

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)

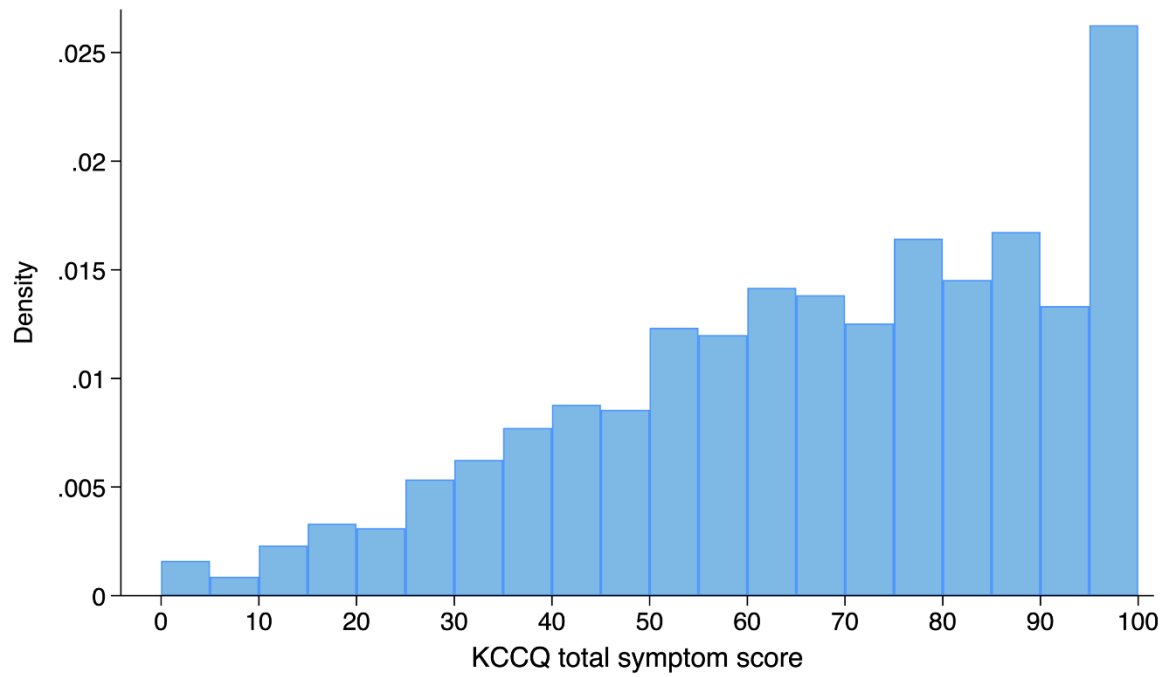
Values are N (%) unless otherwise stated. Safety analyses were carried out in patients who had undergone enrolment and received at least one dose of the randomized treatment (a total of 15 randomized patients were excluded from the safety analysis). Safety events were considered treatment-emergent if 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

