

**SUPPLEMENTAL TABLES**

**Supplemental Table 1. Characteristics of participants by baseline KDIGO risk categories in EMPEROR-Reduced cohort.**

|                                  | <b>Low risk<br/>(n=1174)</b> | <b>Moderate risk<br/>(n= 1059)</b> | <b>High risk<br/>(n=853)</b> | <b>Very high risk<br/>(n=642)</b> | <b>P value<br/>for trend</b> |
|----------------------------------|------------------------------|------------------------------------|------------------------------|-----------------------------------|------------------------------|
| Age, yr                          | 65.0 (56.0-72.0)             | 67.0 (60.0-74.0)                   | 70.0 (63.0-77.0)             | 72.0 (65.0-79.0)                  | <0.001                       |
| Women, n (%)                     | 273 (23.3)                   | 240 (22.7)                         | 214 (25.1)                   | 166 (25.9)                        | 0.146                        |
| Race, n (%)                      |                              |                                    |                              |                                   | 0.019                        |
| Asian                            | 230 (19.6)                   | 212 (20.0)                         | 129 (15.1)                   | 101 (15.7)                        |                              |
| Black OR African American        | 89 (7.6)                     | 74 (7.0)                           | 56 (6.6)                     | 38 (5.9)                          |                              |
| White                            | 805 (68.6)                   | 716 (67.6)                         | 635 (74.4)                   | 471 (73.4)                        |                              |
| Other including mixed race       | 35 (3.0)                     | 39 (3.7)                           | 18 (2.1)                     | 22 (3.4)                          |                              |
| Missing                          | 15 (1.3)                     | 18 (1.7)                           | 15 (1.8)                     | 10 (1.6)                          |                              |
| Geographic region, n (%)         |                              |                                    |                              |                                   | <0.001                       |
| Asia Pacific                     | 154 (13.1)                   | 168 (15.9)                         | 97 (11.4)                    | 74 (11.5)                         |                              |
| West Europe                      | 135 ( 11.5)                  | 148 ( 14.0)                        | 168 ( 19.7)                  | 142 ( 22.1)                       |                              |
| East Europe                      | 279 ( 23.8)                  | 209 ( 19.7)                        | 181 ( 21.2)                  | 90 ( 14.0)                        |                              |
| North America                    | 105 (8.9)                    | 120 (11.3)                         | 101 (11.8)                   | 99 (15.4)                         |                              |
| Latin America                    | 425 (36.2)                   | 371 (35.0)                         | 273 (32.0)                   | 216 (33.6)                        |                              |
| Other                            | 76 (6.5)                     | 43 (4.1)                           | 33 (3.9)                     | 21 (3.3)                          |                              |
| eGFR, ml/min/1.73 m <sup>2</sup> | 77.0 (67.5-88.5)             | 62.0 (53.0-78.0)                   | 48.5 (40.0-58.0)             | 34.5 (28.5-42.0)                  | <0.001                       |
| UACR, mg/g                       | 8.8 (5.0-                    | 33.0 (10.8-                        | 47.4 (12.4-                  | 109.8 (39.8-                      | <0.001                       |

|                                       |                     |                     |                     |                     |        |
|---------------------------------------|---------------------|---------------------|---------------------|---------------------|--------|
|                                       | 15.9)               | 76.9)               | 212.1)              | 466.5)              |        |
| HF hospitalization within 1 yr, n (%) | 344 (29.3)          | 320 (30.2)          | 291 (34.1)          | 196 (30.5)          | 0.140  |
| Body weight, kg                       | 77.0 (64.8-89.5)    | 76.8 (65.5-90.0)    | 77.0 (66.2-90.0)    | 78.3 (66.0-90.7)    | 0.219  |
| Ejection fraction, %                  | 28 (24-30)          | 28 (24 -31)         | 28 (24-32)          | 28 (25-33)          | 0.001  |
| KCCQ-CSS                              | 77.5 (58.3-91.7)    | 76.0 (56.8-88.5)    | 72.4 (53.7-87.5)    | 69.8 (51.6-87.5)    | <0.001 |
| NYHA Class II, n (%)                  | 934 (79.6)          | 797 (75.3)          | 624 (73.2)          | 444 (69.2)          | <0.001 |
| Systolic blood pressure, mm Hg        | 119.0 (109.0-130.0) | 119.0 (108.0-131.0) | 121.0 (110.0-134.0) | 123.0 (110.0-138.0) | <0.001 |
| Heart rate, bpm                       | 70.0 (62.0-78.0)    | 70.0 (63.0-80.0)    | 70.0 (63.0-79.0)    | 70.0 (63.0-78.0)    | 0.225  |
| Hypertension, n (%)                   | 733 (62.4)          | 777 (73.4)          | 656 (76.9)          | 531 (82.7)          | <0.001 |
| Diabetes mellitus, n (%)              | 460 (39.2)          | 537 (50.7)          | 467 (54.7)          | 390 (60.7)          | <0.001 |
| Atrial fibrillation, n (%)            | 306 (27.6)          | 409 (38.6)          | 357 (41.9)          | 297 (46.3)          | <0.001 |
| Ischemic etiology, n (%)              | 588 (50.1)          | 517 (48.8)          | 464 (54.4)          | 359 (55.9)          | 0.005  |
| ACE-I, ARB <sup>a</sup> , ARNI, n (%) | 1067 (90.9)         | 947 (89.4)          | 743 (87.1)          | 535 (83.3)          | <0.001 |
| Diuretic, n (%) <sup>b</sup>          | 962 (81.9)          | 923 (87.2)          | 774 (90.7)          | 588 (91.6)          | <0.001 |
| Loop or high ceiling diuretics        | 930 (79.2)          | 896 (84.6)          | 750 (87.9)          | 573 (89.3)          | <0.001 |
| Thiazides or low ceiling diuretics    | 78 (6.6)            | 64 (6.0)            | 68 (8.0)            | 75 (11.7)           | <0.001 |

|  |                   |                    |                    |                    |        |
|--|-------------------|--------------------|--------------------|--------------------|--------|
| Beta-blocker, n (%)                                | 1112 (94.7)       | 1000 (94.4)        | 808 (94.7)         | 612 (95.3)         | 0.645  |
| MRA, n (%)   | 900 (76.7)        | 781 (73.7)         | 601 (70.5)         | 377 (58.7)         | <0.001 |
| Uric acid, mg/dl                                   | 6.4 (5.2-7.6)     | 6.8 (5.6-8.1)      | 7.4 (6.0-8.8)      | 7.7 (6.2-9.3)      | <0.001 |
| Hematocrit, %                                      | 43.0 (40.0-45.5)  | 42.7 (39.3-46.0)   | 41.9 (38.2-45.0)   | 40.0 (37.0-44.0)   | <0.001 |
| Hemoglobin, g/dl                                   | 14.0 (13.0-14.9)  | 13.9 (12.8-14.9)   | 13.5 (12.4-14.7)   | 13.0 (12.0-14.2)   | <0.001 |
| NT-proBNP, pg/ml                                   | 1362 (844 – 2308) | 1837 (1163 – 3160) | 2346 (1445 – 4172) | 3149 (1758 – 5945) | <0.001 |
| NT-proBNP, pg/ml (patients with AF/AFl history)    | 2023 (1492-3201)  | 2253 (1562-3733)   | 2712 (1806-4559)   | 3788 (2188-6963)   | <0.001 |
| NT-proBNP, pg/ml (patients without AF/AFl history) | 1238 (806-2088)   | 1692 (1016-2932)   | 2131 (1286-3995)   | 2895 (1525-5769)   | <0.001 |

Data are median (IQR) or number (%). The *P* value for NTproBNP and UACR was computed for log-transformed data. Race was self-reported. Those who identified with more than one race or with no race were classified as ‘other’.

<sup>a</sup>ARBs exclude valsartan when taken with sacubitril because sacubitril/valsartan is shown as an ARNI.

<sup>b</sup>Excluding mineralocorticoid receptor antagonists.

ACE-I = angiotensin-converting enzyme inhibitor; AF= atrial fibrillation; AFl= atrial flutter; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor neprilysin inhibitor; eGFR = estimated glomerular filtration rate; HF = heart failure; IQR = interquartile range; KCCQ-CSS = Kansas City Cardiomyopathy Questionnaire-clinical summary score; KDIGO = Kidney Disease Improving Global Outcomes; MRA=mineralocorticoid receptor antagonist; NYHA= New York Heart Association; NT-proBNP = N-terminal pro-B-type natriuretic peptide; SD = standard deviation; UACR = urine albumin-to-creatinine ratio; yr=year.



