University of Glasgow

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Serum Creatine Kinase Concentration and Clinical Outcomes in Patients with HFmrEF/HFpEF: Results from FINEARTS-HF

FINEARTS-HF
FINerenone trial to investigate Efficacy and sAfety superioR to placebo in paTientS with Heart Failure

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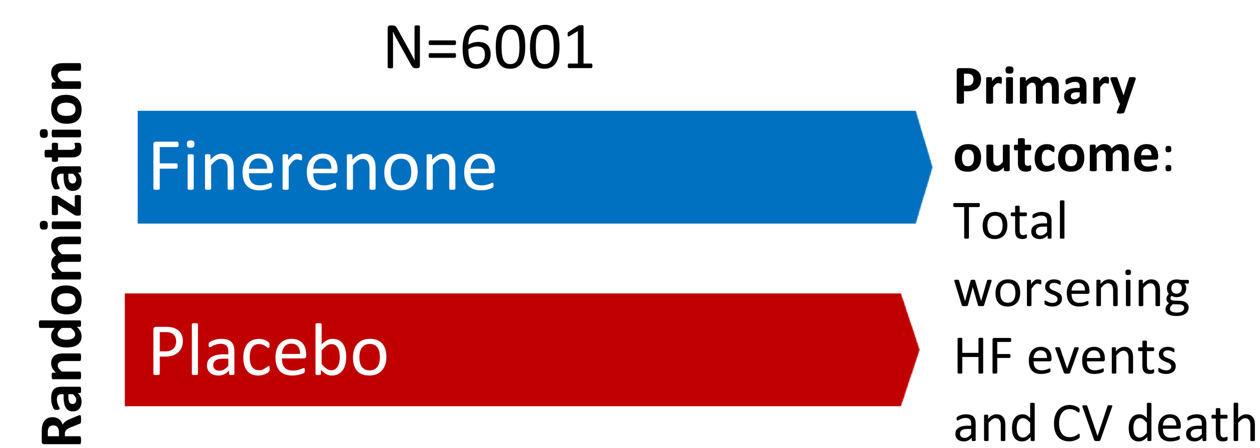
BACKGROUND

- Serum creatine kinase (CK) levels in heart failure may reflect skeletal muscle health and may be prognostically important.
- We aimed to assess the relationship between serum CK levels, clinical characteristics, and outcomes in patients with HFmrEF/HFpEF enrolled in the FINEARTS-HF trial and to evaluate the effect of finerenone, compared with placebo, according to baseline CK concentration, and the effect of finerenone on CK level after randomization.

METHODS

Trial and population

- FINEARTS-HF trial: A multicenter, randomized, double-blind, parallel-group, placebo-controlled study to evaluate the efficacy and safety of finerenone on morbidity and mortality in participants with heart failure (NYHA II-IV) and left ventricular ejection fraction (LVEF) ≥40%



CK

- CK (U/L) levels were measured at randomization, 1 month, 6 months, 9 months, and 12 months after randomization.

STATISICAL ANALYSIS

- Trend tests were applied to assess trends across CK quartiles for both continuous and categorical variables
- The association between serum CK levels and clinical outcomes was evaluated using semiparametric proportional rates models for total events and Cox models for time-to-first-event data, stratified by geographic region and baseline LVEF (<60%, ≥60%)
- Analysis of covariance (ANCOVA) was used to evaluate the effect on change in CK from baseline to 12 months.

