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ORIGINAL RESEARCH

Impact of Empagliflozin in Heart Failure With Reduced Ejection Fraction in Patients With Ischemic Versus Nonischemic Cause

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BACKGROUND: Outcomes and treatment effects of therapy may vary according to the cause of heart failure (HF).

METHODS AND RESULTS: In this post hoc analysis of the EMPEROR-Reduced (Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Reduced Ejection Fraction) trial, the effect of empagliflozin on cardiovascular and renal outcomes was assessed according to the cause of HF. The cause of HF was investigator reported and stratified as ischemic or nonischemic. Cox proportional hazards models were used to calculate hazard ratios (HRs) and 95% CIs. Of the 3730 patients enrolled, 1929 (51.7%) had ischemic cause. In the placebo arm, patients with ischemic cause of HF did not have a significantly higher risk of cardiovascular mortality (HR, 1.21 [95% CI, 0.90–1.63]) and hospitalization for HF (HR, 0.90 [95% CI, 0.72–1.12]) compared with nonischemic cause. Empagliflozin compared with placebo significantly reduced the risk of cardiovascular death or hospitalization for HF in patients with ischemic and nonischemic cause (HR, 0.82 [95% CI, 0.68–0.99] for ischemic and HR, 0.67 [95% CI, 0.55–0.82] for nonischemic cause; *P* interaction=0.15). The benefit of empagliflozin on HF hospitalization, the renal composite end point, estimated glomerular filtration slope changes, and health status scores were also consistent in both groups without treatment by cause modification.

CONCLUSIONS: Empagliflozin offers cardiovascular and renal benefits in patients with heart failure with reduced ejection fraction regardless of the cause of HF.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT03057977.

Key Words: empagliflozin ■ heart failure ■ ischemic cause ■ reduced ejection fraction ■ sodium-glucose co-transporter-2

The cause of heart failure (HF) with reduced ejection fraction (HFrEF) is related to coronary heart disease in the majority of patients.[1–5] Differentiating between ischemic and nonischemic causes of HFrEF is important. First, prognosis may vary by cause, with ischemic HFrEF having a more unfavorable outcome trajectory compared with nonischemic HFrEF cause.[6,7] Second, treatment response to specific therapies for HFrEF may vary according to cause.[8,9] The EMPEROR-Reduced (Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Reduced Ejection Fraction) trial studied the SGLT2 (sodium-glucose co-transporter-2) inhibitor empagliflozin in patients with HFrEF and left ventricular ejection fraction <40% and showed a significant reduction in the risk of cardiovascular death or worsening HF events.[10] In this post hoc analysis, we examined the effect of empagliflozin on cardiovascular and renal outcomes in patients who are ischemic and nonischemic. We also assessed

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CLINICAL PERSPECTIVE

What Is New?

- Contrary to multiple previous studies, ischemic versus nonischemic cause was not significantly associated with a worse prognosis in patients with heart failure with reduced ejection fraction in EMPEROR-Reduced (Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Reduced Ejection Fraction).
- The benefit of treatment with the SGLT2 (sodium-glucose co-transporter-2) inhibitor empagliflozin was not influenced by heart failure cause.

What Are the Clinical Implications?

- Patients with heart failure with reduced ejection fraction, with and without ischemic cause, have a similarly poor prognosis.
- Patients with heart failure with reduced ejection fraction, with and without ischemic cause, derive similar benefit from treatment with the SGLT2 inhibitor empagliflozin.

Nonstandard Abbreviations and Acronyms

DAPA-HF	Dapagliflozin and Prevention of Adverse-outcomes in Heart Failure
EMPEROR-Reduced	Empagliflozin Outcome Trial in Patients With Chronic Heart Failure with Reduced Ejection Fraction
EMPHASIS-HF	Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure
HFrEF	heart failure with reduced ejection fraction
MERIT-HF	Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure
PARADIGM-HF	Prospective Comparison of Angiotensin-Receptor-Neprilysin Inhibitor with Angiotensin-Converting Enzyme Inhibitor to Determine Impact on Global Mortality and Morbidity in Heart Failure
PRAISE	Prospective Randomized Amlodipine Survival Evaluation
SGLT2	sodium-glucose co-transporter-2

the natural history and outcomes in patients with HFrEF according to cause.