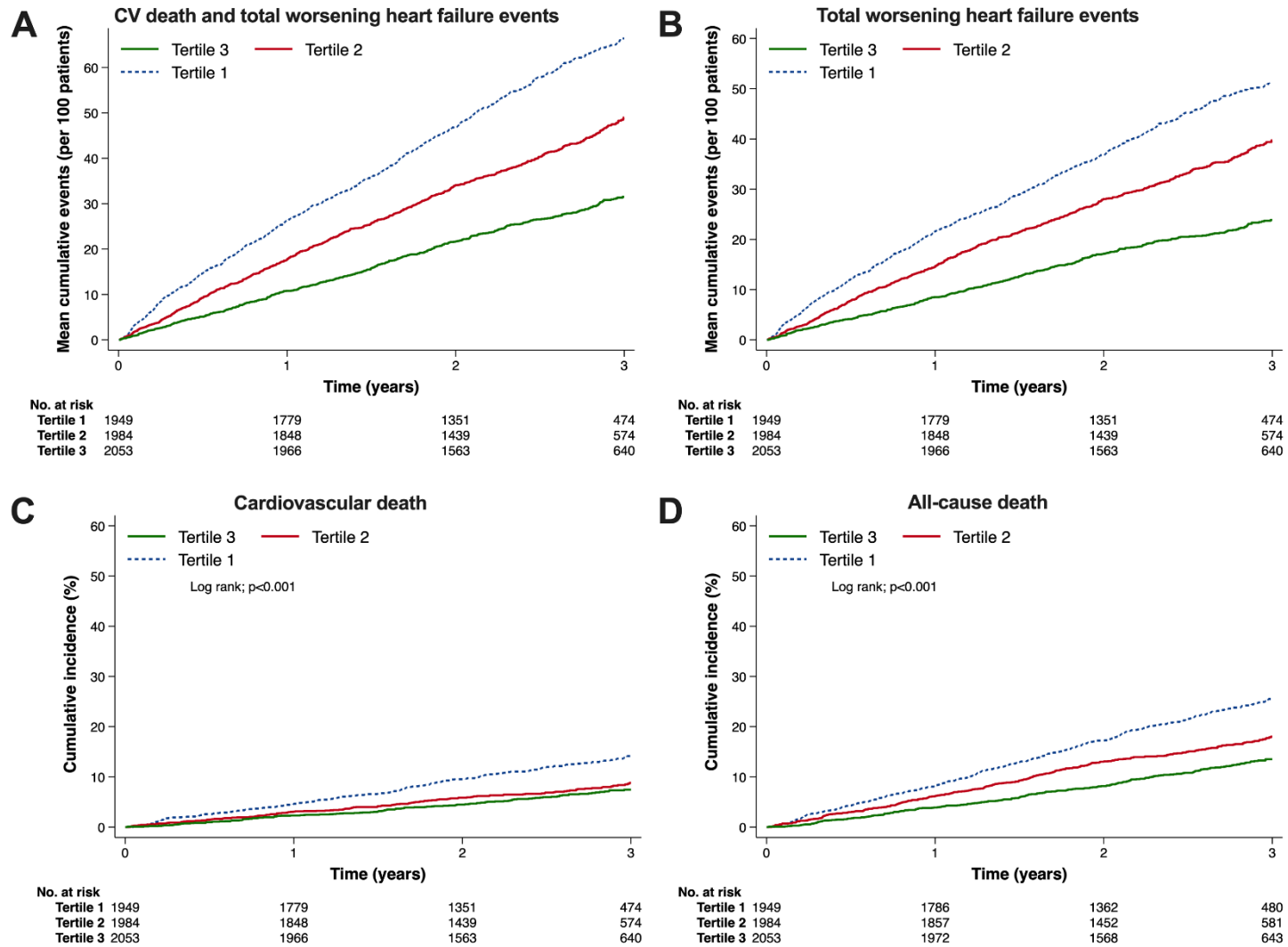
Method	Dataset	Estimate	Lower	Upper	<i>P</i> -value
ANCOVA	Current	1.39	0.28	2.50	0.014
	Imputation	1.40	0.28	2.52	0.014
Mixed model	Current	1.6	0.8	2.4	<0.001
	Imputation	1.4	0.3	2.5	0.011
Responder 5 point improvement	Current	1.04	0.94	1.16	0.45
	Imputation	1.04	0.93	1.16	0.47
Responder 10 point improvement	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.