**Supplemental Table 2. Characteristics of participants by baseline KDIGO risk categories in EMPEROR-Preserved cohort.**

|                                  | <b>Low risk<br/>(n=1931)</b> | <b>Moderate risk<br/>(n=1763)</b> | <b>High risk<br/>(n=1278)</b> | <b>Very high risk<br/>(n=1014)</b> | <b>P value<br/>for trend</b> |
|----------------------------------|------------------------------|-----------------------------------|-------------------------------|------------------------------------|------------------------------|
| Age, yr                          | 70.0 (64.0-76.0)             | 73.0 (67.0-79.0)                  | 76.0 (69.0-80.0)              | 75.0 (68.0-81.0)                   | <0.001                       |
| Women, n (%)                     | 779 (40.3)                   | 812 (46.1)                        | 619 (48.4)                    | 466 (46.0)                         | <0.001                       |
| Race, n (%)                      |                              |                                   |                               |                                    | 0.912                        |
| Asian                            | 262 (13.6)                   | 245 (13.9)                        | 179 (14.0)                    | 138 (13.6)                         |                              |
| Black OR African American        | 82 (4.2)                     | 76 (4.3)                          | 40 (3.1)                      | 59 (5.8)                           |                              |
| White                            | 1456 (75.4)                  | 1351 (76.6)                       | 986 (77.2)                    | 748 (73.8)                         |                              |
| Other including mixed race       | 129 (6.7)                    | 91 (5.2)                          | 73 (5.7)                      | 69 (6.8)                           |                              |
| Missing                          | 2 (0.1)                      | 0                                 | 0                             | 0                                  |                              |
| Geographic region, n (%)         |                              |                                   |                               |                                    | <0.001                       |
| Asia Pacific                     | 207 (10.7)                   | 215 (12.2)                        | 159 (12.4)                    | 105 (10.4)                         |                              |
| West Europe                      | 196 (10.2)                   | 241 (13.7)                        | 224 (17.5)                    | 142 (14.0)                         |                              |
| East Europe                      | 732 (37.9)                   | 574 (32.6)                        | 371 (29.0)                    | 208 (20.5)                         |                              |
| North America                    | 171 (8.9)                    | 202 (11.5)                        | 162 (12.7)                    | 183 (18.3)                         |                              |
| Latin America                    | 500 (25.9)                   | 423 (24.0)                        | 292 (22.8)                    | 300 (29.6)                         |                              |
| Other                            | 125 (6.5)                    | 108 (6.1)                         | 70 (5.5)                      | 76 (7.5)                           |                              |
| eGFR, ml/min/1.73 m <sup>2</sup> | 75.0 (67.0-85.0)             | 59.5 (52.5-74.5)                  | 47.0 (40.0-57.0)              | 35.5 (28.5-42.0)                   | <0.001                       |
| UACR, mg/g                       | 8.0 (5.3-15.9)               | 27.7 (8.8-62.8)                   | 37.1 (10.6-139.3)             | 169 (52.2-723.1)                   | <0.001                       |

|   |                     |                     |                     |                     |        |
|---|---------------------|---------------------|---------------------|---------------------|--------|
| HF hospitalization within 1 year, n (%) | 389 (20.1)          | 376 (21.3)          | 317 (24.8)          | 287 (28.3)          | <0.001 |
| Body weight, kg                         | 80.0 (68.0-94.0)    | 79.0 (67.0-94.1)    | 80.0 (68.2-93.0)    | 80.5 (68.1-95.7)    | 0.454  |
| Ejection fraction, %                    | 52.0 (46.0-60.0)    | 55.0 (47.0-60.0)    | 54.0 (47.0-60.0)    | 55.0 (48.0-61.0)    | <0.001 |
| NYHA Class II, n (%)                    | 1682 (87.1)         | 1459 (82.8)         | 996 (77.9)          | 744 (73.4)          | <0.001 |
| KCCQ-CSS                                | 78.1 (61.5-90.8)    | 75.0 (58.3-88.0)    | 69.3 (51.0-85.4)    | 68.2 (47.9-83.3)    | <0.001 |
| Systolic blood pressure, mm Hg          | 130.0 (120.0-140.0) | 132.0 (120.0-142.0) | 132.0 (120.0-142.0) | 134.0 (121.0-145.0) | <0.001 |
| Heart rate, bpm                         | 69.0 (61.0-78.0)    | 70.0 (62.0-78.0)    | 70.0 (62.0-79.0)    | 70.0 (62.0-78.0)    | 0.018  |
| Hypertension, n (%)                     | 1683 (87.2)         | 1582 (89.7)         | 1188 (93.0)         | 969 (95.6)          | <0.001 |
| Diabetes mellitus                       | 809 (41.9)          | 806 (45.7)          | 665 (52.0)          | 656 (64.7)          | <0.001 |
| Atrial fibrillation, n (%)              | 866 (44.8)          | 934 (53.0)          | 757 (59.2)          | 500 (49.3)          | <0.001 |
| Ischemic etiology, n (%)                | 719 (37.2)          | 594 (33.7)          | 424 (33.2)          | 379 (37.4)          | 0.366  |
| ACE-I, ARB <sup>a</sup> , ARNI, n (%)   | 1598 (82.8)         | 1448 (82.1)         | 1032 (80.8)         | 752 (74.2)          | <0.001 |
| Diuretic, n (%) <sup>b</sup>            | 1434 (74.3)         | 1408 (79.9)         | 1069 (83.6)         | 896 (88.4)          | <0.001 |
| Loop or high ceiling diuretics          | 1129 (58.5)         | 1162 (65.9)         | 941 (73.6)          | 820 (80.9)          | <0.001 |
| Thiazides or low ceiling diuretics      | 429 (22.2)          | 369 (20.9)          | 251 (19.6)          | 190 (18.7)          | 0.014  |

|  |                     |                     |                      |                      |        |
|--|---------------------|---------------------|----------------------|----------------------|--------|
| Beta-blocker, n (%)                                | 1669 (86.4)         | 1528 (86.7)         | 1102 (86.2)          | 866 (85.4)           | 0.494  |
| MRA, n (%)   | 729 (37.8)          | 683 (38.7)          | 503 (39.4)           | 329 (32.4)           | 0.080  |
| Uric acid, mg/dl                                   | 5.9 (5.0-7.1)       | 6.3 (5.2-7.5)       | 6.8 (5.6-8.2)        | 7.4 (6.0-9.0)        | <0.001 |
| Hematocrit, %                                      | 42.0 (39.0-45.0)    | 41.0 (38.0-44.0)    | 40.0 (37.0-43.5)     | 39.0 (35.4-42.0)     | <0.001 |
| Hemoglobin, g/dl                                   | 13.8 (12.8-14.7)    | 13.4 (12.4-14.4)    | 13.1 (12.1-14.2)     | 12.6 (11.4-13.6)     | <0.001 |
| NT-proBNP, pg/ml                                   | 722<br>(390 – 1289) | 943<br>(483 – 1612) | 1213<br>(608 – 2129) | 1516<br>(783 – 2807) | <0.001 |
| NT-proBNP, pg/ml (patients with AF/AFl history)    | 1335 (953-1710)     | 1558 (1121-2168)    | 1827 (1263-2749)     | 2228 (1511-3785)     | <0.001 |
| NT-proBNP, pg/ml (patients without AF/AFl history) |                     |                     |                      |                      |        |

Data are median (IQR) or number (%). The *P* value for NTproBNP and UACR was computed for log-transformed data. Race was self-reported. Those who identified with more than one race or with no race were classified as ‘other’.

<sup>a</sup>ARBs exclude valsartan when taken with sacubitril because sacubitril/valsartan is shown as an ARNI.

<sup>b</sup>Excluding mineralocorticoid receptor antagonists.

ACE-I = angiotensin-converting enzyme inhibitor; AF= atrial fibrillation; AFl= atrial flutter; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor neprilysin inhibitor; eGFR = estimated glomerular filtration rate; HF = heart failure; IQR = interquartile range; KCCQ-CSS = Kansas City Cardiomyopathy Questionnaire-clinical summary score; KDIGO = Kidney Disease Improving Global Outcomes; MRA=mineralocorticoid receptor antagonist; NYHA= New York Heart Association; NT-proBNP = N-terminal pro-B-type natriuretic peptide; SD = standard deviation; UACR = urine albumin-to-creatinine ratio; yr=year.

