**Supplemental material**

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**Supplemental Table 1:** Patients completed KCCQ total and domain scores at baseline and during follow-up

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Baseline** | **6 months and baseline** | **9 months and baseline** | **12 months and baseline** |
| **N** | 6001 | 6001 | 6001 | 6001 |
| **Total scores** |  |  |  |  |
| Total symptom score | 5986 (99.8) | 5356 (89.3) | 5036 (83.9) | 5004 (83.4) |
| Clinical summary score | 5987 (99.8) | 5359 (89.3) | 5037 (83.9) | 5006 (83.4) |
| Overall summary score | 5987 (99.8) | 5359 (89.3) | 5037 (83.9) | 5006 (83.4) |
| **Domain scores\*** |  |  |  |  |
| Physical limitation | 5892 (98.2) | 5215 (86.9) | 4872 (81.2) | 4848 (80.8) |
| Symptom frequency | 5986 (99.8) | 5356 (89.3) | 5035 (83.9) | 5003 (83.4) |
| Symptom burden | 5985 (99.7) | 5355 (89.2) | 5035 (83.9) | 5003 (83.4) |
| Quality of life | 5986 (99.8) | 5355 (89.2) | 5036 (83.9) | 5004 (83.4) |
| Social limitation | 5574 (92.9) | 4772 (79.5) | 4460 (74.3) | 4465 (74.4) |

Data are presented as N (%).

\*Domain scores used to create summary scores.

KCCQ, Kansas City Cardiomyopathy Questionnaire.