RESULTS

Table 1: Baseline characteristics

	Q1: <56	Q2: 56 to <80	Q3: 80 to <118	Q4: ≥118	P for trend
N, %	1465 (25.0)	1455 (24.8)	1449 (24.7)	1495 (25.5)	
Demographics and physiologic measures					
Age, yr	73.5 ± 9.5	72.2 ± 9.2	71.8 ± 9.5	70.4 ± 10.2	<0.001
Female	640 (43.7)	781 (53.7)	813 (56.1)	967 (64.7)	<0.001
SBP, mmHg	128.1 ± 15.5	129.1 ± 15.7	129.4 ± 14.8	130.9 ± 15.4	<0.001
≥140	331 (22.6)	354 (24.3)	360 (24.9)	413 (27.6)	0.002
BMI, kg/m^2	30.1 ± 6.4	29.9 ± 6.2	29.7 ± 6.1	30.1 ± 5.8	0.69
≥30	691 (47.3)	653 (45.0)	625 (43.2)	668 (44.8)	0.12
Comorbidities					
AF	934 (63.8)	806 (55.4)	739 (51.0)	703 (47.0)	<0.001
Hypertension	1326 (90.5)	1280 (88.0)	1271 (87.7)	1326 (88.7)	0.12
MI	315 (21.5)	369 (25.4)	400 (27.6)	432 (28.9)	<0.001
Stroke	168 (11.5)	184 (12.6)	165 (11.4)	172 (11.5)	0.76
DM	686 (46.9)	582 (40.1)	557 (38.5)	564 (37.9)	<0.001
CKD	765 (52.2)	676 (46.5)	666 (46.0)	708 (47.4)	0.01
Heart failure history and characteristics					
Previous HF hospitalization	1020 (69.6)	914 (62.8)	814 (56.2)	781 (52.2)	<0.001
KCCQ-TSS	62.1 ± 24.8	67.3 ± 23.5	69.6 ± 23.4	69.2 ± 23.3	<0.001
NYHA III/IV	567 (38.7)	434 (29.8)	408 (28.2)	397 (26.6)	<0.001
KCCQ-CSS	64.1 (45.8-80.2)	68.8 (50.0-84.3)	71.9 (56.8-85.4)	70.1 (56.3-82.6)	<0.001
LVEF, %	52.8 ± 7.7	52.3 ± 7.8	52.4 ± 7.7	52.8 ± 8.1	0.99
NT-proBNP, pg/ml	1316 (570-2579)	1064 (450-1924)	963 (426-1820)	861 (400-1587)	<0.001
UACR, mg/g	128.6 ± 376.0	137.5 ± 465.4	139.5 ± 597.2	227.1 ± 836.4	<0.001
eGFR, ml/min/1.73 m^2	60.5 ± 20.0	63.1 ± 19.7	62.8 ± 19.2	62.3 ± 19.9	0.02
Background therapy at baseline					
Loop diuretics	1334 (91.1)	1281 (88.0)	1229 (84.8)	1277 (85.4)	<0.001
Beta-blocker	1265 (86.3)	1233 (84.7)	1225 (84.5)	1259 (84.2)	0.11
CCB	457 (31.2)	470 (32.3)	472 (32.6)	527 (35.3)	0.02
ACEi/ARB/ARNI	1107 (75.6)	1161 (79.8)	1182 (81.6)	1207 (80.7)	<0.001
SGLT2i	261 (17.8)	196 (13.5)	190 (13.1)	154 (10.3)	<0.001
CRT-P or CRT-D	7 (0.5)	4 (0.3)	9 (0.6)	9 (0.6)	0.38

Data are presented as mean ± SD or median (IQR) for continuous measures, and n (%) for categorical measures.
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; AF, atrial fibrillation; BMI, body mass index; CCB, calcium channel blocker; CKD, chronic kidney disease; CRT-D, cardiac resynchronization therapy with defibrillator; CRT-P, cardiac resynchronization therapy with pacemaker; DM, Diabetes Mellitus; eGFR, estimated glomerular filtration rate; HF, heart failure; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire total symptom score; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NT-proBNP, N-terminal pro B-type natriuretic peptide; NYHA, New York Heart Association; SBP, systolic blood pressure; SGLT2i, sodium-glucose cotransporter-2 inhibitors; UACR, urine albumin-to-creatinine ratio; yr, year.

CONCLUSIONS

- High serum CK concentrations are associated with better clinical outcomes in patients with HFmrEF/HFpEF, possibly because they reflect better skeletal muscle health in this population.
- The effects of finerenone compared to placebo were consistent across CK groups.
- Improving muscular health could potentially improve clinical outcomes in this population.

