# Blood Pressure and Cardiorenal Outcomes With Finerenone in Chronic Kidney Disease in Type 2 Diabetes

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**Supplemental Material**

## Methods

### Study Design and Participants

At the run-in and screening visits, patients were required to have serum potassium levels less than or equal to 4.8 mEq/L. Key exclusion criteria were known nondiabetic kidney disease, chronic symptomatic heart failure with reduced ejection fraction (New York Heart Association class II–IV), a recent history of dialysis for acute kidney failure or a kidney transplant, or uncontrolled hypertension.

Signed informed consent was obtained from all patients prior to enrollment. The trial conformed to the Declaration of Helsinki, and the protocol was approved by relevant regulatory authorities and ethics committees at each trial site. The study was registered with the European Union Clinical Trials Register (EudraCT 2015-000990-11) and ClinicalTrials.gov (NCT02540993).

### Procedures and Outcomes

Initial dosing of finerenone of 10 or 20 mg once daily was based on an estimated glomerular filtration rate (eGFR) at the screening visit of 25–<60 or ≥60 mL/min/1.73 $m^2$, respectively. Randomization was stratified by geographic region (North America, Europe, Asia, Latin America, and other), eGFR (25–<45, 45–<60, or ≥60 mL/min/1.73 $m^2$), and albuminuria categories (urine albumin-to-creatinine ratio 30–<300 or ≥300 mg/g) at screening; all patients and study personnel were blinded to treatment assignment.