METHODS

Trial Design and Patient Population

The EMPEROR-Reduced trial was a randomized, double-blind, parallel-group, placebo-controlled, event-driven study. The study was approved by an institutional review committee, and subjects gave informed consent. The design and primary results of EMPEROR-Reduced have been published previously.[11] Briefly, adult patients who had chronic HF with New York Heart Association functional class II to IV symptoms with a left ventricular ejection fraction ≤40% were enrolled. Because the trial intended to enroll patients at higher risk, the eligibility criteria mandated either a hospitalization for HF within 12 months or ejection fraction ≤30% with an NT-proBNP (N-terminal pro-B-type natriuretic peptide) level of ≥600 pg/mL, or ≥1000 pg/mL or ≥2500 pg/mL in those with an ejection fraction of 31% to 35% or 36% to 40%, respectively. Patients with symptomatic hypotension or a systolic blood pressure of <100 mm Hg and an estimated glomerular filtration rate (eGFR) <20 mL/min per 1.73 m^2 body surface area or requiring dialysis were excluded. Patients were randomized (1:1) to receive empagliflozin 10 mg or placebo daily.

Cause of Heart Failure

Information on HF cause was collected from the case report form. The cause of HF was completed by the investigators as ischemic, hypertensive, valvular heart disease, alcoholism, diabetic, idiopathic, or other. Other cause was considered in the nonischemic group.

Outcomes

The primary end point of the EMPEROR-Reduced trial was the time-to-first-event analysis of the combined risk of cardiovascular death or hospitalization for HF. The key secondary end points were the total number of adjudicated hospitalizations for HF, and the slope of the change in eGFR. A composite renal end point was defined as the need for chronic dialysis or renal transplant or a ≥40% decrease in eGFR (Chronic Kidney Disease Epidemiology Collaboration), or a sustained

eGFR <15 mL/min per 1.73 m^2 (if the baseline eGFR was ≥30), or <10 mL/min per 1.73 m^2 (if the baseline eGFR was <30 mL/min per 1.73 m^2). Safety end points included adverse events leading to discontinuation of study drug, hypotension, volume depletion, bone fracture, and hypoglycemia.

Statistical Analysis

Continuous variables are reported as mean±SD or median (interquartile range), whereas categorical variables are reported as frequency and percentage. Comparison was done using a *t* test for continuous variables and a χ^2 test for categorical variables. Baseline characteristics of the enrolled patients were stratified according to cause of HF (ischemic versus nonischemic). Incidence rates for each outcome of interest are presented per 100 patient-years of follow-up. Time-to-event data for the clinical outcomes according to cause of HF were evaluated using Cox proportional hazard models to calculate hazard ratios (HRs), 95% CIs, and 2-sided *P* values. The HRs were adjusted for age, sex, region, ejection fraction, eGFR, and diabetes status. For total hospitalizations for HF, a joint frailty model (with cardiovascular death as a competing risk) was used, adjusted by the same covariates as the Cox model. For the analysis of the primary outcome, the assumption of proportional hazards was investigated, and no violations were observed. Proportionality of hazards of the primary end point in the ischemic versus nonischemic subgroup was checked by visual inspection of the cumulative incidence curves, and no relevant deviations from the assumption of proportional hazards were observed. Between-group differences in the slope of change in eGFR were analyzed using a mixed-effects regression model including both a random intercept and a random slope based on on-treatment data. All available on-treatment change from baseline eGFR values were used for the slope analysis. The frequencies of the prespecified safety outcomes were investigated in a logistic regression model adjusted with the same covariates as the Cox model. To assess the consistency of effects across various subgroups, subgroup-by-treatment interaction terms were also added in the models. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC). A *P* value of <0.05 was considered significant.

Data Sharing Statement

To ensure independent interpretation of clinical study results and enable authors to fulfill their role and obligations under the International Committee of Medical Journal Editors criteria, Boehringer Ingelheim grants all external authors access to relevant clinical study data. In adherence with the Boehringer Ingelheim Policy on Transparency and Publication of Clinical Study Data, scientific and medical researchers can request access to clinical study data after publication of the primary article in a peer-reviewed journal, regulatory activities are complete, and other criteria are met. Researchers should use the https://vivli.org/ link to request access to study data and visit https://www.mystudywindow.com/msw/datasharing for further information.

