Finerenone and Serum Sodium in Patients with Heart Failure and Mildly Reduced or Preserved Ejection Fraction: An Analysis of FINEARTS-HF

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Background: Serum sodium in FINEARTS-HF

- Serum sodium concentration is a fundamental marker of fluid homeostasis, and hyponatraemia is associated with adverse outcomes in heart failure (HF), particularly in HF with reduced ejection fraction; however, its prognostic significance in HF with preserved ejection fraction is less well established.[1,2]
- Steroidal mineralocorticoid receptor antagonists (sMRAs), such as spironolactone, reduce aldosterone-mediated sodium retention, and observational studies in HF and cirrhosis have reported associations between sMRA use and hyponatraemia.[3]
- However, the effect of the nonsteroidal MRA, finerenone, on serum sodium concentration is still unknown.

1. Eur J Heart Fail 2012;14:1147-1154. 2. Curr Heart Fail Rep 2024;21:252-261. 3. JAMA 1973;225:40-43.

Objectives and methods: Serum sodium in FINEARTS-HF

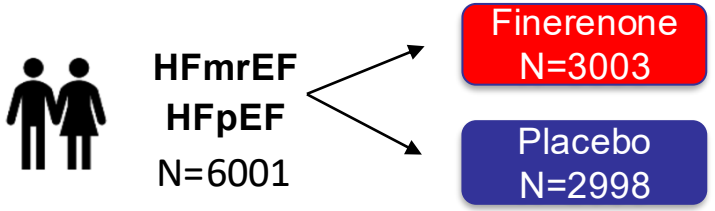
Objectives

- To examine the distribution and prognostic significance of serum sodium concentration, and the effects of finerenone on serum sodium concentration and clinical outcomes.

Key inclusion criteria

- LVEF ≥ 40% + structural heart disease
- NYHA functional class II-IV
- Elevated natriuretic peptides
- Diuretics in the 30 days prior to randomization

No exclusion criteria related to serum sodium



Primary endpoint

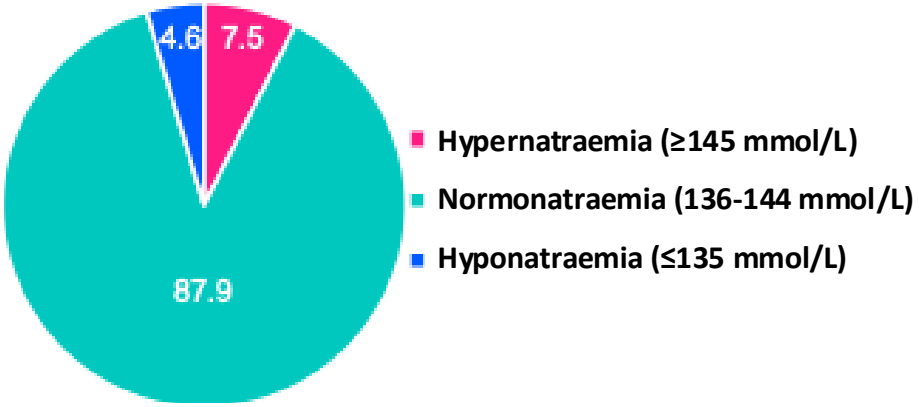
The composite of total (first and recurrent) HF events (i.e. HF hospitalisation or an urgent HF visit) and CV death

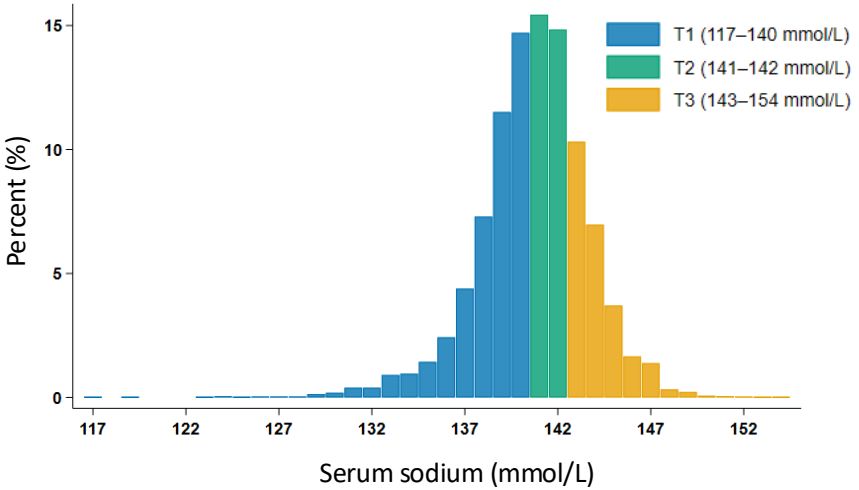
Serum sodium measurement

- Serum sodium level was measured in a central laboratory at baseline, as well as 1, 3, 6, 9, 12, 16, 20 and 24 months after randomization.