**Table S1.** Patient Baseline Characteristics by Treatment Arm and Baseline Office SBP Quartile.

| Characteristic | Baseline Office SBP | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Q1 (≤128.7 mm Hg) | | Q2 (>128.7–≤138.3 mm Hg) | | Q3 (>138.3–≤148.0 mm Hg) | | Q4 (>148.0 mm Hg) | |
| | Finerenone (n=726) | Placebo (n=722) | Finerenone (n=662) | Placebo (n=684) | Finerenone (n=778) | Placebo (n=714) | Finerenone (n=664) | Placebo (n=719) |
| Age, y, mean (SD) | 64.0 (9.1) | 64.6 (9.8) | 65.4 (8.9) | 64.9 (9.0) | 65.9 (8.7) | 66.6 (8.7) | 66.5 (9.0) | 66.6 (9.0) |
| Gender, male, n (%) | 509 (70.1) | 526 (72.9) | 461 (69.6) | 478 (69.9) | 542 (69.7) | 514 (72.0) | 441 (66.4) | 511 (71.1) |
| Race, n (%) | | | | | | | | |
| White | 403 (55.5) | 413 (57.2) | 423 (63.9) | 433 (63.3) | 515 (66.2) | 465 (65.1) | 435 (65.5) | 503 (70.0) |
| Black/African American | 30 (4.1) | 29 (4.0) | 29 (4.4) | 28 (4.1) | 34 (4.4) | 29 (4.1) | 46 (6.9) | 38 (5.3) |
| Asian | 247 (34.0) | 242 (33.5) | 161 (24.3) | 180 (26.3) | 176 (22.6) | 173 (24.2) | 133 (20.0) | 128 (17.8) |
| Office SBP, mm Hg, mean (SD) | 120.1 (7.3) | 119.7 (7.7) | 133.5 (2.7) | 133.6 (2.7) | 142.9 (3.0) | 142.7 (2.9) | 156.6 (7.3) | 155.9 (6.9) |
| Office DBP, mm Hg, mean (SD) | 70.5 (9.0) | 70.2 (9.0) | 75.2 (8.5) | 75.4 (8.8) | 77.5 (9.0) | 77.4 (8.7) | 80.3 (9.5) | 80.3 (9.2) |
| BMI, $kg/m^2$, mean (SD) | 30.3 (6.1) | 30.2 (6.0) | 31.4 (5.9) | 31.3 (6.2) | 31.4 (6.0) | 31.4 (5.9) | 31.5 (6.1) | 31.5 (5.9) |
| Duration of diabetes, y, mean (SD) | 16.2 (8.6) | 16.0 (8.7) | 16.8 (9.1) | 16.5 (8.7) | 16.7 (8.6) | 16.3 (8.7) | 16.6 (8.8) | 17.3 (9.0) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| HbA1c, %, mean (SD) | 7.6 (1.3) | 7.6 (1.3) | 7.7 (1.4) | 7.7 (1.4) | 7.7 (1.3) | 7.7 (1.4) | 7.7 (1.3) | 7.7 (1.4) |
| Serum potassium, mEq/L, mean (SD) | 4.4 (0.5) | 4.4 (0.5) | 4.4 (0.5) | 4.4 (0.4) | 4.4 (0.5) | 4.4 (0.5) | 4.4 (0.4) | 4.3 (0.5) |
| eGFR, mL/min/1.73 $m^2$, mean (SD) | 44.2 (12.5) | 43.7 (12.1) | 45.2 (12.6) | 44.4 (12.9) | 44.4 (12.6) | 45.1 (12.7) | 43.8 (12.4) | 44.1 (12.6) |
| eGFR, mL/min/1.73 $m^2$, n (%) | | | | | | | | |
| <25 | 16 (2.2) | 19 (2.6) | 14 (2.1) | 17 (2.5) | 16 (2.1) | 18 (2.5) | 20 (3.0) | 15 (2.1) |
| 25–<45 | 379 (52.2) | 387 (53.6) | 312 (47.1) | 371 (54.2) | 416 (53.5) | 357 (50.0) | 367 (55.3) | 390 (54.2) |
| 45–<60 | 247 (34.0) | 240 (33.2) | 269 (40.6) | 213 (31.1) | 253 (32.5) | 247 (34.6) | 203 (30.6) | 227 (31.6) |
| ≥60 | 84 (11.6) | 76 (10.5) | 67 (10.1) | 83 (12.1) | 93 (12.0) | 92 (12.9) | 74 (11.1) | 87 (12.1) |
| UACR, mg/g, median (IQR) | 671.3 (374.5–1269.6) | 704.0 (377.5–1226.6) | 826.7 (422.7–1501.8) | 836.9 (429.4–1623.5) | 899.3 (465.2–1702.0) | 958.9 (514.5–1789.7) | 1040.8 (581.9–1950.7) | 1004.8 (531.9–1906.1) |
| UACR, mg/g, n (%)* | | | | | | | | |
| <30 | 8 (1.1) | 5 (0.7) | 0 (0.0) | 4 (0.6) | 1 (0.1) | 1 (0.1) | 2 (0.3) | 2 (0.3) |
| 30–<300 | 120 (16.5) | 122 (16.9) | 89 (13.4) | 88 (12.9) | 88 (11.3) | 63 (8.8) | 53 (8.0) | 62 (8.6) |
| ≥300 | 598 (82.4) | 595 (82.4) | 573 (86.6) | 592 (86.5) | 689 (88.6) | 650 (91.0) | 608 (91.6) | 655 (91.1) |
| Heart rate, bpm, mean (SD) | 73.6 (12.0) | 73.1 (11.4) | 72.6 (11.1) | 72.6 (10.6) | 72.0 (10.8) | 72.2 (11.5) | 71.0 (12.0) | 71.0 (11.6) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| History of CVD, n (%)[†] | 328 (45.2) | 327 (45.3) | 319 (48.2) | 306 (44.7) | 374 (48.1) | 357 (50.0) | 281 (42.3) | 311 (43.3) |
| Current smoker, n (%) | 131 (18.0) | 120 (16.6) | 98 (14.8) | 84 (12.3) | 89 (11.4) | 96 (13.4) | 96 (14.5) | 92 (12.8) |
| Medication use at baseline, n (%) | | | | | | | | |
| ACEi | 225 (31.0) | 250 (34.6) | 231 (34.9) | 236 (34.5) | 282 (36.2) | 259 (36.3) | 209 (31.5) | 246 (34.2) |
| ARB | 499 (68.7) | 472 (65.4) | 430 (65.0) | 448 (65.5) | 495 (63.6) | 453 (63.4) | 455 (68.5) | 472 (65.6) |
| Beta-blockers | 347 (47.8) | 370 (51.2) | 360 (54.4) | 332 (48.5) | 406 (52.2) | 405 (56.7) | 348 (52.4) | 398 (55.4) |
| Diuretics | 359 (49.4) | 377 (52.2) | 366 (55.3) | 372 (54.4) | 437 (56.2) | 422 (59.1) | 414 (62.3) | 464 (64.5) |
| Statins | 544 (74.9) | 529 (73.3) | 483 (73.0) | 516 (75.4) | 572 (73.5) | 530 (74.2) | 504 (75.9) | 533 (74.1) |
| Potassium supplements | 23 (3.2) | 22 (3.0) | 26 (3.9) | 20 (2.9) | 15 (1.9) | 24 (3.4) | 21 (3.2) | 19 (2.6) |
| Potassium-lowering agents | 24 (3.3) | 19 (2.6) | 14 (2.1) | 12 (1.8) | 19 (2.4) | 13 (1.8) | 13 (2.0) | 22 (3.1) |

ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; IQR, interquartile range; Q, quartile; SBP, systolic blood pressure; SD, standard deviation; and UACR, urine albumin-to-creatinine ratio.

*n=1 (0.2%) patient with data missing in Q4 of the finerenone group.

[†]History of CVD was defined as investigator-reported medical history of coronary artery disease (myocardial infarction, coronary revascularization, or angiography-proven stenosis ≥50% in at least 1 major coronary artery), ischemic stroke, or peripheral artery disease.