RESULTS

Baseline Characteristics

Of the 3730 patients who were assigned to receive either placebo or empagliflozin, 1929 (51.7%) had ischemic cause of HF. Among the 1801 (48.3%) patients with nonischemic cause, 453 (25.2%) had hypertensive cause noted, 637 (35.4%) had idiopathic dilated cardiomyopathy, 105 (5.8%) had valvular heart disease, and 506 (28.1%) had other causes. The median follow-up time was 16 months. Table 1 shows the baseline characteristics of the enrolled patients stratified according to cause of HF. Compared with patients with nonischemic cause, those with ischemic cause were older, more often White, men, and more likely to have a history of diabetes and coronary artery disease. Patients with ischemic cause of HF had a lower diastolic blood pressure, heart rate, eGFR, and NT-proBNP.

Outcomes According to Cause in Placebo Arm

The rate of the primary composite outcome of cardiovascular death or hospitalization for HF, its components, and all-cause mortality according to cause in the placebo arm are shown in Table 2. There was no significant difference in the risk of cardiovascular death or hospitalization for HF, all-cause, or cardiovascular mortality in patients with and without ischemic cause of HF.

Empagliflozin and Outcomes According to Cause of HF

Cardiovascular Outcomes

The effect of empagliflozin on the primary outcome was not influenced by the cause of HF. In patients with ischemic cause, the primary outcome occurred in 207 of 983 (17.1/100 patient-years) in the empagliflozin group and 236 of 946 (20.6/100 patient-years) in the placebo group (HR, 0.82 [95% CI, 0.68–0.99]). Among patients without an ischemic cause, the primary outcome occurred in 154 of 880 (14.3/100 patient-years) in the empagliflozin group and 226 of 921 (21.4/100 patient-years) in the placebo group (HR, 0.67 [95% CI, 0.55–0.82]). The effect of empagliflozin compared with placebo on other secondary end points is shown in Table 3. There was no significant subgroup interaction

Table 1. Baseline Characteristics According to Cause of Heart Failure

Characteristic	Ischemic, n=1929	Nonischemic, n=1801	*P* value
Age, y	68.4 (9.9)	65.2 (11.9)	<0.001
Men	1578 (81.8)	1259 (69.9)	<0.001
Race			<0.001
White	1440 (74.7)	1189 (66.0)	
Black	67 (3.5)	190 (10.5)	
Asian	324 (16.8)	348 (19.3)	
Other	52 (2.7)	62 (3.4)	
Missing	46 (2.4)	12 (0.7)	
Geographic region			<0.001
North America	222 (11.5)	203 (11.3)	
Latin America	511 (26.5)	775 (43.0)	
Europe	885 (45.9)	468 (26.0)	
Asia Pacific	213 (11.0)	280 (15.5)	
Other	98 (5.1)	75 (4.2)	
HF hospitalization within 1 y	534 (27.7)	617 (34.3)	<0.001
BMI, kg/m^2	27.8 (5.2)	27.9 (5.6)	0.668
Ejection fraction at screening, %	27.5 (5.9)	27.5 (6.2)	0.954
New York Heart Association class I/II	1441 (74.7)	1359 (75.5)	0.594
Systolic blood pressure, mm Hg	122.4 (15.5)	121.5 (15.8)	0.071
Heart rate, bpm	70.3 (11.1)	72.3 (12.3)	<0.001
Hypertension	1469 (76.2)	1229 (68.2)	<0.001
Diabetes	1067 (55.3)	789 (43.8)	<0.001
Atrial fibrillation	289 (15.0)	444 (24.7)	<0.001
Coronary artery disease	1815 (94.1)	331 (18.4)	<0.001
Cause of heart failure			
Ischemic	1929 (100)	0.0	<0.001
Hypertensive		453 (25.2)	
Valvular heart disease		105 (5.8)	
Diabetic		47 (2.6)	
Alcoholism		41 (2.3)	
Idiopathic		637 (35.4)	
Other		518 (28.8)	
ACEI, ARB, ARNI	1680 (87.1)	1613 (89.6)	0.019
Diuretic	1688 (87.5)	1560 (86.6)	0.419
β-Blocker	1833 (95.0)	1700 (94.4)	0.389
Mineralocorticoid receptor antagonist	1338 (69.4)	1323 (73.5)	0.006
Statin	1676 (86.9)	878 (48.8)	<0.001
eGFR, mL/min per 1.73 m^2	59.7 (20.5)	64.5 (22.5)	<0.001
NT-proBNP, pg/mL	1811 (1072–3319)	1987 (1171–3625)	0.002