**Supplemental Table 2:** Clinical outcomes according to baseline KCCQ-TSS category divided by tertile

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Tertile 1: 0 to <57** | **Tertile 2: 57 to <81** | **Tertile 3: 81 to 100** |
| **N** | 1949 | 1984 | 2053 |
| **CV death and total worsening HF events** |  |  |  |
| No. of events (%) | 1031 (568, 29.1%) | 786 (441, 22.2%) | 540 (329, 16.0%) |
| Rate per 100 patient-years (95%CI) | 22.8 (20.6, 25.1) | 16.3 (14.5, 18.3) | 10.5 (9.2, 11.9) |
| RR (95%CI)\* | Ref. | 0.69 (0.59, 0.80) | 0.40 (0.34, 0.48) |
| Adjusted RR (95%CI)\*\* | Ref. | 0.85 (0.72, 0.99) | 0.59 (0.49, 0.72) |
| **Total worsening HF events** |  |  |  |
| No. of events (%) | 805 (446, 22.9%) | 639 (352, 17.7%) | 414 (249, 12.1%) |
| Rate per 100 patient-years (95%CI) | 17.8 (15.9, 19.9) | 13.3 (11.7, 15.1) | 8.0 (7.0, 9.3) |
| RR (95%CI)\* | ref | 0.71 (0.60, 0.85) | 0.38 (0.31, 0.47) |
| Adjusted RR (95%CI)\*\* | ref | 0.88 (0.74, 1.05) | 0.57 (0.45, 0.71) |
| **Total HF hospitalizations** |  |  |  |
| No. of events (%) | 712 (418, 21.4%) | 545 (322, 16.2%) | 356 (219, 10.7%) |
| Rate per 100 patient-years (95%CI) | 15.7 (14.1, 17.6) | 11.3 (9.9, 12.9) | 6.9 (5.9, 8.1) |
| RR (95%CI)\* | ref | 0.69 (0.58, 0.82) | 0.37 (0.30, 0.46) |
| Adjusted RR (95%CI)\*\* | ref | 0.86 (0.72, 1.03) | 0.55 (0.43, 0.70) |
| **Total urgent HF visits** |  |  |  |
| No. of events (%) | 93 (70, 3.6%) | 94 (67, 3.4%) | 58 (49, 2.4%) |
| Rate per 100 patient-years (95%CI) | 2.1 (1.6, 2.7) | 1.9 (1.5, 2.6) | 1.1 (0.8, 1.5) |
| RR (95%CI)\* | ref | 0.88 (0.61, 1.27) | 0.47 (0.31, 0.71) |
| Adjusted RR (95%CI)\*\* | ref | 1.04 (0.70, 1.50) | 0.69 (0.42, 1.12) |
| **CV death or worsening HF** |  |  |  |
| No. of events (%) | 568 (568, 29.1%) | 441 (441, 22.2%) | 329 (329, 16%) |
| Rate per 100 patient-years (95%CI) | 14.4 (13.2, 15.6) | 10.0 (9.1, 11.0) | 6.8 (6.1, 7.6) |
| HR (95%CI)\* | ref | 0.67 (0.59, 0.76) | 0.41 (0.36, 0.48) |
| Adjusted HR (95%CI)\*\* | ref | 0.82 (0.72, 0.94) | 0.59 (0.50, 0.69) |
| **Worsening HF** |  |  |  |
| No. of events (%) | 446 (446, 22.9%) | 352 (352, 17.7%) | 249 (249, 12.1%) |
| Rate per 100 patient-years (95%CI) | 11.3 (10.2, 12.4) | 8.0 (7.2, 8.9) | 5.1 (4.5, 5.8) |
| HR (95%CI)\* | ref | 0.67 (0.58, 0.78) | 0.39 (0.33, 0.45) |
| Adjusted HR (95%CI)\*\* | ref | 0.85 (0.73, 0.98) | 0.56 (0.47, 0.67) |
| **CV death** |  |  |  |
| No. of events (%) | 226 (226, 11.6%) | 147 (147, 7.4%) | 128 (128, 6.2%) |
| Rate per 100 patient-years (95%CI) | 5.0 (4.4, 5.7) | 3.0 (2.6, 3.6) | 2.5 (2.1, 3.0) |
| HR (95%CI)\* | ref | 0.61 (0.49, 0.75) | 0.48 (0.38, 0.60) |
| Adjusted HR (95%CI)\*\* | ref | 0.72 (0.57, 0.90) | 0.70 (0.54, 0.90) |
| **CV death or first HF hospitalization** |  |  |  |
| No. of events (%) | 541 (541, 27.8%) | 415 (415, 20.9%) | 302 (302, 14.7%) |
| Rate per 100 patient-years (95%CI) | 13.5 (12.4, 14.7) | 9.3 (8.5, 10.3) | 6.2 (5.5, 6.9) |
| HR (95%CI)\* | ref | 0.66 (0.58, 0.76) | 0.40 (0.34, 0.46) |
| Adjusted HR (95%CI)\*\* | ref | 0.82 (0.71, 0.94) | 0.57 (0.48, 0.67) |
| **First HF hospitalization** |  |  |  |
| No. of events (%) | 418 (418, 21.4%) | 322 (322, 16.2%) | 219 (219, 10.7%) |
| Rate per 100 patient-years (95%CI) | 10.4 (9.4, 11.5) | 7.2 (6.5, 8.1) | 4.5 (3.9, 5.1) |
| HR (95%CI)\* | ref | 0.66 (0.57, 0.76) | 0.36 (0.30, 0.43) |
| Adjusted HR (95%CI)\*\* | ref | 0.83 (0.71, 0.97) | 0.52 (0.43, 0.64) |
| **All cause death** |  |  |  |
| No. of events (%) | 444 (444, 22.8%) | 324 (324, 16.3%) | 241 (241, 11.7%) |
| Rate per 100 patient-years (95%CI) | 9.8 (8.9, 10.7) | 6.7 (6.0, 7.4) | 4.7 (4.1, 5.3) |
| HR (95%CI)\* | ref | 0.66 (0.57, 0.76) | 0.44 (0.37, 0.52) |
| Adjusted HR (95%CI)\*\* | ref | 0.77 (0.66, 0.90) | 0.62 (0.52, 0.75) |

Values are N (n, %), unless otherwise indicated.

\*Stratified by/adjusted for geographic region and baseline LVEF (<60%, ≥60%).

\*\*Adjusted for age, sex, heart rate, systolic blood pressure, body mass index, prior hospitalization for HF, NYHA functional class III/IV, left ventricular ejection fraction, estimated glomerular filtration rate, NT-proBNP (log-transformed), atrial fibrillation, myocardial infarction, and diabetes mellitus.