**Supplemental Table 3. Safety Outcomes in Participant Subgroups Defined by Baseline KDIGO Risk Categories in the EMPEROR-Program.**

|   | Placebo          | Empagliflozin    | OR (95% CI)       | P value for trend |
|---|------------------|------------------|-------------------|-------------------|
|   | n/N (%)          | n/N              |                   |                   |
| Any AEs   |                  |                  |                   |                   |
| Overall   | 4048/4852 (83.4) | 3994/4859 (82.2) | 0.91 (0.82, 1.01) | 0.584             |
| Low risk  | 1231/1575 (78.2) | 1183/1528 (77.4) | 0.95 (0.80, 1.13) |                   |
| Moderate risk                                   | 1141/1380 (82.7) | 1170/1440 (81.3) | 0.89 (0.74, 1.09) |                   |
| High risk                                       | 915/1060 (86.3)  | 898/1070 (83.9)  | 0.81 (0.64, 1.04) |                   |
| Very high risk                                  | 759/834 (91.0)   | 743/820 (90.6)   | 0.95 (0.68, 1.34) |                   |
| Serious AEs                                     |                  |                  |                   |                   |
| Overall   | 2439/4852 (50.3) | 2208/4859 (45.4) | 0.82 (0.75, 0.89) | 0.808             |
| Low risk  | 642/1575 (40.8)  | 553/1528 (36.2)  | 0.82 (0.71, 0.95) |                   |
| Moderate risk                                   | 665/1380 (48.2)  | 617/1440 (42.8)  | 0.80 (0.69, 0.93) |                   |
| High risk                                       | 603/1060 (56.9)  | 545/1070 (50.9)  | 0.79 (0.66, 0.94) |                   |
| Very high risk                                  | 528/834 (63.3)   | 493/820 (60.1)   | 0.87 (0.71, 1.06) |                   |
| Any AE leading to discontinuation of trial drug |                  |                  |                   |                   |
| Overall   | 879/4852 (18.1)  | 893/4859 (18.4)  | 1.02 (0.92, 1.13) | 0.287             |
| Low risk  | 182/1575 (11.6)  | 214/1528 (14.0)  | 1.25 (1.01, 1.54) |                   |
| Moderate risk                                   | 244/1380 (17.7)  | 230/1440 (16.0)  | 0.87 (0.72, 1.07) |                   |



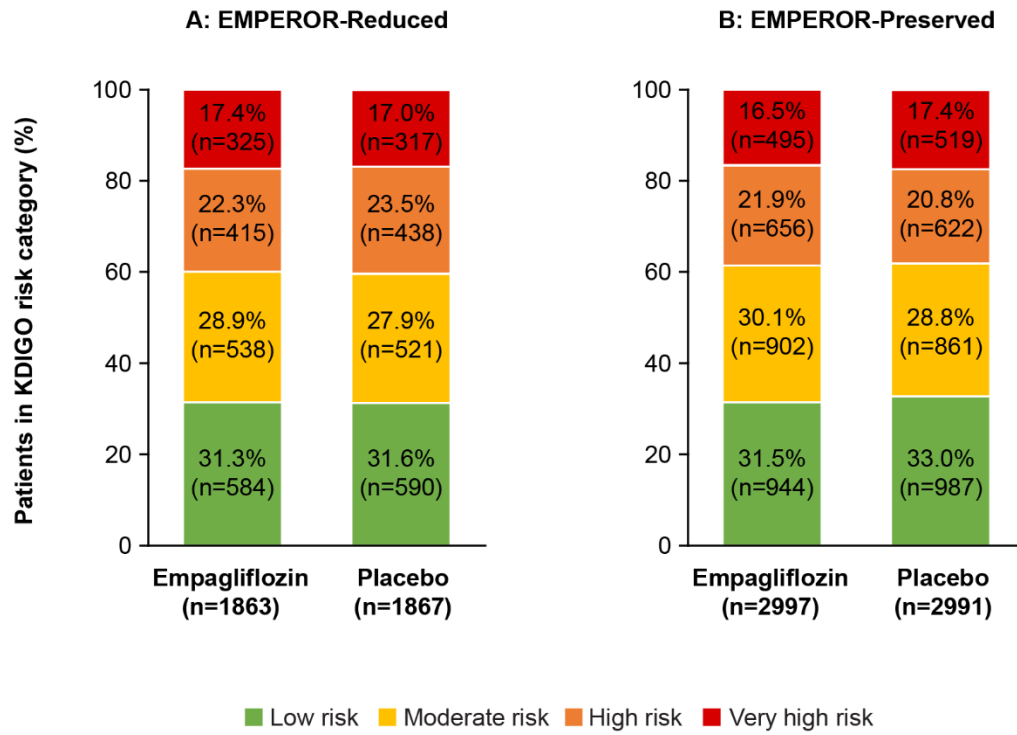
|                         |                 |                 |                   |       |
|-------------------------|-----------------|-----------------|-------------------|-------|
| High risk               | 214/1060 (20.2) | 215/1070 (20.1) | 1.00 (0.81, 1.24) |       |
| Very high risk          | 238/834 (28.5)  | 234/820 (28.5)  | 1.00 (0.81, 1.24) |       |
| Acute renal failure     |                 |                 |                   | 0.103 |
| Overall                 | 576/4852 (11.9) | 538/4859 (11.1) | 0.92 (0.81, 1.04) |       |
| Low risk                | 105/1575 (6.7)  | 78/1528 (5.1)   | 0.76 (0.56, 1.03) |       |
| Moderate risk           | 138/1380 (10.0) | 135/1440 (9.4)  | 0.93 (0.72, 1.19) | 0.103 |
| High risk               | 157/1060 (14.8) | 139/1070 (13.0) | 0.86 (0.67, 1.09) |       |
| Very high risk          | 176/834 (21.1)  | 186/820 (22.7)  | 1.09 (0.86, 1.37) |       |
| Volume depletion        |                 |                 |                   |       |
| Overall                 | 470/4852 (9.7)  | 553/4859(11.4)  | 1.20 (1.05, 1.36) |       |
| Low risk                | 127/1575 (8.1)  | 135/1528 (8.8)  | 1.10 (0.85, 1.42) |       |
| Moderate risk           | 131/1380 (9.5)  | 174/1440 (12.1) | 1.30 (1.02, 1.65) | 0.957 |
| High risk               | 113/1060 (10.7) | 138/1070 (12.9) | 1.25 (0.96, 1.63) |       |
| Very high risk          | 99/834 (11.9)   | 106/820 (12.9)  | 1.11 (0.83, 1.49) |       |
| Urinary tract infection |                 |                 |                   |       |
| Overall                 | 326/4852 (6.7)  | 388/4859 (8.0)  | 1.22 (1.04, 1.42) |       |
| Low risk                | 74/1575 (4.7)   | 100/1528 (6.5)  | 1.47 (1.08, 2.01) |       |
| Moderate risk           | 86/1380 (6.2)   | 110/1440 (7.6)  | 1.26 (0.94, 1.70) | 0.080 |
| High risk               | 81/1060 (7.6)   | 99/1070 (9.3)   | 1.16 (0.85, 1.59) |       |
| Very high risk          | 85/834 (10.2)   | 79/820 (9.6)    | 0.99 (0.71, 1.37) |       |
| Bone fracture           |                 |                 |                   |       |
| Overall                 | 168/4852 (3.5)  | 179/4859 (3.7)  | 1.07 (0.86, 1.33) |       |

|                        |                |                |                    |       |
|------------------------|----------------|----------------|--------------------|-------|
| Low risk               | 42/1575 (2.7)  | 45/1528 (2.9)  | 1.14 (0.74, 1.78)  | 0.897 |
| Moderate risk          | 45/1380 (3.3)  | 49/1440 (3.4)  | 1.05 (0.69, 1.59)  |       |
| High risk              | 44/1060 (4.2)  | 46/1070 (4.3)  | 0.98 (0.64, 1.50)  |       |
| Very high risk         | 37/834 (4.4)   | 39/820 (4.8)   | 1.13 (0.71, 1.80)  |       |
| Confirmed hypoglycemia |                |                |                    |       |
| Overall                | 106/4852 (2.2) | 100/4859 (2.1) | 0.94 (0.71, 1.24)  |       |
| Low risk               | 23/1575 (1.5)  | 17/1528 (1.1)  | 0.78 (0.41, 1.47)  | 0.447 |
| Moderate risk          | 19/1380 (1.4)  | 21/1440 (1.5)  | 1.05 (0.56, 1.97)  |       |
| High risk              | 23/1060 (2.2)  | 17/1070 (1.6)  | 0.73 (0.39, 1.38)  |       |
| Very high risk         | 41/834 (4.9)   | 45/820 (5.5)   | 1.09 (0.70, 1.69)  |       |
| Genital infection      |                |                |                    |       |
| Overall                | 34/4852 (0.7)  | 98/4859 (2.0)  | 2.94 (1.98, 4.35)  |       |
| Low risk               | 8/1575 (0.5)   | 33/1528 (2.2)  | 4.34 (1.99, 9.43)  | 0.749 |
| Moderate risk          | 16/1380 (1.2)  | 31/1440 (2.2)  | 1.89 (1.02, 3.47)  |       |
| High risk              | 5/1060 (0.5)   | 21/1070 (2.0)  | 4.29 (1.61, 11.45) |       |
| Very high risk         | 5/834 (0.6)    | 13/820 (1.6)   | 2.69 (0.95, 7.60)  |       |