Figure 1: Cumulative incidence of clinical outcomes according to quartiles of baseline CK

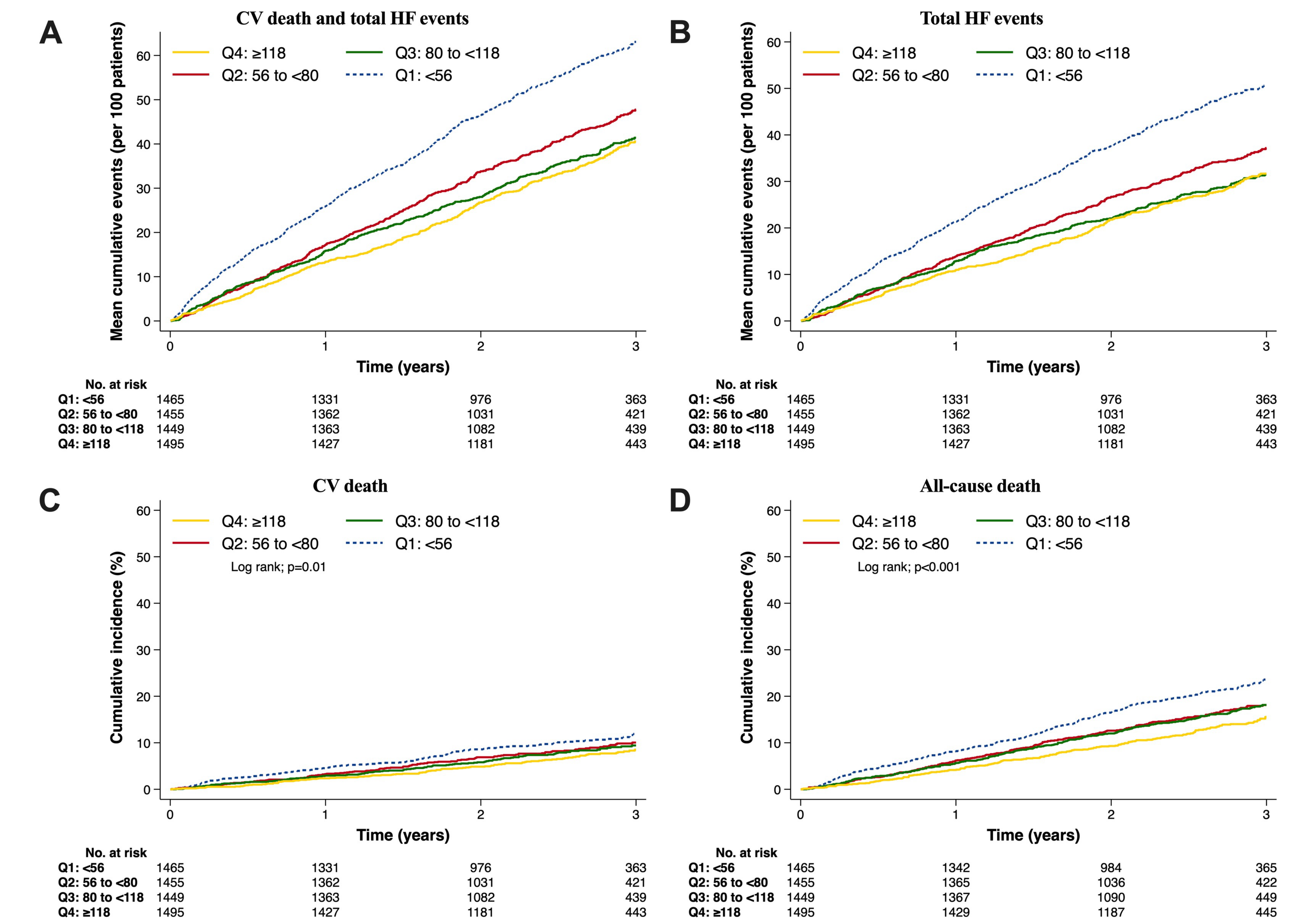


Figure 2: Effect of finerenone on clinical outcome according to quartiles of baseline CK