**Table S2. Antihypertensive Therapies by Baseline Office SBP Quartile**

| Patients With Antihypertensive Therapies, n (%) | Baseline Office SBP | | | |
|---|---|---|---|---|
| | **Q1 (≤128.7 mm Hg) n=1448** | **Q2 (>128.7–≤138.3 mm Hg) n=1346** | **Q3 (>138.3–≤148.0 mm Hg) n=1492** | **Q4 (>148.0 mm Hg) n=1383** |
| Any antihypertensive | 1447 (>99.9) | 1346 (100.0) | 1491 (>99.9) | 1383 (100.0) |
| RAS inhibitors | 1445 (99.8) | 1343 (99.8) | 1488 (99.7) | 1379 (99.7) |
| ACEi | 475 (32.8) | 467 (34.7) | 541 (36.3) | 455 (32.9) |
| ARB | 971 (67.1) | 878 (65.2) | 948 (63.5) | 927 (67.0) |
| Beta-blockers | 717 (49.5) | 692 (51.4) | 811 (54.4) | 746 (53.9) |
| Alpha-blocking agents | 332 (22.9) | 307 (22.8) | 368 (24.7) | 399 (28.9) |
| Calcium channel blockers | 864 (59.7) | 820 (60.9) | 957 (64.1) | 941 (68.0) |
| Diuretics | 736 (50.8) | 738 (54.8) | 859 (57.6) | 878 (63.5) |
| Loop diuretics | 363 (25.1) | 371 (27.6) | 414 (27.7) | 469 (33.9) |
| Thiazide diuretics | 318 (22.0) | 309 (23.0) | 357 (23.9) | 370 (26.8) |
| Centrally acting antihypertensives | 88 (6.1) | 104 (7.7) | 122 (8.2) | 157 (11.4) |
| Nitrates | 106 (7.3) | 87 (6.5) | 96 (6.4) | 82 (5.9) |

| | | | | |
|---|---|---|---|---|
| Mean number of antihypertensives | 3.1 | 3.2 | 3.3 | 3.5 |

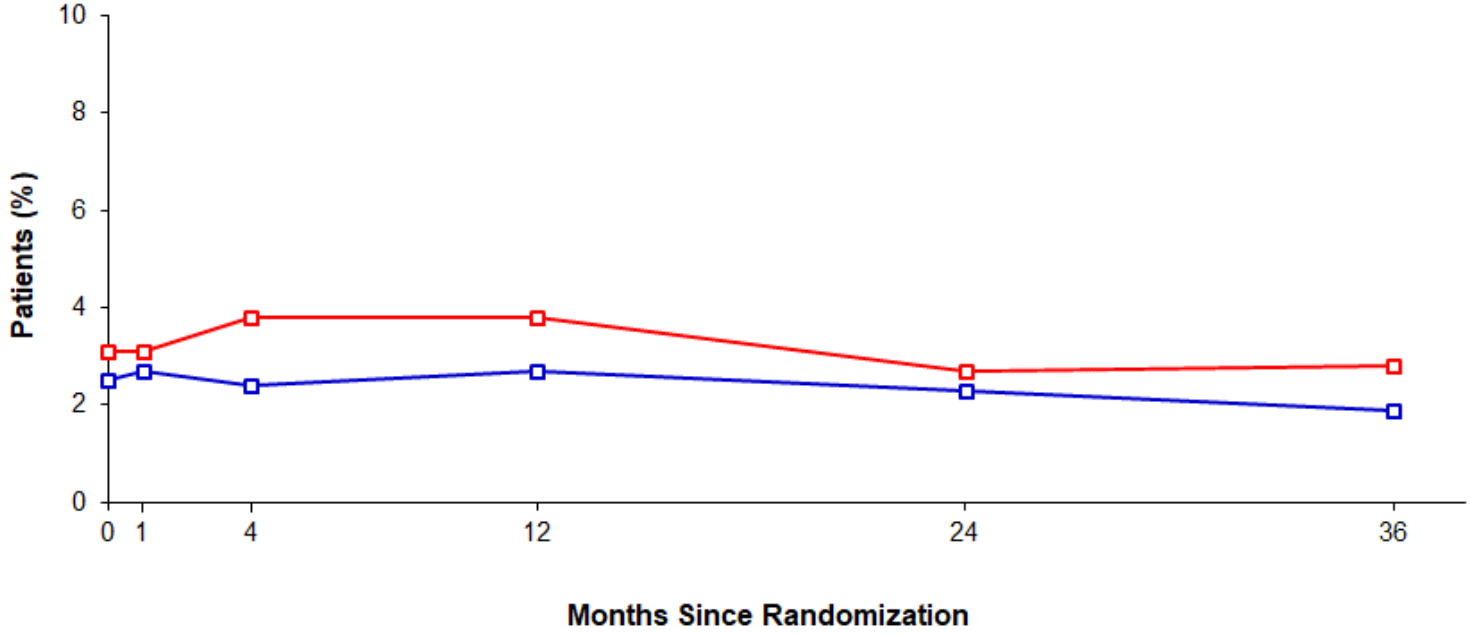
Patients who took ≥1 antihypertensive medication at baseline. Multiple drug groups per drug are possible; therefore, the same drug may be counted in >1 category for the same patient. ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; Q, quartile; RAS, renin-angiotensin system; and SBP, systolic blood pressure.