Data are mean (SD) or number (%), except NT-proBNP is median (interquartile range). Other includes "American Indian or Alaska Native," "Native Hawaiian or Other Pacific Islander" and patients who identified with more than one race. ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibition; BMI, body mass index; eGFR, estimated glomerular filtration rate; HF, heart failure; and NT-proBNP, N-terminal pro-B-type natriuretic peptide.

in patients with and without an ischemic cause of HF in any of the end points.

Renal Outcomes

The effect of empagliflozin on eGFR slope change was consistent across both groups (placebo-corrected eGFR slope change, 1.57 [95% CI, 0.70–2.44] in ischemic HFrEF and 1.93 [95% CI, 1.01–2.86] in nonischemic HFrEF; *P* interaction=0.572; Table 3). Similarly, empagliflozin reduced the risk of renal composite events in patients with and without an ischemic cause of HF (HR, 0.42 [95% CI, 0.24–0.75]) in ischemic HFrEF and HR, 0.62 [95% CI, 0.31–1.23] in nonischemic HFrEF; *P* interaction=0.399.

Table 2. Natural History of Heart Failure Patients With Ischemic or Nonischemic Cause Receiving Placebo

History	Ischemic, n=946	Nonischemic, n=921	*P* value
Time to first event of cardiovascular death or HHF			
Incidence rates per 100 patient-y	20.64	21.41	
Comparison vs nonischemic, HR (95% CI)	0.98 (0.81–1.19)		0.861
Time to first HHF			
Incidence rates per 100 patient-y	14.60	16.57	
Comparison vs nonischemic, HR (95% CI)	0.90 (0.72–1.12)		0.342
Time to cardiovascular death			
Incidence rates per 100 patient-y	8.85	7.38	
Comparison vs nonischemic, HR (95% CI)	1.21 (0.90–1.63)		0.199
Time to first renal composite outcome			
Incidence rates per 100 patient-y	3.69	2.41	
Comparison vs nonischemic, HR (95% CI)	1.63 (0.92–2.88)		0.093

HHF indicates hospitalization for heart failure; and HR, hazard ratio.

Health Status

Empagliflozin improved Kansas City Cardiomyopathy Questionnaire-Clinical Summary Score in both of the groups (+1.70, +0.79, and +1.07 in ischemic HFrEF and +2.21, +1.96, and +2.22 in nonischemic HFrEF at 12, 32, and 52 weeks, respectively; *P* interaction=0.61, 0.29, and 0.36 at 12, 32, and 52 weeks, respectively) without any evidence of treatment modification.

Safety

The rates of adverse events were similar across treatment arms in patients with and without ischemic cause of HF (Table 4).

DISCUSSION

In this prespecified analysis of the EMPEROR-Reduced trial, we show several key findings. First, patients with ischemic cause of HF did not have a higher risk of all-cause and cardiovascular mortality compared with patients who had nonischemic cause of HF. Second, empagliflozin reduced the risk of primary composite outcome, its components, and composite renal outcomes in patients with HF irrespective of cause. Empagliflozin also improved quality of life measured by Kansas City Cardiomyopathy Questionnaire in both groups. These data outline the important benefit of empagliflozin across a broad range of patients.