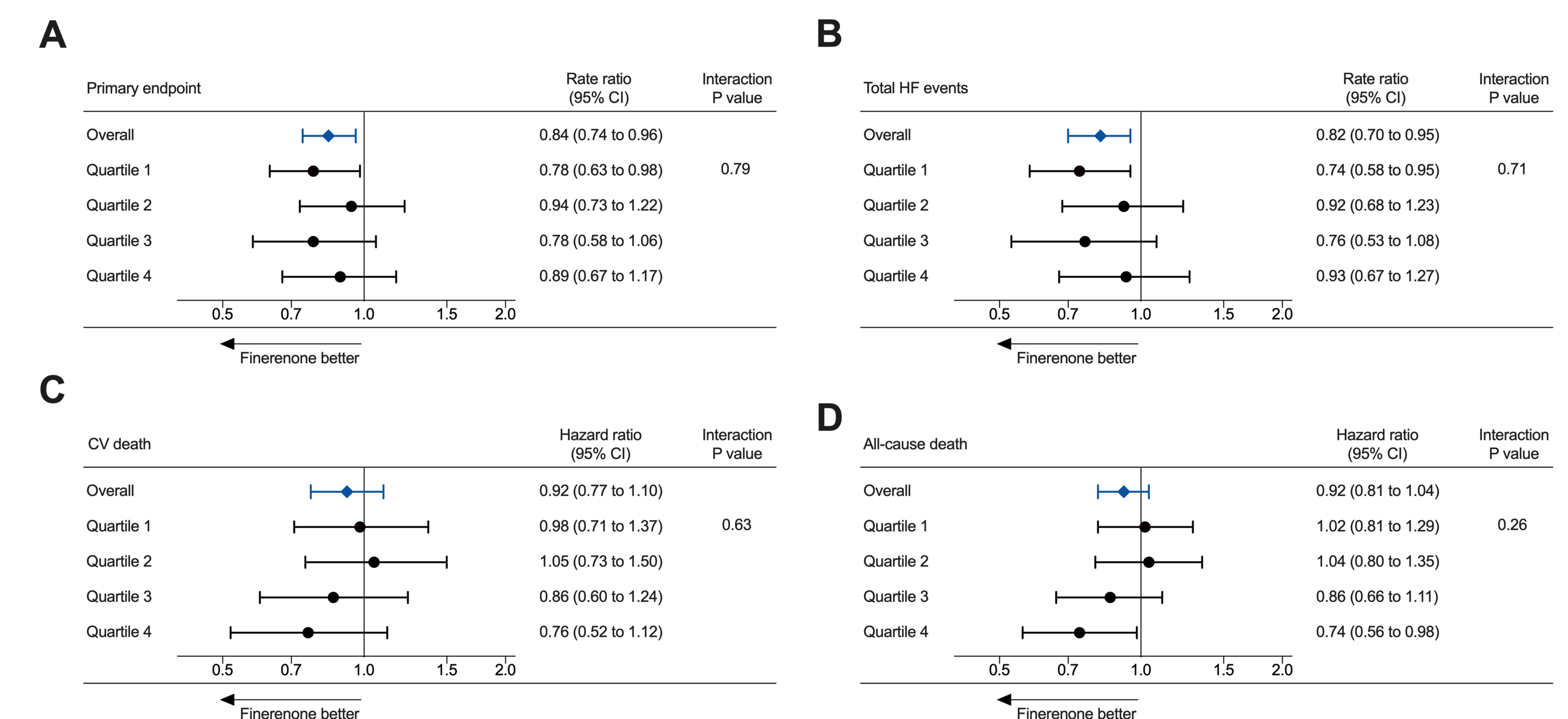


Table 2: Mean change of CK from baseline to 12 months by treatment assignment

	Mean ± SD		48 weeks from baseline	
	Baseline	12 months	Mean change	Mean difference (95% CI)
Finerenone (n=2330)	103.7±150.6	105.9±104.7	1.6 (-2.6 to 5.8)	1.4 (-3.8 to 6.5)
Placebo (n=2349)	103.5±96.0	107.3±83.8	0.2 (-4.0 to 4.4)	P = 0.60

Analysis were adjusted for baseline value, geographic region and baseline LVEF (<60%, ≥60%). CI, confidence interval; IQR, interquartile range; SD, standard deviation.

DISCLOSURES: The FINEARTS- HF trial was funded by Bayer.