**Table S3. Hyperkalemia and Acute Kidney Injury Outcomes by Baseline Office SBP Quartile**

| Patients With Treatment-emergent AEs, n (%) | Baseline Office SBP | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Q1 (≤128.7 mm Hg) | | Q2 (>128.7–≤138.3 mm Hg) | | Q3 (>138.3–≤148.0 mm Hg) | | Q4 (>148.0 mm Hg) | |
| | Finerenone (n=726) | Placebo (n=721) | Finerenone (n=662) | Placebo (n=683) | Finerenone (n=777) | Placebo (n=712) | Finerenone (n=661) | Placebo (n=715) |
| Any hyperkalemia | 132 (18.2) | 77 (10.7) | 112 (16.9) | 62 (9.1) | 145 (18.7) | 56 (7.9) | 127 (19.2) | 60 (8.4) |
| Related to study drug | 83 (11.4) | 39 (5.4) | 73 (11.0) | 38 (5.6) | 86 (11.1) | 26 (3.7) | 91 (13.8) | 32 (4.5) |
| Leading to hospitalization | 12 (1.7) | 2 (0.3) | 9 (1.4) | 2 (0.3) | 8 (1.0) | 2 (0.3) | 11 (1.7) | 2 (0.3) |
| Leading to discontinuation | 18 (2.5) | 4 (0.6) | 12 (1.8) | 8 (1.2) | 17 (2.2) | 7 (1.0) | 17 (2.6) | 6 (0.8) |
| SAE | 13 (1.8) | 3 (0.4) | 10 (1.5) | 2 (0.3) | 10 (1.3) | 2 (0.3) | 11 (1.7) | 5 (0.7) |
| Leading to death | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Any acute kidney injury | 24 (3.3) | 35 (4.9) | 40 (6.0) | 23 (3.4) | 34 (4.4) | 36 (5.1) | 31 (4.7) | 42 (5.9) |
| Related to study drug | 6 (0.8) | 6 (0.8) | 12 (1.8) | 3 (0.4) | 8 (1.0) | 4 (0.6) | 8 (1.2) | 5 (0.7) |
| Leading to hospitalization | 12 (1.7) | 15 (2.1) | 20 (3.0) | 9 (1.3) | 13 (1.7) | 7 (1.0) | 8 (1.2) | 16 (2.2) |
| Leading to discontinuation | 1 (0.1) | 3 (0.4) | 1 (0.2) | 1 (0.1) | 2 (0.3) | 1 (0.1) | 1 (0.2) | 2 (0.3) |
| SAE | 13 (1.8) | 15 (2.1) | 20 (3.0) | 11 (1.6) | 14 (1.8) | 8 (1.1) | 9 (1.4) | 17 (2.4) |
| Leading to death | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |

Q indicates quartile; SAE, serious adverse event; and SBP, systolic blood pressure.

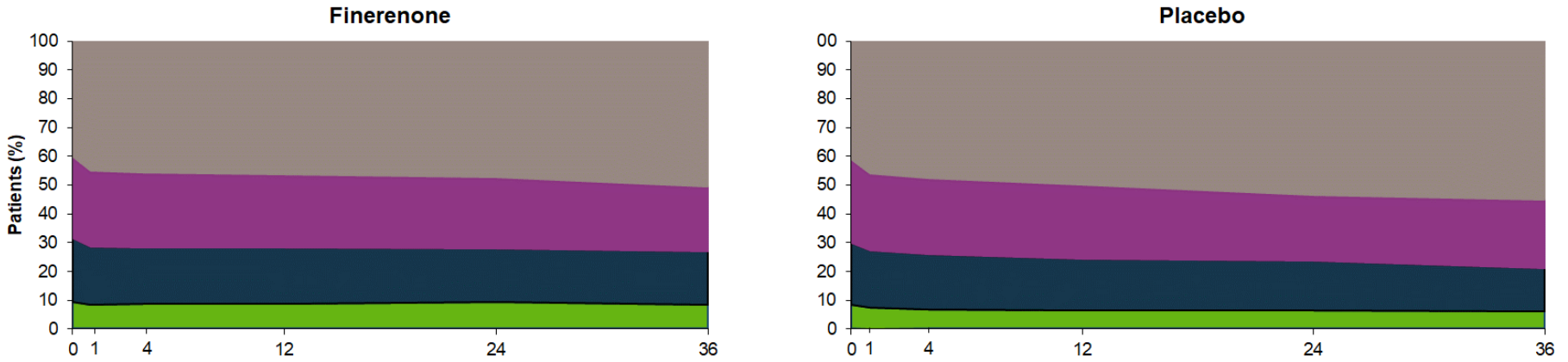
**Figure S1. Patients With an Office Blood Pressure of ≥140/90 mm Hg and on ≥3 Antihypertensive Therapies Including a Diuretic.**




**Patients With an Office Blood Pressure of ≥140/90 mm Hg and on ≥3 Antihypertensive Therapies Including a Diuretic, n/N (%)**

| | | | | | |
|---|---|---|---|---|---|
| Finerenone | 71/2833 (2.5) | 68/2799 (2.4) | 73/2734 (2.7) | 47/2026 (2.3) | 19/981 (1.9) |
| Placebo | 89/2841 (3.1) | 105/2798 (3.8) | 103/2734 (3.8) | 54/2037 (2.7) | 27/969 (2.8) |

