment due to under-prescription of beta-blockers. Consequently, additional effective therapies are especially relevant in patients with COPD. In DAPA-HF, compared to placebo, the sodium-glucose cotransporter 2 (SGLT-2) inhibitor, dapagliflozin, reduced risk of cardiovascular (CV) death or worsening heart failure (HF) in patients with HF with reduced ejection fraction (HFrEF).

Purpose: To examine effect of dapagliflozin, compared with placebo, in patients with and without COPD.

Methods: Primary composite outcome of DAPA-HF was time-to-first CV death or worsening HF event (hospitalization for HF or outpatient visit requiring intravenous therapy). We examined whether effect of dapagliflozin was modified by investigator reported COPD at baseline.

Results: Overall, 585 (12.3%) of the 4744 patients randomized had an investigator-reported history of COPD, 299 (12.6%) in dapagliflozin group and 286 (12.1%) in placebo group. Incidence of primary composite outcome, in the placebo group, was higher in patients with COPD than in those without (22.8; 95% CI 18.4–28.3 vs. 14.9; 13.5–16.4) (Table). Hazard ratio (HR) for the effect of dapagliflozin, compared with placebo, on the primary outcome, was consistent in patients with and without COPD (Table); P-value for interaction was 0.467. Findings for other outcomes were similar (Figure).

Conclusions: Patients in DAPA-HF with COPD were at substantially higher risk than those without. Treatment with dapagliflozin, compared to placebo, reduced risk of CV death and worsening HF, similarly, in patients with and without COPD.

Hazard ratios (HR) stratified by baseline diabetes status

	No COPD		COPD		Interaction p-value
	Placebo (N=2,085)	Dapagliflozin (N=2,074)	Placebo (N=286)	Dapagliflozin (N=299)	
Primary outcome					
Events (%)	419 (20.1)	325 (15.7)	83 (29.0)	61 (20.4)	
Event rate/100 pt. yrs.	14.9 (13.5–16.4)	11.2 (10.1–12.5)	22.8 (18.4–28.3)	15.3 (11.9–19.7)	
HR	0.76 (0.65–0.87)		0.67 (0.48–0.93)		0.467
All-cause death					
Events (%)	272 (13.1)	226 (10.9)	57 (19.9)	50 (16.7)	
Event rate/100 pt. yrs.	9.1 (8.1–10.2)	7.5 (6.6–8.5)	13.8 (10.7–17.9)	11.7 (8.8–15.4)	
HR	0.83 (0.69–0.99)		0.83 (0.57–1.22)		0.956

Primary composite outcome adjusted for previous HF hospitalization.