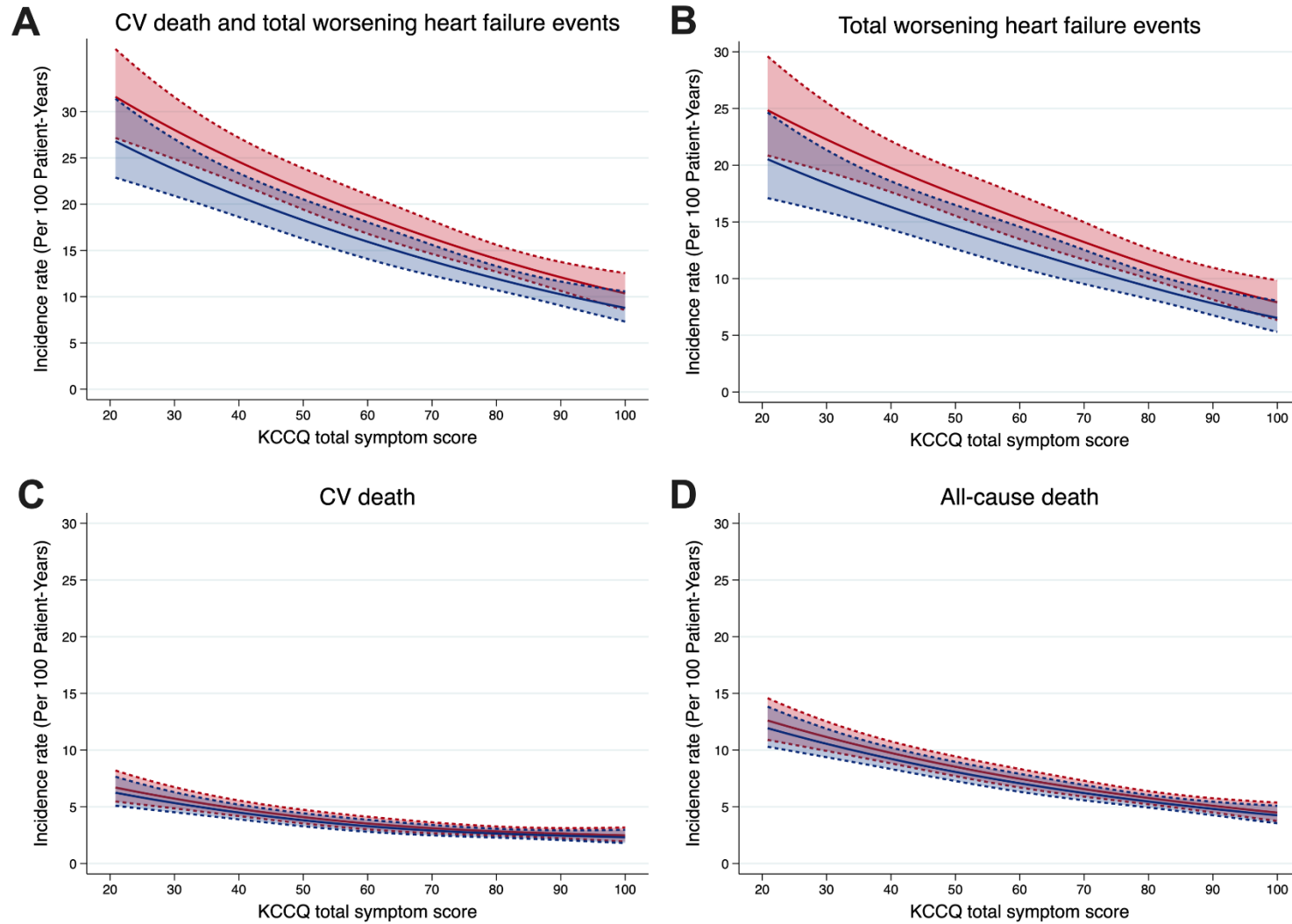
Supplemental Figure 1: Distribution of KCCQ-TSS at baseline
KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire total symptom score.