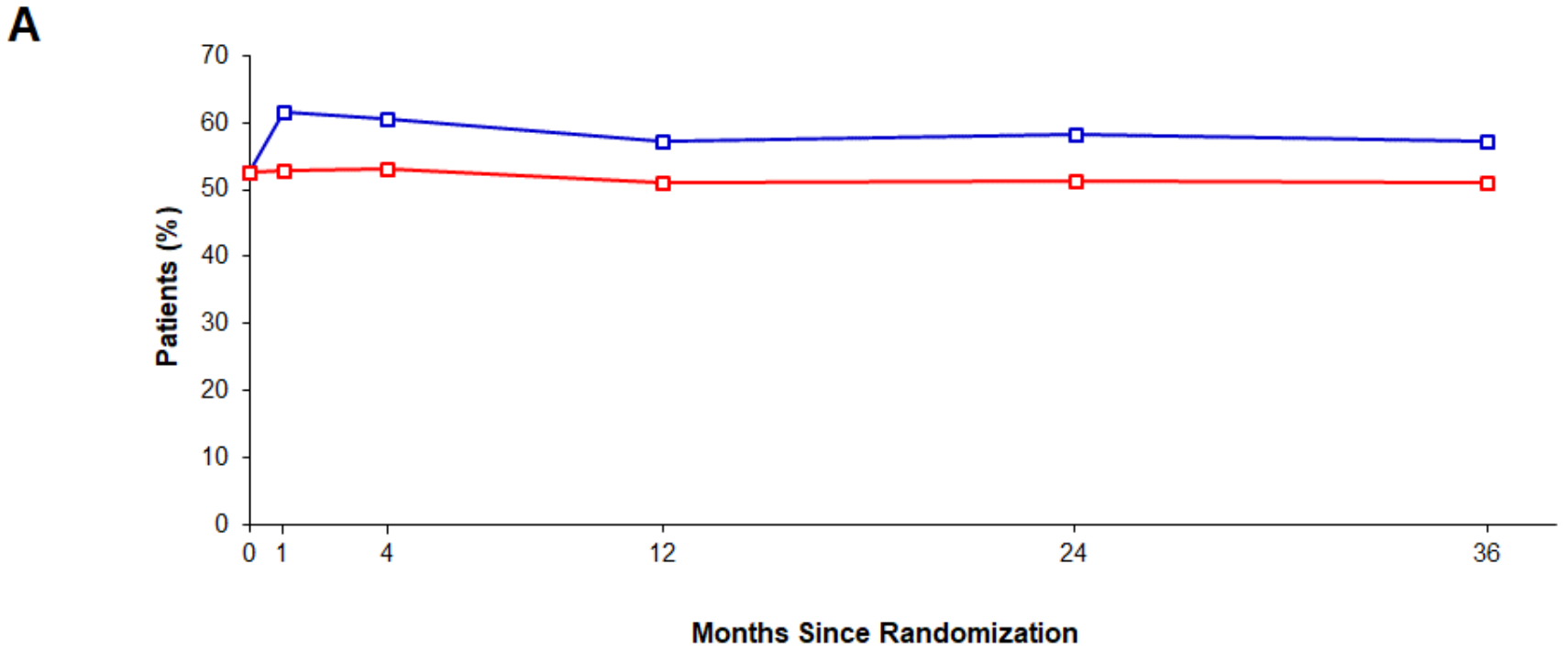
**Figure S2. Number of Antihypertensive Therapies Taken During the Trial.**




**Number of Antihypertensive Agents per Patient, n (%)**

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 1 (<0.1) | 2 (<0.1) | 7 (0.3) | 5 (0.2) | 3 (0.3) | 1 (<0.1) | 2 (<0.1) | 2 (<0.1) | 8 (0.4) | 3 (0.3) |
| **1** | 265 (9.4) | 243 (8.6) | 237 (8.5) | 209 (9.2) | 95 (8.1) | 238 (8.4) | 188 (6.7) | 177 (6.4) | 137 (6.0) | 69 (5.9) |
| **2** | 629 (22.2) | 557 (19.7) | 547 (19.6) | 423 (18.7) | 218 (18.5) | 608 (21.4) | 543 (19.2) | 499 (18.0) | 392 (17.2) | 174 (14.8) |
| **3** | 802 (28.3) | 732 (25.9) | 703 (25.2) | 556 (24.5) | 267 (22.7) | 826 (29.1) | 743 (26.3) | 716 (25.8) | 525 (23.0) | 281 (23.9) |
| **≥4** | 1136 (40.1) | 1287 (45.6) | 1291 (46.4) | 1075 (47.4) | 594 (50.5) | 1168 (41.1) | 1349 (47.8) | 1383 (49.8) | 1216 (53.4) | 649 (55.2) |

