**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/m2** | **BMI 25 to <30 kg/m2** | **BMI 30 to <35 kg/m2** | **BMI 35 to <40 kg/m2** | **BMI ≥40 kg/m2** | **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/m2** | **25 to <30 kg/m2** | **30 to <35 kg/m2** | **35 to <40 kg/m2** | **≥40 kg/m2** |
|  | PlaceboN=638 | EmpagliflozinN=672 | PlaceboN=1003 | EmpagliflozinN=982 | PlaceboN=760 | EmpagliflozinN=793 | PlaceboN=388 | EmpagliflozinN=382 | PlaceboN=200 | EmpagliflozinN=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.