The most common investigator reported cause was ischemic heart disease. Of note, the proportion of patients with ischemic cause in EMPEROR-Reduced was much less than those reported previously.[12,13] Considerable differences in clinical profiles were seen between the 2 groups, with patients with ischemic cause being older and more likely to have comorbidities such as diabetes and coronary artery disease. Consistent with previous data, the most common cause of nonischemic HF was idiopathic (35.4% of the nonischemic cases), followed by hypertension (25.2%).[14,15] Data from 1924 Danish patients with <40% left ventricular ejection fraction showed that 48% of patients had ischemic HF, followed by idiopathic dilated cardiomyopathy (11.6%) and hypertension (10.6%).[6]

Among patients with HFrEF caused by ischemic heart disease in the placebo arm, survival was similar compared with those with nonischemic cause of HFrEF. This is in contrast with several large clinical trials of HF therapy such as the PRAISE (Prospective Randomized Amlodipine Survival Evaluation) trial and Veterans Administration Cooperative study, in which HF mortality was significantly higher among patients with ischemic HF in the placebo arm.[16] However, the community-based Framingham Heart Study showed worse long-term survival among patients with nonischemic HF.[17] Of note, patients with nonischemic cause of HFrEF form a heterogeneous population, with certain causes linked to a better prognosis, whereas others have a poorer prognosis. It is also possible that with improved treatment of ischemic heart disease as well as for HF in general, the outcomes differences historically seen between ischemic and nonischemic causes in patients have been mitigated.

Our results are in line with previous trials of SGLT2 inhibitors in patients with HFrEF. In DAPA-HF (Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure), dapagliflozin reduced the risk of worsening HF and death and improved symptoms similarly in patients with ischemic and nonischemic cause.[17] Similarly, previous studies have shown β-blockers, angiotensin receptor–neprilysin inhibitors, angiotensin-converting enzyme inhibitors, and mineralocorticoid receptor antagonists are effective in HFrEF regardless of the cause. The MERIT-HF (Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart

Table 3. Effect of Empagliflozin on Outcomes According to Cause of Heart Failure

Effect	Placebo		Empagliflozin		HR (95% CI)	*P* value interaction
	n/N	Events/100 patient-y	n/N	Events/100 patient-y		
Cardiovascular death or HHF						
Ischemic	236/946	20.6	207/983	17.1	0.82 (0.68 to 0.99)	0.149
Nonischemic	226/921	21.4	154/880	14.3	0.67 (0.55 to 0.82)	
HHF, first and recurrent						
Ischemic	281		221		0.73 (0.56 to 0.95)	0.620
Nonischemic	272		167		0.66 (0.50 to 0.88)	
First HHF						
Ischemic	167/946	14.6	135/983	11.1	0.76 (0.61 to 0.96)	0.240
Nonischemic	175/921	16.6	111/880	10.3	0.62 (0.49 to 0.79)	
Cardiovascular death						
Ischemic	113/946	8.9	113/983	8.6	0.96 (0.74 to 1.25)	0.609
Nonischemic	89/921	7.4	74/880	6.4	0.86 (0.63 to 1.17)	
All-cause mortality						
Ischemic	151/946	11.8	156/983	11.9	0.99 (0.79 to 1.24)	0.318
Nonischemic	115/921	9.5	93/880	8.0	0.82 (0.63 to 1.08)	
Composite renal end points						
Ischemic	36/946	3.7	17/983	1.7	0.42 (0.24 to 0.75)	0.399
Nonischemic	22/921	2.4	13/880	1.5	0.62 (0.31 to 1.23)	
		Mean (SE)	Mean (SE)		Difference (95% CI)	
eGFR (CKD-EPI) slope change per year						
Ischemic		−2.31 (0.32)	−0.66 (0.31)		1.57 (0.70 to 2.44)	0.572
Nonischemic		−2.33 (0.33)	−0.39 (0.34)		1.93 (1.01 to 2.86)	
KCCQ-CSS						
Change at 12 weeks						
Ischemic		3.32 (0.50)	5.02 (0.49)		1.70 (0.33 to 3.07)	0.609
Nonischemic		3.45 (0.52)	5.66 (0.52)		2.21 (0.79 to 3.63)	
Change at 52 weeks						
Ischemic		4.09 (0.62)	5.17 (0.60)		1.07 (−0.62 to 2.76)	0.361
Nonischemic		4.00 (0.64)	6.22 (0.65)		2.22 (0.44 to 4.00)	

CKD-EPI indicates Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; HHF, hospitalization for heart failure; HR, hazard ratio; and KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire-Clinical Summary Score.