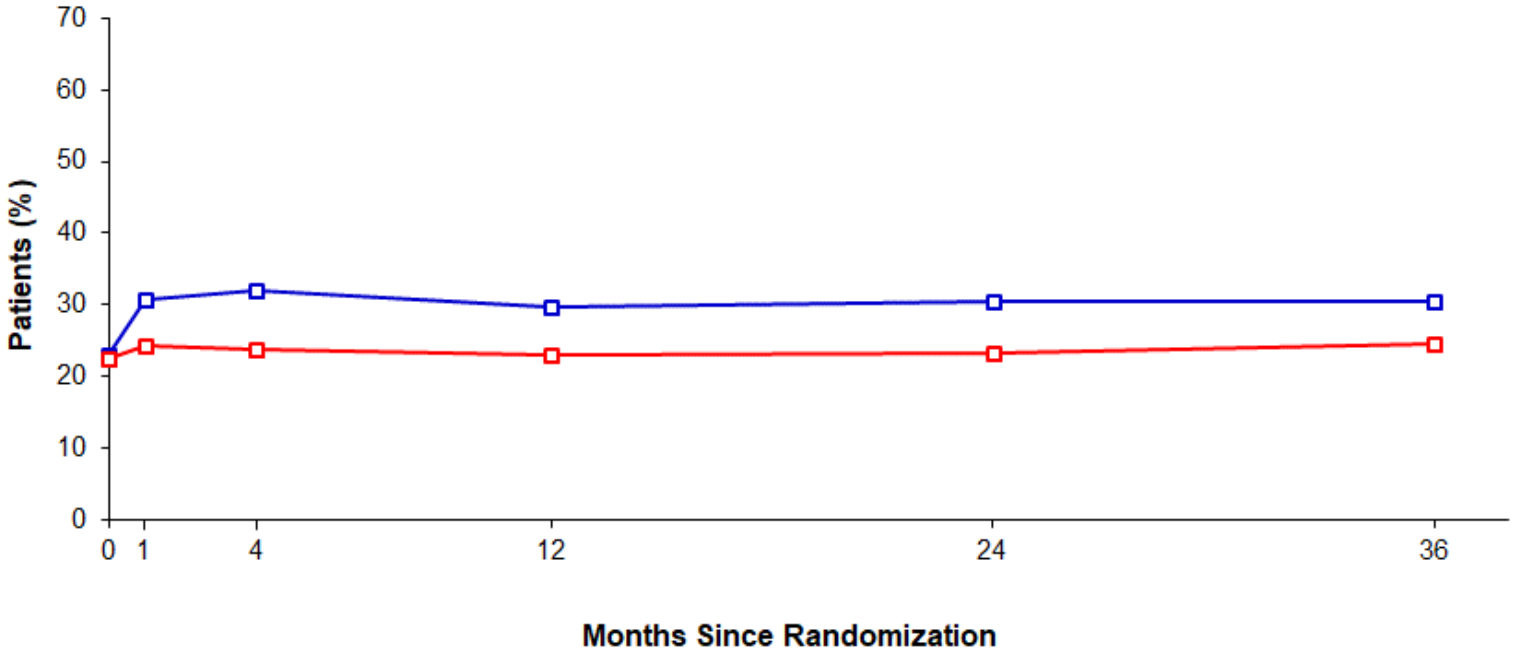
**Figure S3. Patients With a Target Office Blood Pressure of <140/90 mm Hg and <130/80 mm Hg.**




**Patients With a Target Office Blood Pressure of <140/90 mm Hg, n/N (%)**

| | | | | | |
|---|---|---|---|---|---|
| Finerenone | 1490/2833 (52.6) | 1695/2799 (60.6) | 1562/2734 (57.1) | 1180/2026 (58.2) | 561/981 (57.2) |
| Placebo | 1494/2841 (52.6) | 1483/2798 (53.0) | 1394/2734 (51.0) | 1042/2037 (51.2) | 494/969 (51.0) |

**B**




**Patients With a Target Office Blood Pressure of <130/80 mm Hg, n/N (%)**

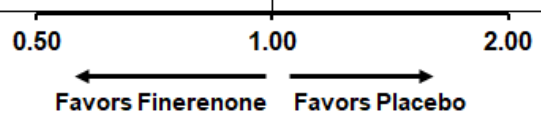
| | | | | | |
|---|---|---|---|---|---|
| Finerenone | 653/2833 (23.0) | 895/2799 (32.0) | 808/2734 (29.6) | 615/2026 (30.4) | 299/981 (30.5) |
| Placebo | 638/2841 (22.5) | 663/2798 (23.7) | 628/2734 (23.0) | 474/2037 (23.3) | 237/969 (24.5) |

**Finerenone** **Placebo**

Percentage of patients with a target office blood pressure of (**A**) <140/90 mm Hg and (**B**) <130/80 mm Hg.