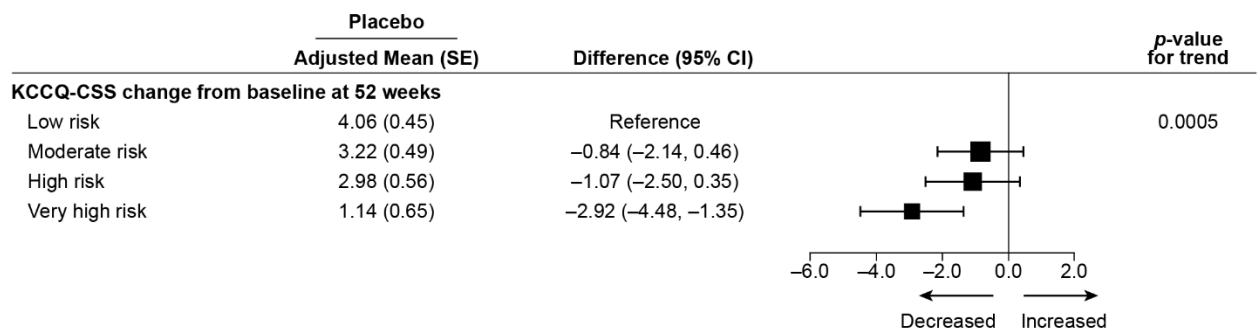
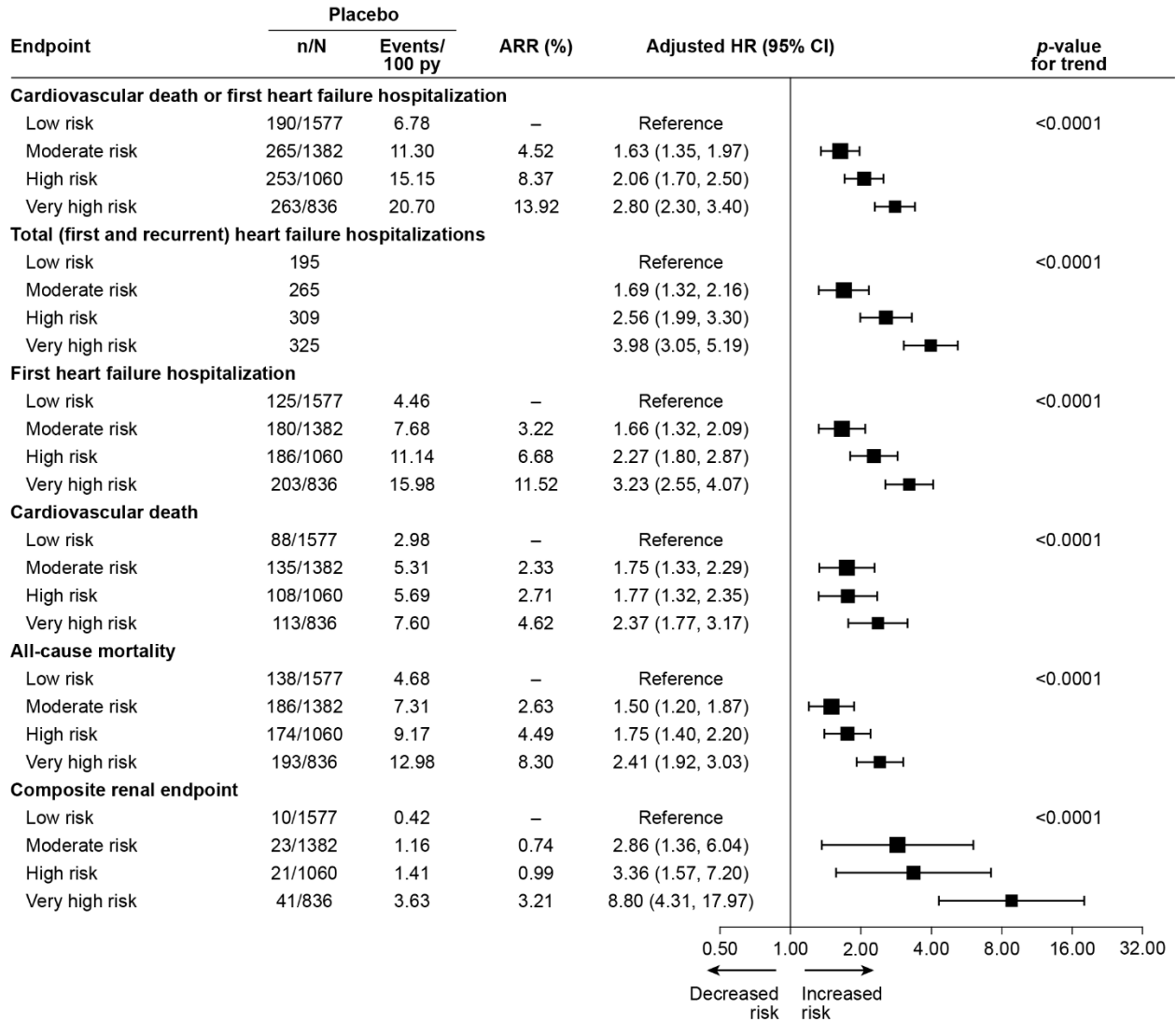
AE = adverse event; CI = confidence interval; KDIGO = Kidney Disease Improving Global Outcomes; OR = odds ratio.

## SUPPLEMENTAL FIGURES

**Supplemental Figure 1. Proportion of empagliflozin and placebo treated participants in each of the KDIGO risk categories.**

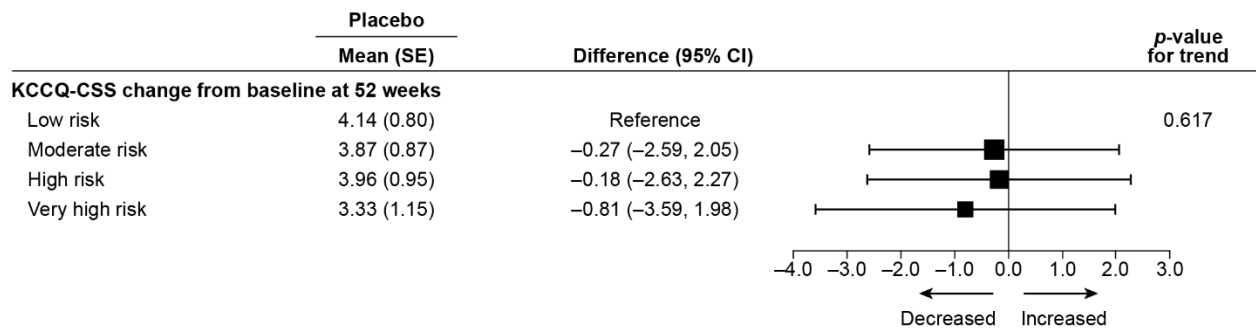
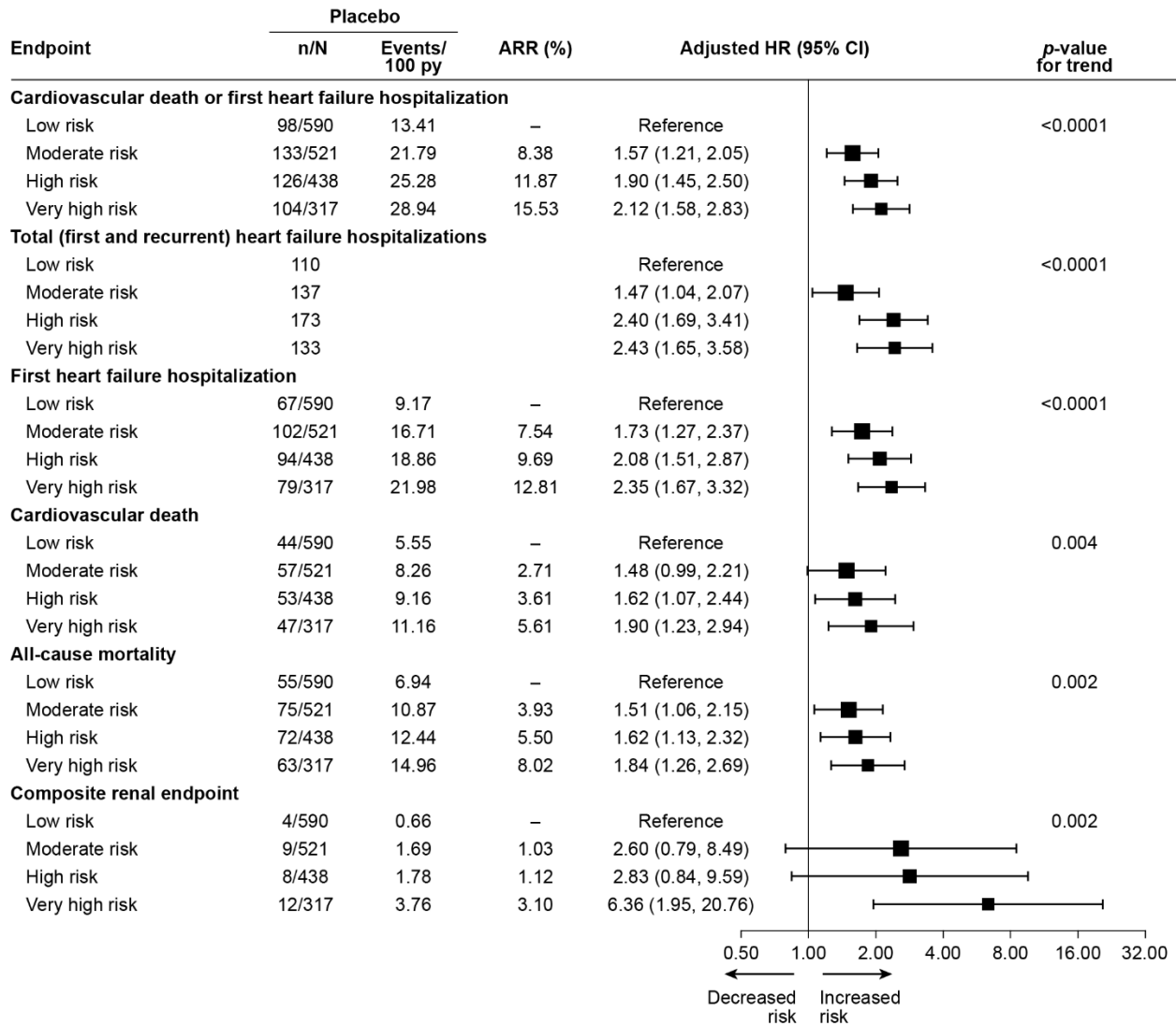