Baseline clinical characteristics by serum sodium category

Prevalence of hypernatraemia, normonatraemia, and hyponatraemia

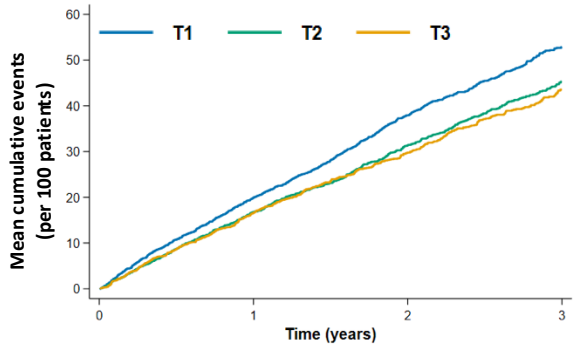




Serum sodium tertile (T)	T1 Na 117-140 (n = 2,632)	T2 Na 141-142 (n = 1,773)	T3 Na 143-154 (n = 1,450)	P for trend
Age (years)	72	72	72	0.57
Sex, male (%)	58	53	51	**<0.001**
NYHA III/IV (%)	31	30	31	0.90
Body mass index (kg/m²)	30	30	30	**0.023**
LVEF (%)	53	53	53	0.37
NT-proBNP (pg/mL)	994	1014	1138	**0.002**
Serum creatinine (mmol/L)	102	98	98	**<0.001**
eGFR (mL/min/1.73m²)	62	63	63	**0.040**
Serum potassium (mmol/L)	4.4	4.4	4.3	**<0.001**
Haematocrit (%)	40	41	41	**<0.001**
Diabetes (%)	45	38	36	**<0.001**
Atrial fibrillation/flutter (%)	53	54	60	**<0.001**
Prior HF hospitalization (%)	63	57	59	**0.010**
ACE-I/ARB/ARNI (%)	78	80	81	0.061
Beta-blocker (%)	84	84	88	**0.001**
Thiazide diuretic (%)	15	13	13	0.10
Loop diuretic (%)	86	88	89	**0.024**
Loop diuretic dose (mg) (furosemide equivalent)	40	40	40	0.96

Clinical outcomes according to serum sodium tertile/level

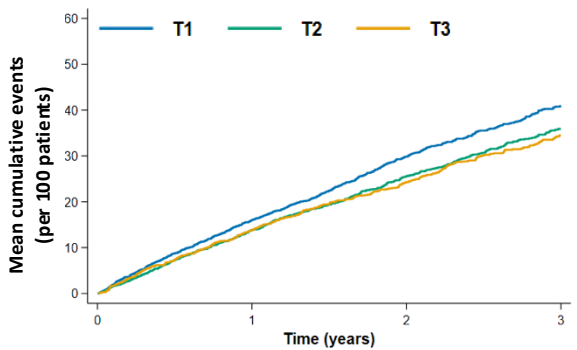
Total HF events and CV death



No. at risk

T1	2632	2422	1840	663
T2	1773	1681	1338	525
T3	1450	1371	1088	476

Total HF events



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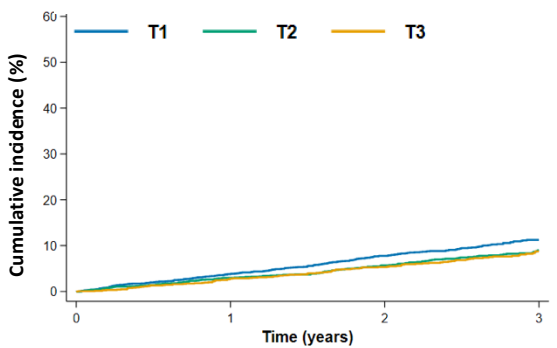
CV death