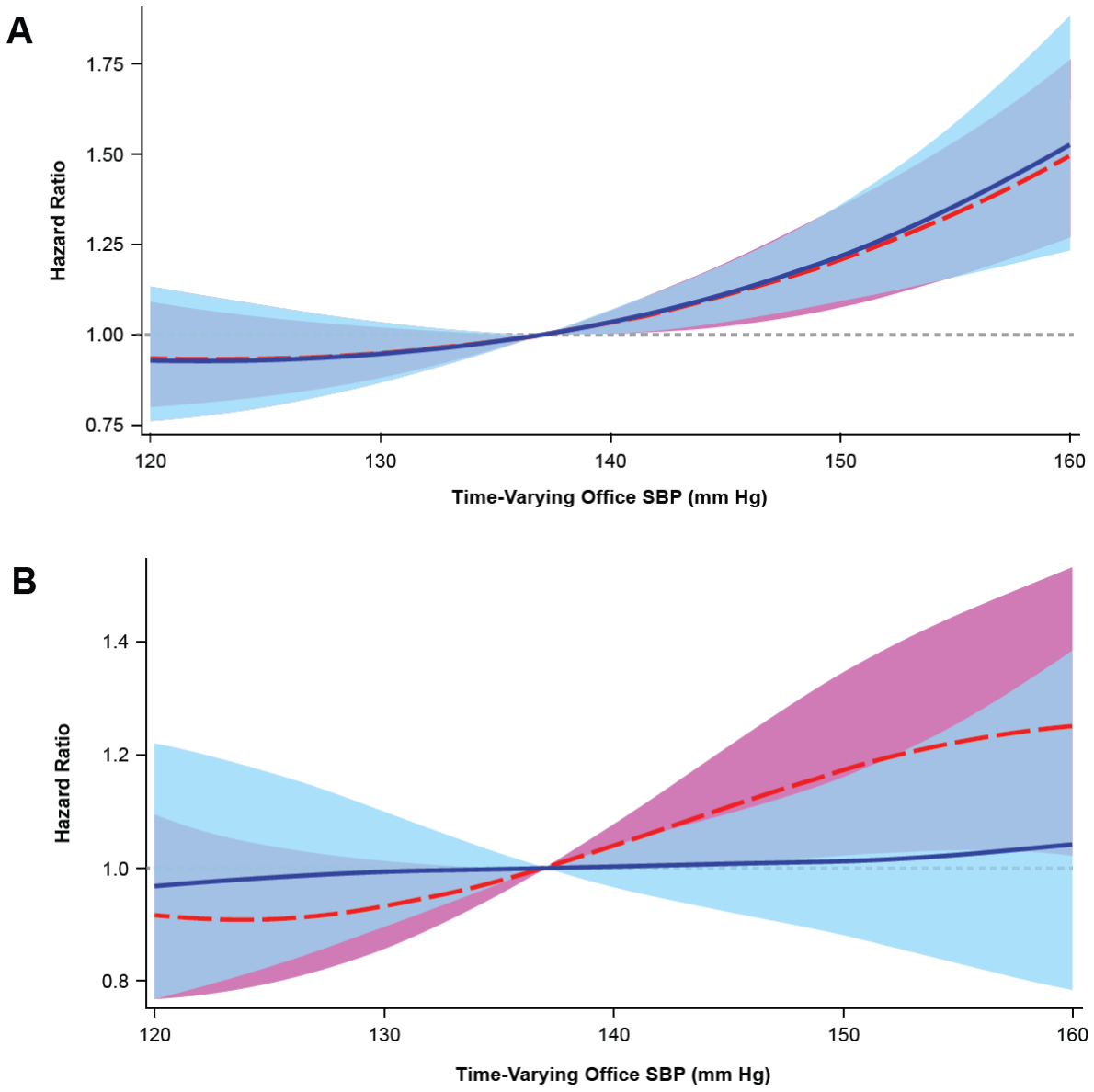
**Figure S4. Change in UACR From Baseline to Month 4 by SBP Quartile.**

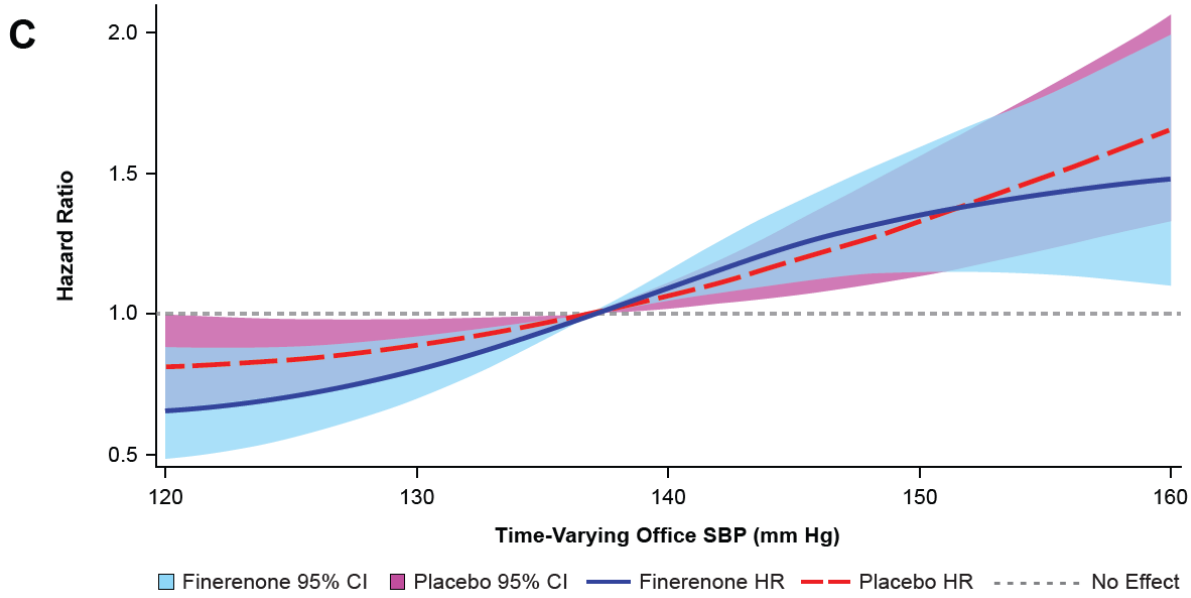
| Outcome | Finerenone | | Placebo | | Ratio of LS-mean (95% CI) |
|---|---|---|---|---|---|
| | N | gMean | N | gMean | |
| **Change in UACR From Baseline to Month 4** | | | | | |
| SBP Q1 (≤128.7 mm Hg) | 696 | 0.70 | 691 | 1.00 | 0.70 (0.65–0.76) |
| SBP Q2 (>128.7–≤138.3 mm Hg) | 635 | 0.66 | 654 | 0.95 | 0.69 (0.63–0.75) |
| SBP Q3 (>138.3–≤148.0 mm Hg) | 750 | 0.63 | 682 | 0.93 | 0.68 (0.63–0.73) |
| SBP Q4 (>148.0 mm Hg) | 629 | 0.64 | 678 | 0.93 | 0.69 (0.64–0.74) |




gMean indicates geometric mean; LS, least squares; Q, quartile; SBP, systolic blood pressure; and UACR, urine albumin-to-creatinine ratio.