**Supplemental Figure 2. Effects of placebo on outcomes across KDIGO categories in the EMPEROR-program.**



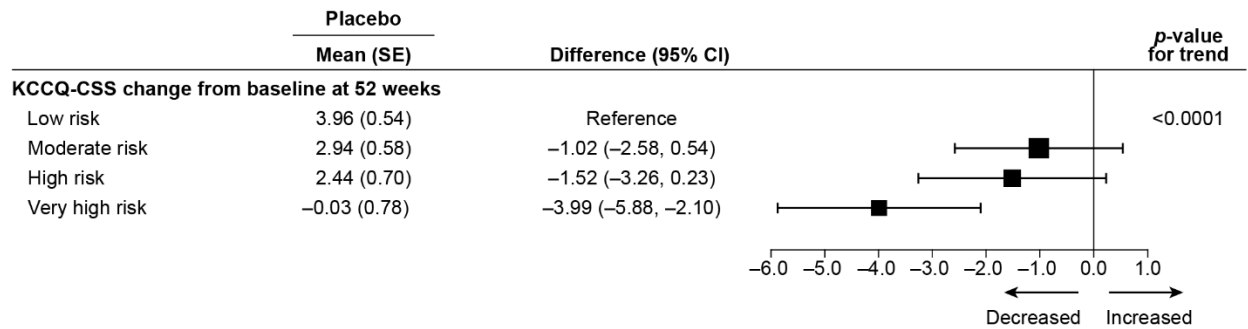
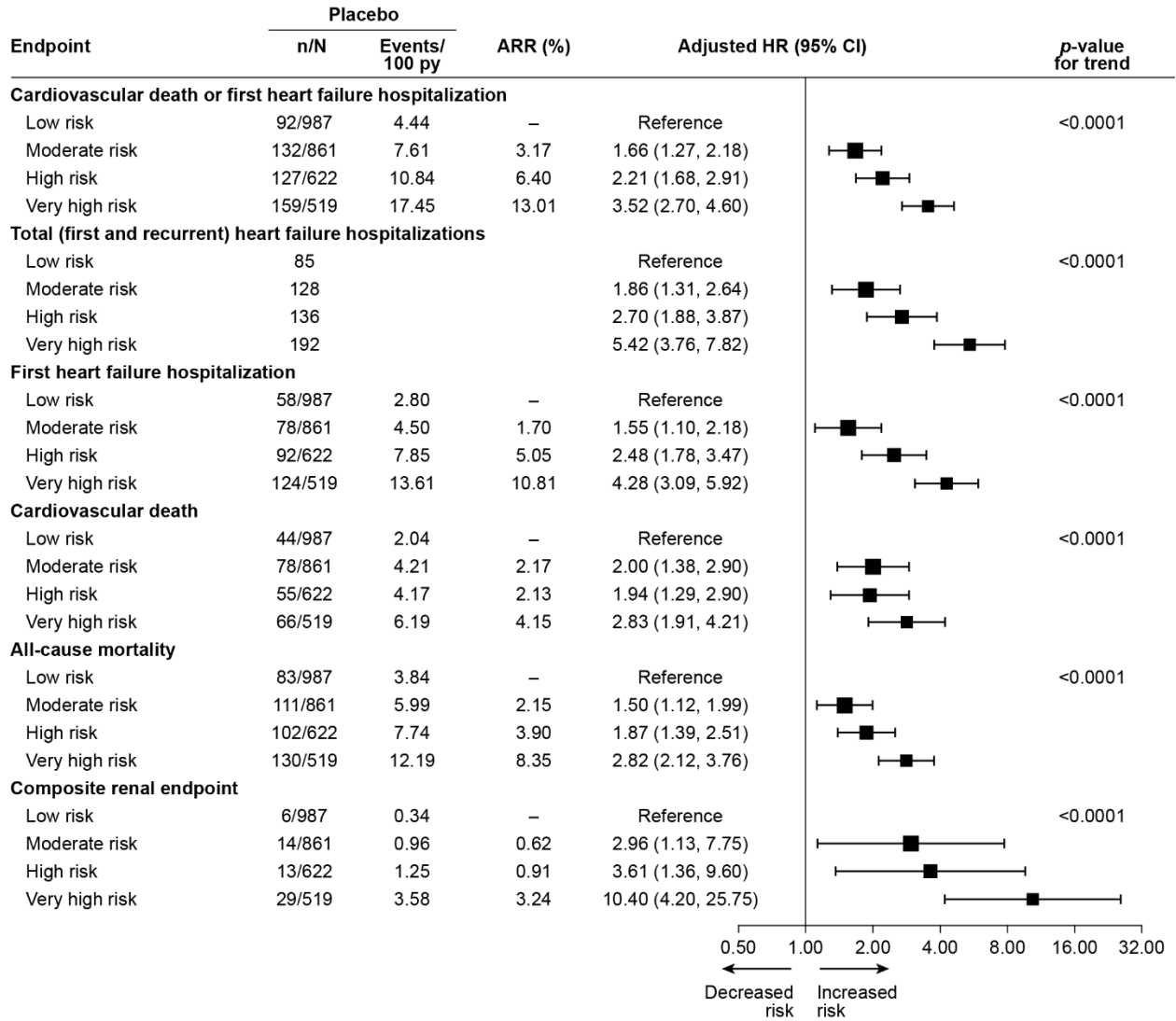
ARR = Absolute Risk Reduction; CI = confidence interval; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; eGFR = estimated glomerular filtration rate; KCCQ-CSS = Kansas City Cardiomyopathy Questionnaire-clinical summary score; KDIGO = Kidney Disease Improving Global Outcomes; py = patient years; SE = standard error.

**Supplemental Figure 3. Effects of placebo on outcomes across KDIGO categories in the EMPEROR-Reduced.**



ARR = Absolute Risk Reduction; CI = confidence interval; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; eGFR = estimated glomerular filtration rate; KCCQ-CSS = Kansas City Cardiomyopathy Questionnaire-clinical summary score; KDIGO = Kidney Disease Improving Global Outcomes; py = patient years; SE = standard error.

