Body Mass Index and Cardiorenal Outcomes in the EMPEROR-Preserved Trial: Principal Findings and Meta-Analysis with the DELIVER Trial

Supplementary

Supplementary Table 1. Effect of empagliflozin versus placebo on the secondary endpoints by baseline BMI categories

Outcome	Overall	BMI <25 kg/m^2	BMI 25 to <30 kg/m^2	BMI 30 to <35 kg/m^2	BMI 35 to <40 kg/m^2	BMI ≥40 kg/m^2	p-value for trend
		N=1310	N=1986	N=1553	N=771	N=368	
Total HHF (First and recurrent HHFs)	0.73 (0.61, 0.88)	0.41 (0.28, 0.61)	0.86 (0.62, 1.19)	1.31 (0.89, 1.93)	0.72 (0.45, 1.16)	0.51 (0.25, 1.02)	0.19
Time to first HHF	0.71 (0.60, 0.83)	0.48 (0.34, 0.68)	0.84 (0.63, 1.13)	0.96 (0.68, 1.37)	0.68 (0.45, 1.02)	0.56 (0.33, 0.96)	0.53
Time to CV death	0.91 (0.76, 1.09)	0.66 (0.45, 0.97)	0.98 (0.71, 1.34)	1.01 (0.68, 1.50)	1.29 (0.79, 2.09)	0.72 (0.36, 1.45)	0.20
Time to all-cause mortality	1.00 (0.87, 1.15)	0.85 (0.65, 1.12)	0.98 (0.77, 1.24)	1.10 (0.83, 1.46)	1.38 (0.95, 2.00)	0.79 (0.47, 1.35)	0.24
Time to first renal composite	0.95 (0.73, 1.24)	0.78 (0.43, 1.44)	0.95 (0.59, 1.54)	1.08 (0.63, 1.85)	1.02 (0.54, 1.93)	1.05 (0.43, 2.60)	0.51

BMI, body mass index; HHF, Hospitalisation for heart failure; CV, cardiovascular.

Supplementary Table 2. Adverse events by BMI categories

BMI	<25 kg/m^2				25 to <30 kg/m^2				30 to <35 kg/m^2				35 to <40 kg/m^2				≥40 kg/m^2			
	Placebo N=638		Empagliflozin N=672		Placebo N=1003		Empagliflozin N=982		Placebo N=760		Empagliflozin N=793		Placebo N=388		Empagliflozin N=382		Placebo N=200		Empagliflozin N=167	
	N (%)	IR/100	N (%)	IR/100	N (%)	IR/100	N (%)	IR/100	N (%)	IR/100	N (%)	IR/100	N (%)	IR/100	N (%)	IR/100	N (%)	IR/100	N (%)	IR/100
Patients with any AE	563 (88.2)	170.88	610 (90.8)	157.21	866 (86.3)	143.25	824 (83.9)	127.17	642 (84.5)	132.10	666 (84.0)	124.31	338 (87.1)	219.73	332 (86.9)	145.39	176 (88.0)	172.85	142 (85.0)	141.72
Patients with AEs leading to drug discontinuation	134 (21.0)	11.77	126 (18.8)	10.04	176 (17.5)	9.31	186 (18.9)	10.33	116 (15.3)	7.97	148 (18.7)	9.72	77 (19.8)	10.54	81 (21.2)	11.70	48 (24.0)	12.98	30 (18.0)	8.92
Patients with serious AEs	352 (55.2)	44.89	315 (46.9)	32.94	518 (51.6)	38.80	437 (44.5)	31.53	360 (47.4)	33.87	397 (50.1)	35.80	205 (52.8)	40.93	202 (52.9)	40.34	108 (54.0)	43.29	85 (50.9)	36.48
Hypotension*	50 (7.8)	4.57	58 (8.6)	4.80	84 (8.4)	4.64	103 (10.5)	6.10	64 (8.4)	4.58	94 (11.9)	6.65	42 (10.8)	6.06	40 (10.5)	6.06	17 (8.5)	4.80	16 (9.6)	5.04
Symptomatic hypotension**	25 (3.9)	2.23	40 (6.0)	3.26	55 (5.5)	2.98	67 (6.8)	3.87	40 (5.3)	2.81	55 (6.9)	3.75	24 (6.2)	3.39	25 (6.5)	3.70	12 (6.0)	3.31	10 (6.0)	3.07
Acute renal failure#	74 (11.6)	6.89	58 (8.6)	4.84	132 (13.2)	7.36	106 (10.8)	6.21	70 (9.2)	4.98	107 (13.5)	7.47	76 (19.6)	11.44	60 (15.7)	9.41	32 (16.0)	9.11	32 (19.2)	10.40
Confirmed hypoglycemia	17 (2.7)	1.52	17 (2.5)	1.37	26 (2.6)	1.39	16 (1.6)	0.89	19 (2.5)	1.32	21 (2.6)	1.39	11 (2.8)	1.52	13 (3.4)	1.90	5 (2.5)	1.35	6 (3.6)	1.81
Genital infection*	3 (0.5)	0.26	6 (0.9)	0.48	4 (0.4)	0.21	23 (2.3)	1.28	7 (0.9)	0.48	26 (3.3)	1.73	2 (0.5)	0.27	7 (1.8)	1.01	6 (3.0)	1.65	5 (3.0)	1.51

* Based on pre-defined terms (BIcMQ)
** Investigator defined, primary system organ class and preferred term
# based on pre-defined terms (narrow SMQ)
Adverse events (AEs) are shown up to 7 days after discontinuation of study medication.
AE, adverse event; BMI, body mass index; IR, incidence rate.