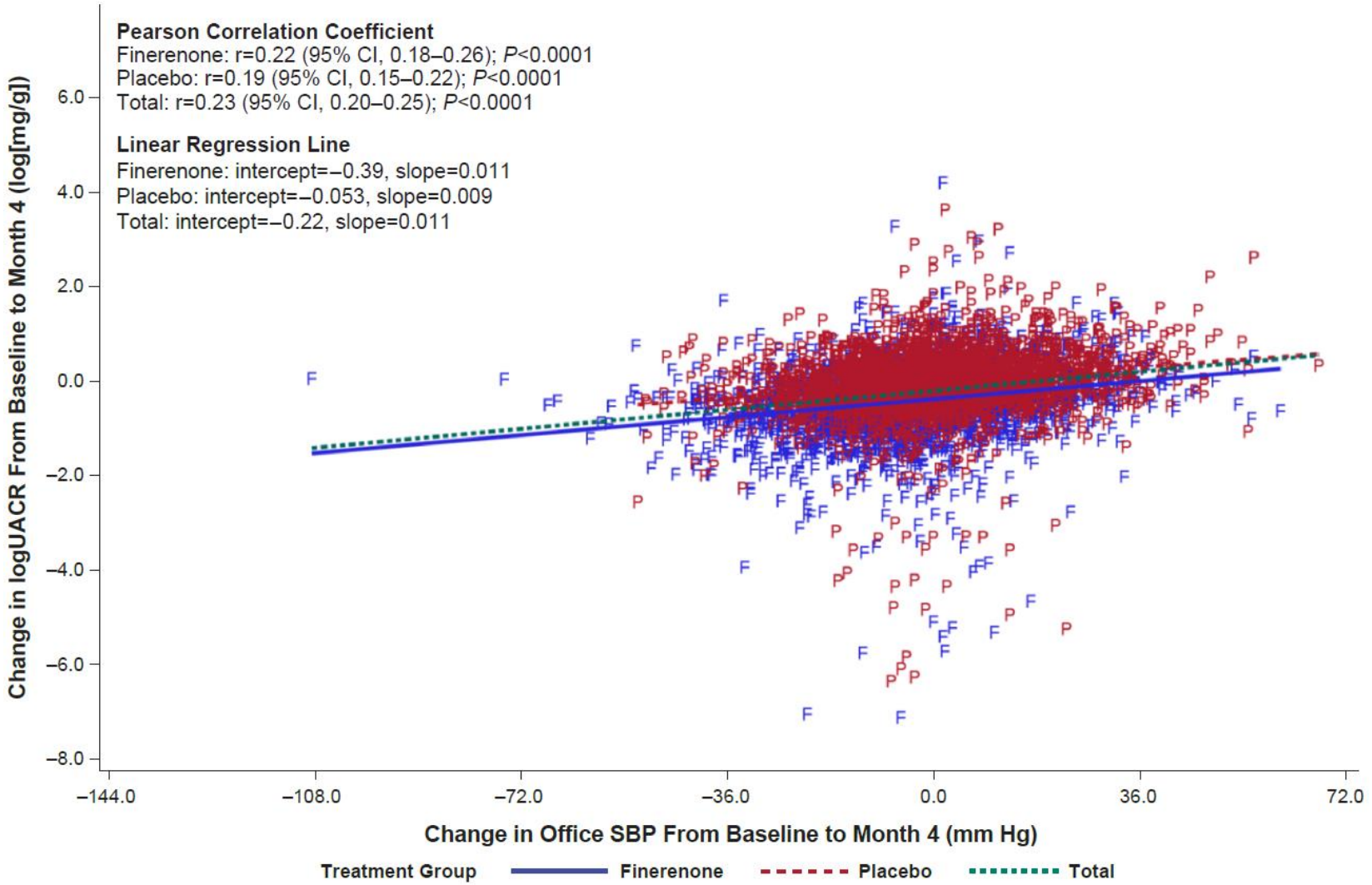
**Figure S5. Relationship of Time-varying Office SBP With Kidney Composite and CV Composite Outcomes.**






Cox proportional hazards models fitted separately by treatment group using cubic B-splines for office SBP and multivariable adjustment for (**A**) primary kidney composite outcome, (**B**) key secondary CV composite outcome, and (**C**) secondary kidney composite outcome. CV indicates cardiovascular; and SBP, systolic blood pressure.

**Figure S6. Correlation for Change From Baseline to Month 4 of SBP Versus Log UACR.**




F indicates finerenone; P, placebo; SBP, systolic blood pressure; and UACR, urine albumin-to-creatinine ratio.