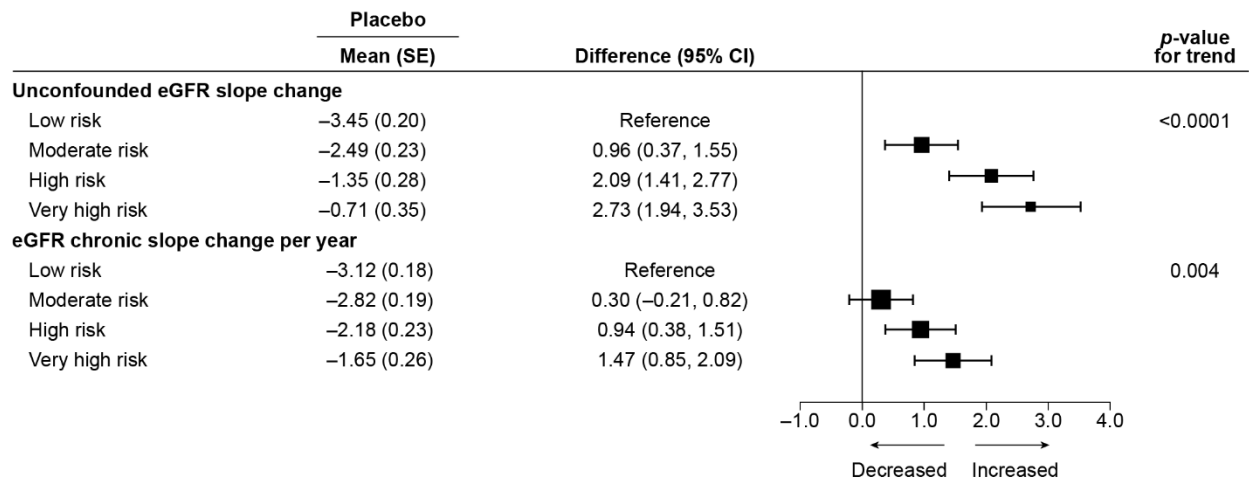
**Supplemental Figure 4. Effects of placebo on outcomes across KDIGO categories in the EMPEROR-Preserved.**





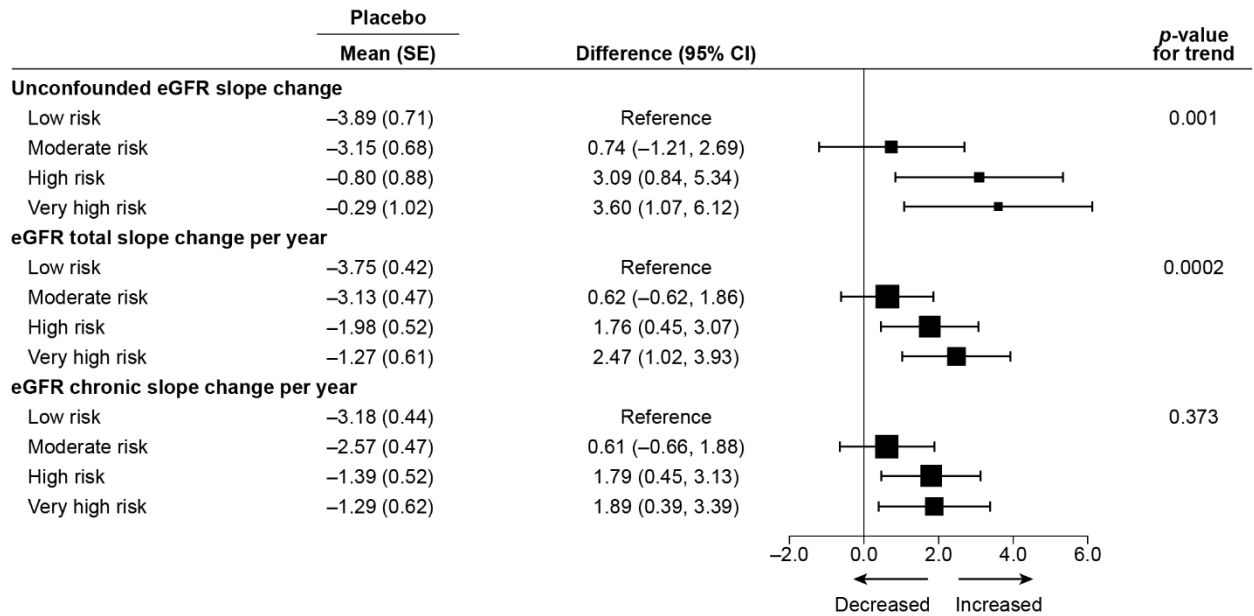
ARR = Absolute Risk Reduction; CI = confidence interval; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; eGFR = estimated glomerular filtration rate; KCCQ-CSS = Kansas City Cardiomyopathy Questionnaire-clinical summary score; KDIGO = Kidney Disease Improving Global Outcomes; py = patient years; SE = standard error.