Abbreviations and definitions as in **Table 2**.

**Supplemental Table 3:** Safety outcomes according to baseline KCCQ-TSS category divided by tertile

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Tertile 1: 0 to <57** | **Tertile 2: 57 to <81** | **Tertile 3: 81 to 100** |
| **N** | 1949 | 1984 | 2053 |
| **Systolic blood pressure < 100 mmHg** | 248 (13.2) | 257 (13.4) | 391 (19.6) |
| **Creatinine ≥3 mg/dL** | 42 (2.3) | 27 (1.4) | 22 (1.1) |
| **Creatinine ≥2.5 mg/dL** | 97 (5.2) | 67 (3.5) | 66 (3.3) |
| **Potassium >6 mmol/L** | 39 (2.1) | 51 (2.7) | 36 (1.8) |
| **Potassium >5.5 mmol/L** | 198 (10.6) | 214 (11.2) | 198 (9.9) |
| **Potassium <3.5 mmol/L** | 159 (8.5) | 101 (5.3) | 147 (7.4) |

Values are N (%) unless otherwise stated. Safety analyses were carried out in patients who had undergone enrolment and received at least one dose of the randomized treatment (a total of 15 randomized patients were excluded from the safety analysis). Safety events were considered treatment-emergent if they occurred between the day of treatment initiation up to and including 3 days after treatment discontinuation.

KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire total symptom score.

**Supplemental Table 4:** Effect of finerenone on KCCQ-TSS from baseline to 12 months

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Method | Dataset | Estimate | Lower | Upper | *P*-value |
| ANCOVA | Current | 1.39 | 0.28 | 2.50 | 0.014 |
| Imputation | 1.40 | 0.28 | 2.52 | 0.014 |
| Mixed model | Current | 1.6 | 0.8 | 2.4 | <0.001 |
| Imputation | 1.4 | 0.3 | 2.5 | 0.011 |
| Responder  5 point improvement | Current | 1.04 | 0.94 | 1.16 | 0.45 |
| Imputation | 1.04 | 0.93 | 1.16 | 0.47 |
| Responder  10 point improvement | Current | 1.08 | 0.97 | 1.2 | 0.16 |
| Imputation | 1.08 | 0.97 | 1.2 | 0.16 |
| Responder  20 point improvement | Current | 1.15 | 1.03 | 1.28 | 0.01 |
| Imputation | 1.14 | 1.03 | 1.27 | 0.01 |
| Decrease  5 point deterioration | Current | 0.92 | 0.81 | 1.03 | 0.14 |
| Imputation | 0.92 | 0.92 | 1.03 | 0.15 |

ANCOVA, Analysis of covariance; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire total symptom score.

**Supplemental Figure 1:** Distribution of KCCQ-TSS at baseline

KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire total symptom score.



**Supplemental Figure 2:** Cumulative incidence of clinical outcomes according to baseline KCCQ-TSS category divided by tertile. (A) CV death and total worsening HF events; (B) HF events; (C) CV death; (D) all-cause death.

CV, cardiovascular; HF, heart failure; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire Total Symptom Score.



**Supplemental Figure 3:** Incidence rates of outcomes across baseline KCCQ-TSS. (A) CV death and total worsening HF events; (B) HF events; (C) CV death; (D) all-cause death. Placebo: red (upper line); finerenone: blue (lower line).

CV, cardiovascular; HF, heart failure; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire Total Symptom Score.



**Supplemental Figure 4:** Adjusted mean difference in KCCQ-CSS, -TSS, -OSS, and subdomains by randomized treatment allocation at 6, 9, and 12 months.

KCCQ, Kansas City Cardiomyopathy Questionnaire; CSS, Clinical Summary Score; OSS, Overall Summary Score; TSS, Total Symptom Score.



**Supplemental Figure 5:** Overall average mean difference in KCCQ-CSS, TSS, OSS, and subdomains attributable to finerenone over the follow-up period (across 0, 6, 9, and 12 months).

KCCQ, Kansas City Cardiomyopathy Questionnaire; CSS, Clinical Summary Score; OSS, Overall Summary Score; TSS, Total Symptom Score.