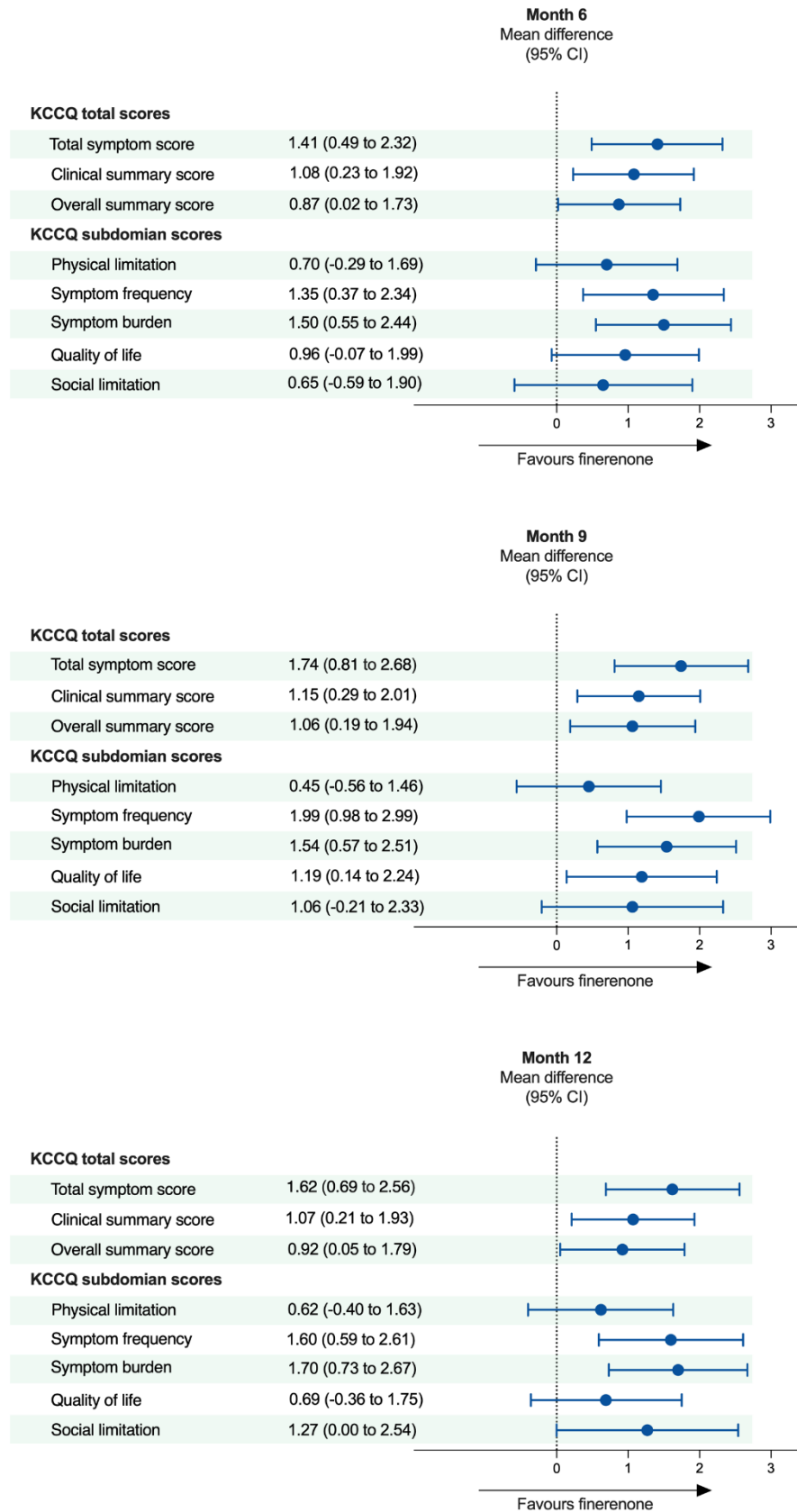
Supplemental Figure 2: Cumulative incidence of clinical outcomes according to baseline KCCQ-TSS category divided by tertile. (A) CV death and total worsening HF events; (B) HF events; (C) CV death; (D) all-cause death. CV, cardiovascular; HF, heart failure; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire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