**Supplemental Figure 5. Effect of placebo on different eGFR slopes in the EMPEROR-program.**

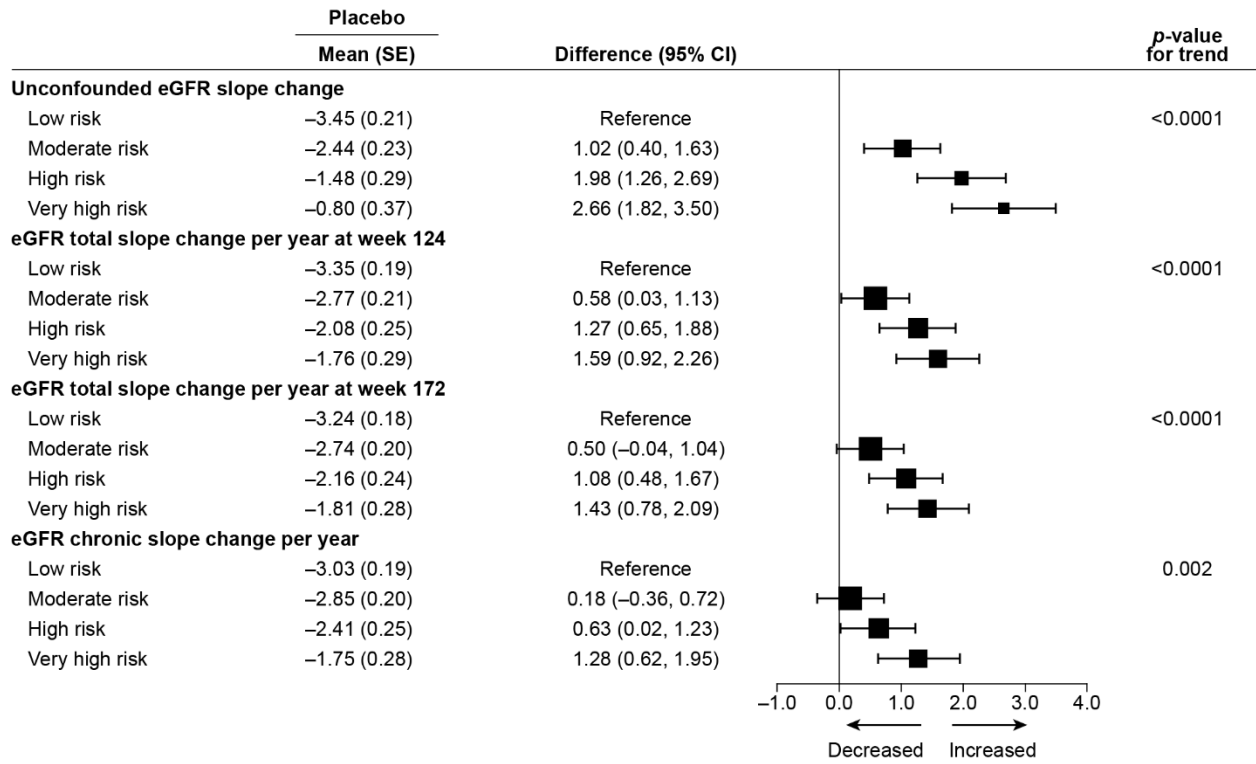


**Supplemental Figure 6. Effect of placebo on different eGFR slopes in EMPEROR-**

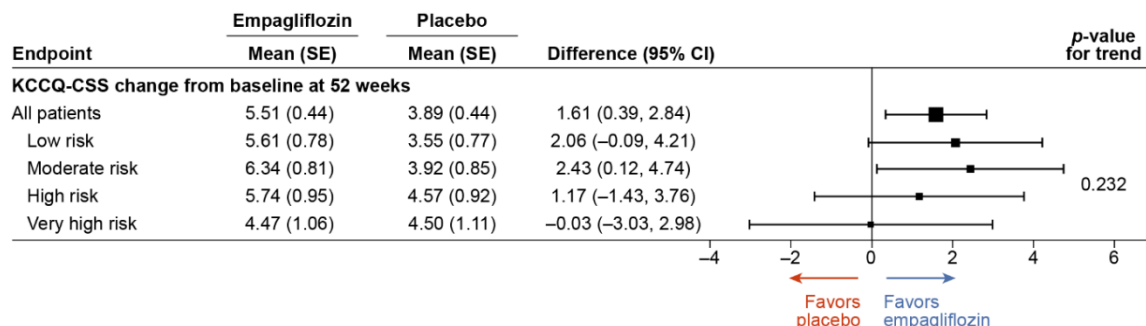
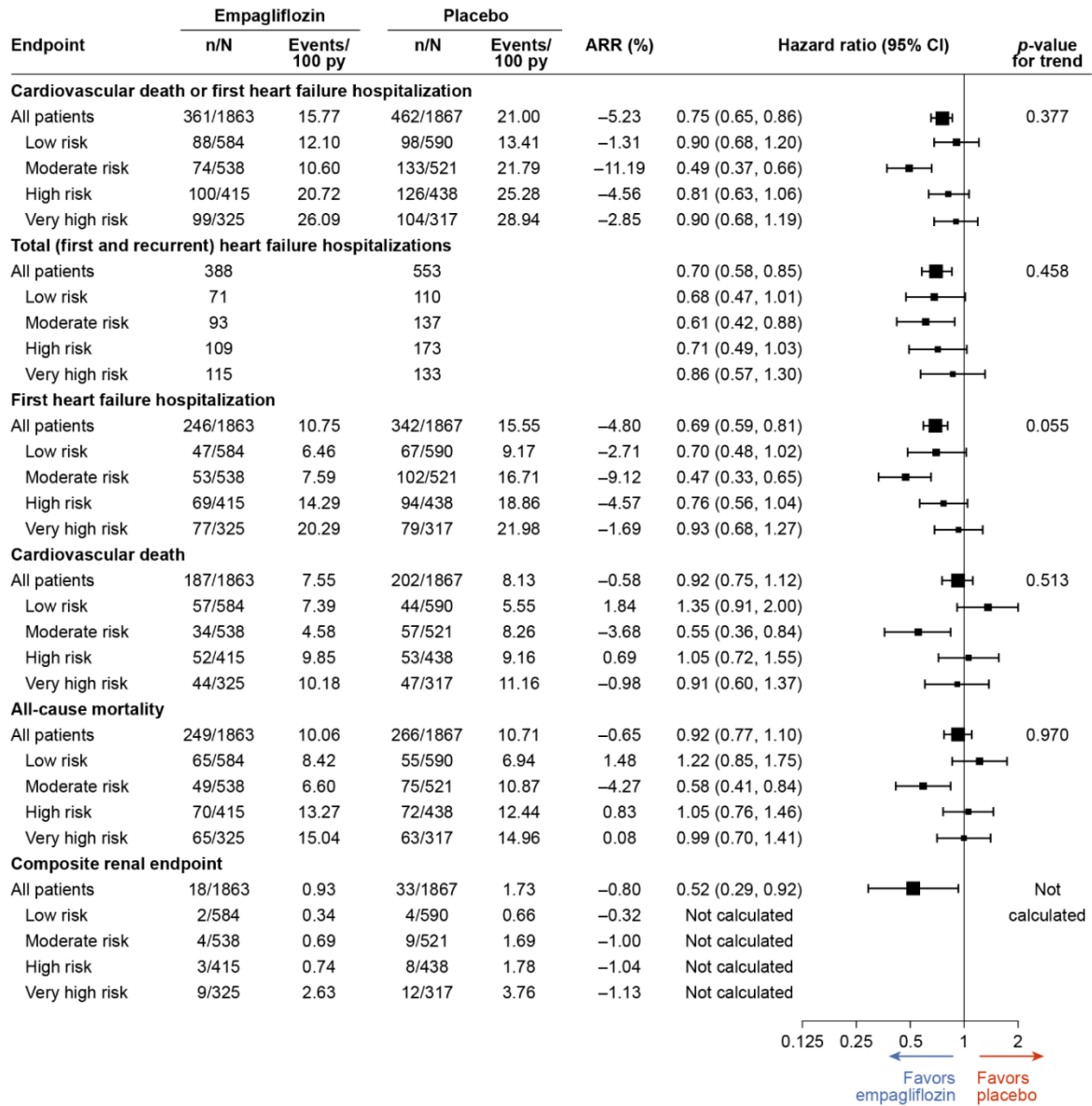
**Reduced.**



**Supplemental Figure 7. Effect of placebo on different eGFR slopes in EMPEROR- Preserved.**

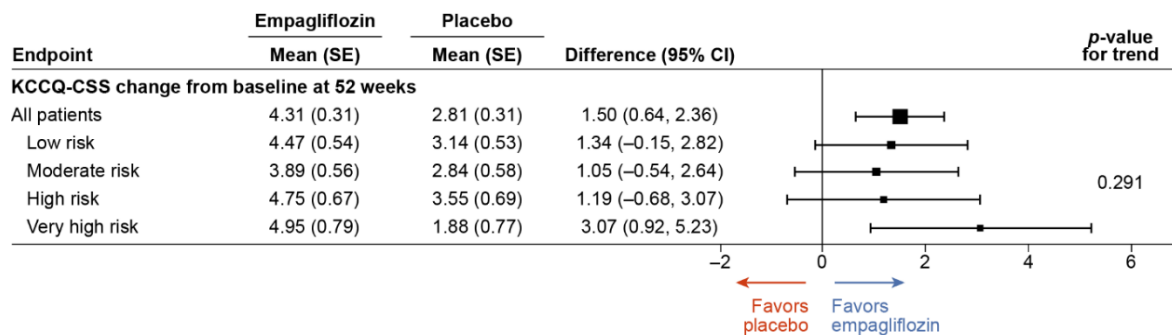
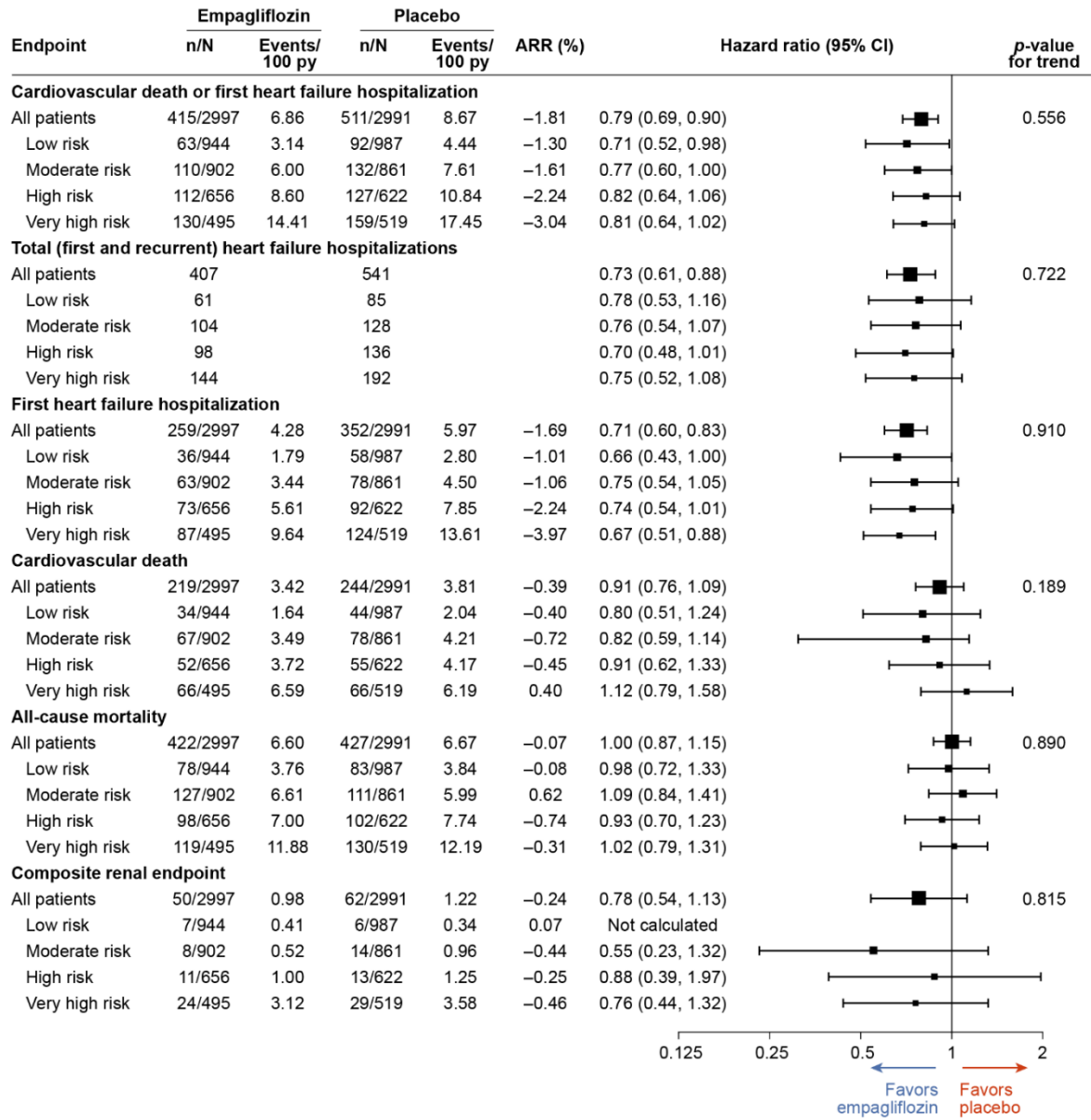


**Supplemental Figure 8. Effects of empagliflozin versus placebo on outcomes across KDIGO categories in the EMPEROR-Reduced.**



If there were fewer than 14 patients with events in one subgroup, then that subgroup was not included in the model, and if this left only one subgroup, the subgroup analysis was not conducted and stated as not calculated. ARR = Absolute Risk Reduction; CI = confidence interval; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; eGFR = estimated glomerular filtration rate; KCCQ-CSS = Kansas City Cardiomyopathy Questionnaire-clinical summary score; KDIGO = Kidney Disease Improving Global Outcomes; py = patient years; SE = standard error.