Failure) trial showed that metoprolol reduces the risk of all-cause mortality by 38% in ischemic HFrEF and by 27% in nonischemic cause.[18] The PARADIGM-HF (Prospective Comparison of Angiotensin Receptor-Neprilysin Inhibitor With Angiotensin-Converting Enzyme Inhibitor to Determine Impact on Global Mortality and Morbidity in Heart Failure) trial, which enrolled 8399 patients with HFrEF, showed that adjusted outcomes were similar across cause categories, as was the benefit of sacubitril/valsartan over enalapril.[19] EMPHASIS-HF (Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure) showed that the drug eplerenone reduced the risk of cardiovascular mortality and HF hospitalization in patients with both ischemic and nonischemic causes of HFrEF without any significant treatment interaction (*P* interaction=0.73).[20] These data suggest that once left ventricular dilation and consequent dysfunction have ensued, regardless of prior cause journey progression of HF syndrome, a quadruple therapy regimen is effective and can be broadly used.

Cause may be more important in the context of cardiac devices. Prophylactic implantation of cardioverter-defibrillator implantation has been shown to reduce the risk of sudden cardiac death and all-cause mortality in ischemic HFrEF.[9] However, their effectiveness in nonischemic HFrEF today is debatable. Resynchronization therapy in HFrEF because of nonischemic cause may achieve greater improvement in left ventricular function than in patients with ischemic cause.[10]

A key goal of management of HF is to improve patients' health status. Like HF outcomes, improvements

Table 4. Effect of Empagliflozin on Safety Outcomes According to Cause of Heart Failure

Effect	Placebo n/N (%)	Empagliflozin n/N (%)	OR (95% CI)	*P* value interaction
Discontinuation of study drug for any reason excluding serious fatal events leading to discontinuation				
Ischemic	170/944 (18.0)	173/983 (17.6)	0.96 (0.76–1.22)	0.358
Nonischemic	176/919 (19.2)	143/880 (16.3)	0.82 (0.64–1.05)	
AEs leading to discontinuation				
Ischemic	182/944 (19.3)	193/983 (19.6)	1.02 (0.81–1.28)	0.478
Nonischemic	146/919 (15.9)	129/880 (14.7)	0.90 (0.69–1.17)	
Volume depletion				
Ischemic	92/944 (9.7)	106/983 (10.8)	1.11 (0.82–1.49)	0.786
Nonischemic	92/919 (10.0)	91/880 (10.3)	1.05 (0.77–1.42)	
Fractures				
Ischemic	23/944 (2.4)	22/983 (2.2)	0.89 (0.49–1.60)	0.417
Nonischemic	19/919 (2.1)	23/880 (2.6)	1.26 (0.68–2.35)	
Confirmed hypoglycemia*				
Ischemic	15/944 (1.6)	17/983 (1.7)	1.05 (0.52–2.12)	0.673
Nonischemic	13/919(1.4)	10/880 (1.1)	0.83 (0.36–1.91)	

Treatment emergent adverse events up to 7 days following discontinuation of study medication are included. AEs indicates adverse events; and OR, odds ratio.

*Hypoglycemic AEs with a plasma glucose value of ≤70 mg/dL or that required assistance.

in health-related quality of life were similar with empagliflozin in HFrEF with ischemic cause compared with nonischemic cause. Similarly, data on tolerability and safety are assuring, with serious adverse events and discontinuation of drugs being mostly low, with no significant differences between the 2 groups.

The results of this study should be interpreted in context of potential limitations. Cause was investigator reported, and no instructions as how to identify cause were provided; therefore, some degree of misclassification of HF cause cannot be precluded. Although analysis by cause was predefined, the evaluation of secondary outcomes by cause was done post hoc.

In conclusion, treatment with empagliflozin reduced the risk of HF hospitalization and cardiovascular death regardless of HF cause. These data outline the important benefit of empagliflozin across a broad range of patients.

ARTICLE INFORMATION

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