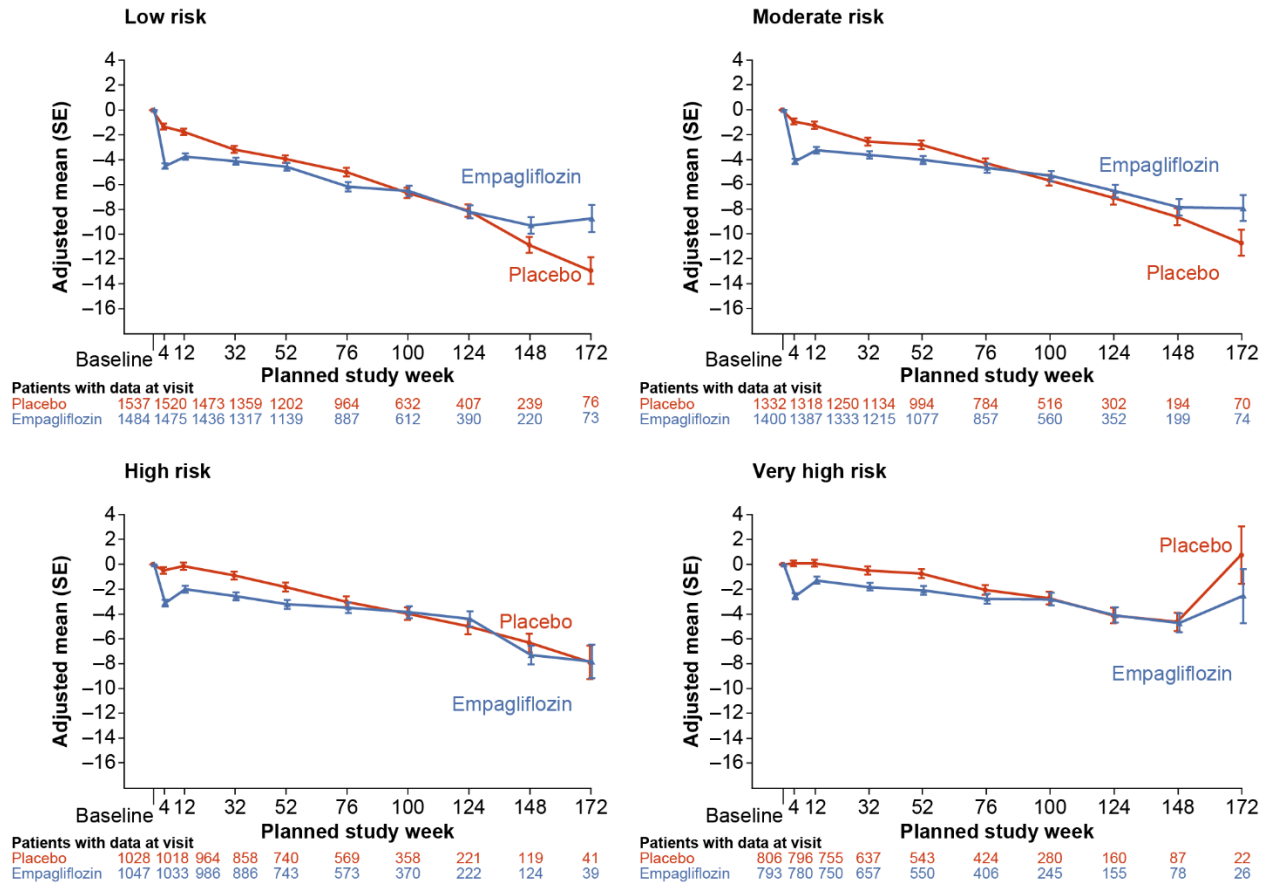
**Supplemental Figure 9. Effects of empagliflozin versus placebo on outcomes across KDIGO categories in the EMPEROR-Preserved cohort.**



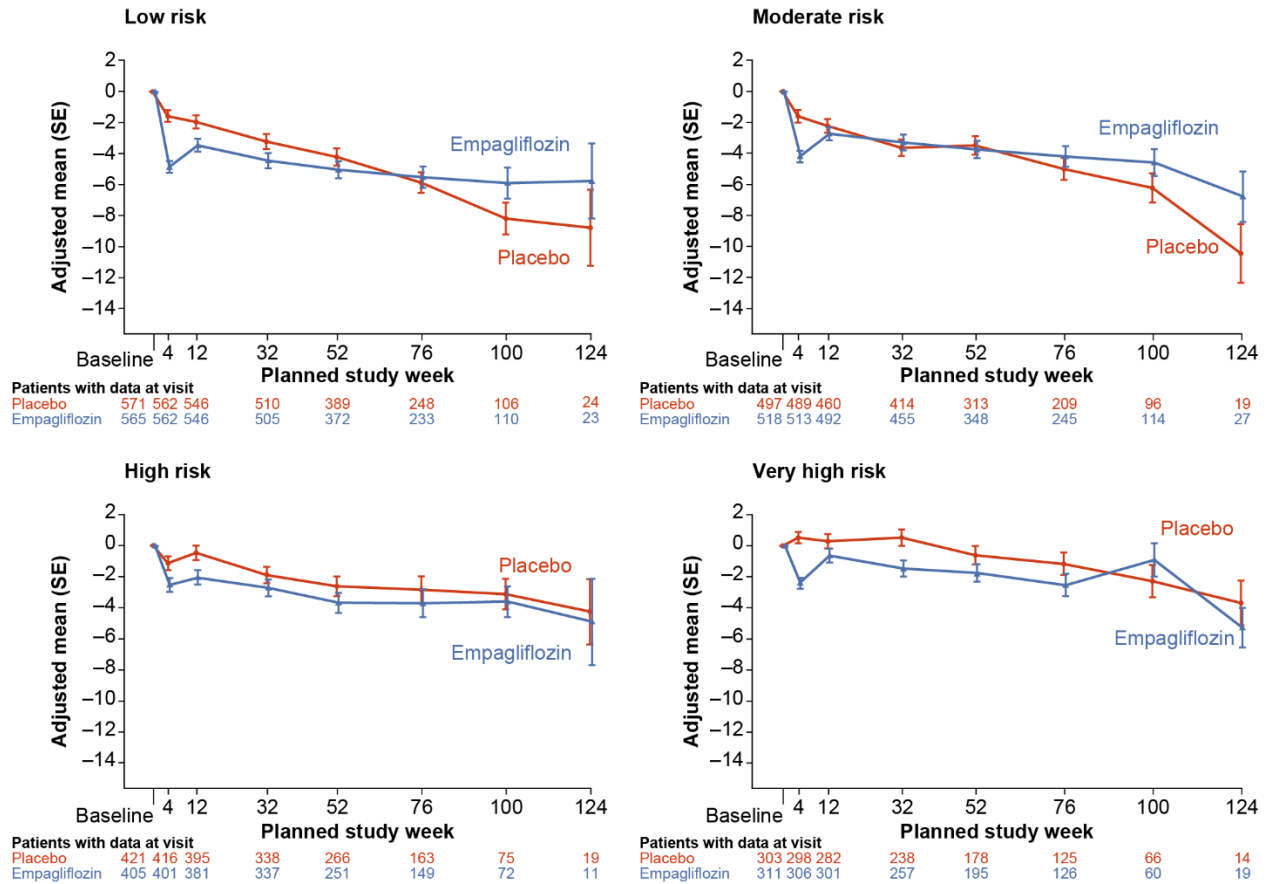
If there were fewer than 14 patients with events in one subgroup, then that subgroup was not included in the model, and if this left only one subgroup, the subgroup analysis was not conducted and stated as not calculated. ARR = Absolute Risk Reduction; CI = confidence interval; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; eGFR = estimated glomerular filtration rate; KCCQ-CSS = Kansas City Cardiomyopathy Questionnaire-clinical summary score; KDIGO = Kidney Disease Improving Global Outcomes; py = patient years; SE = standard error.



**Supplemental Figure 10. Adjusted mean changes in eGFR (CKD-EPI) from baseline over time and mean slope of change in eGFR by baseline KDIGO risk categories based on on-treatment data in EMPEROR-program.**



**Supplemental Figure 11. Adjusted mean changes in eGFR from baseline over time and mean slope of change in eGFR by baseline KDIGO risk categories based on on-treatment data in the EMPEROR-Reduced.**



**Supplemental Figure 12. Adjusted mean changes in eGFR from baseline over time and mean slope of change in eGFR by baseline KDIGO risk categories based on on-treatment data in the EMPEROR-Preserved.**