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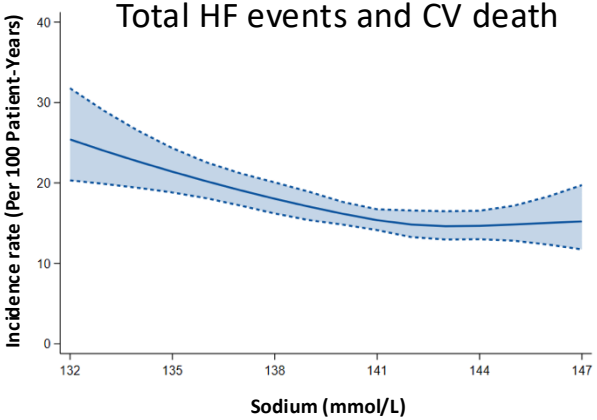
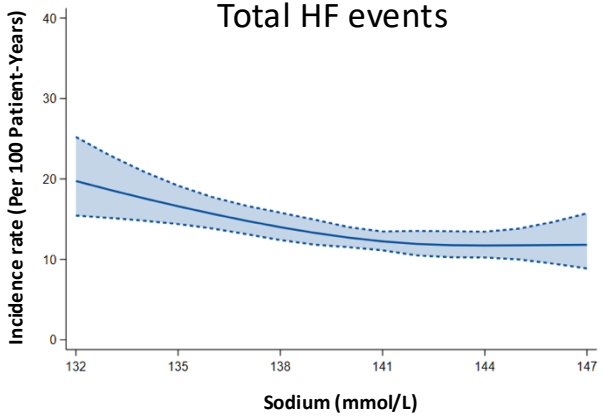
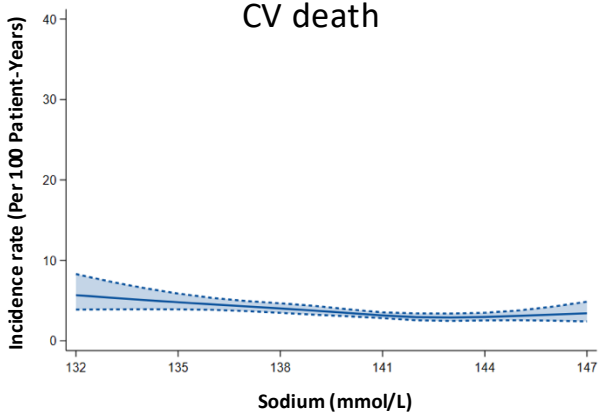


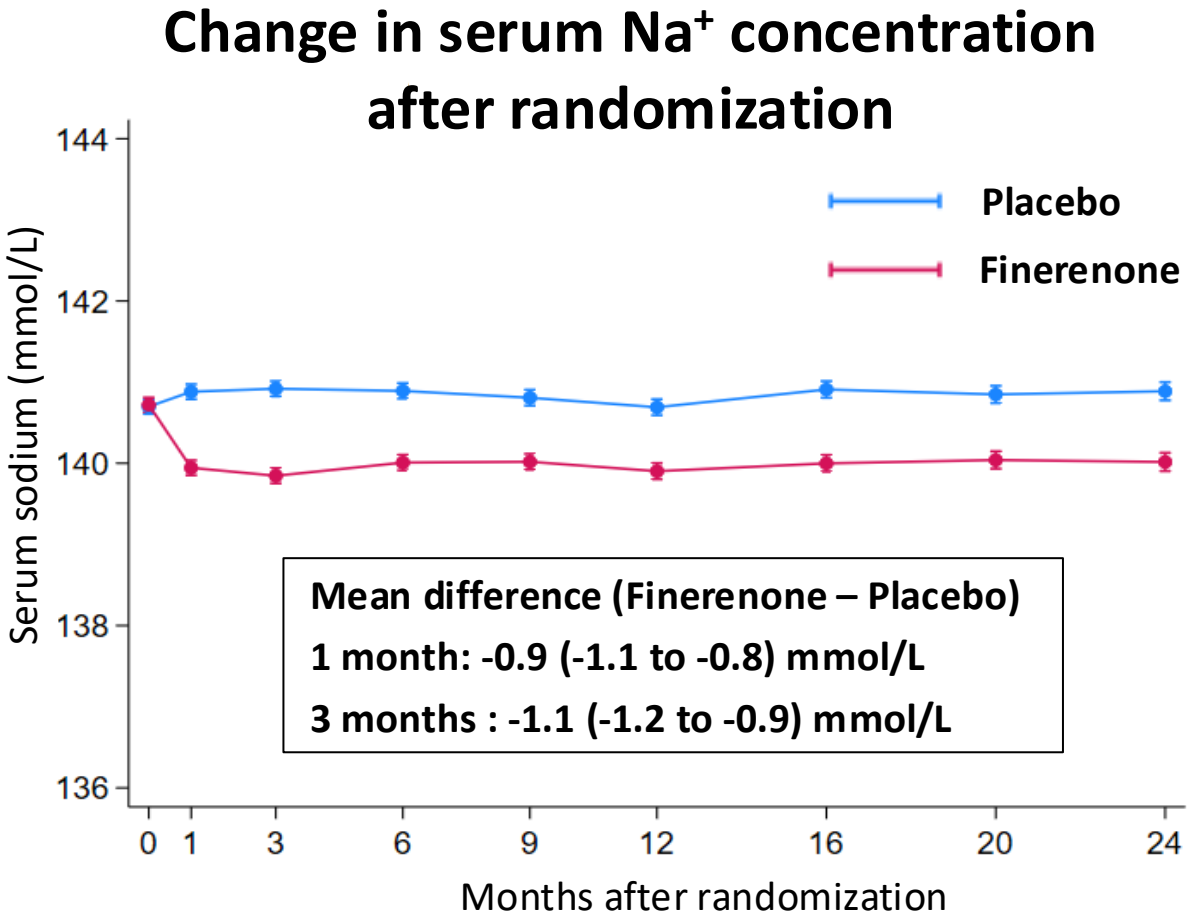
Total HF events



CV death

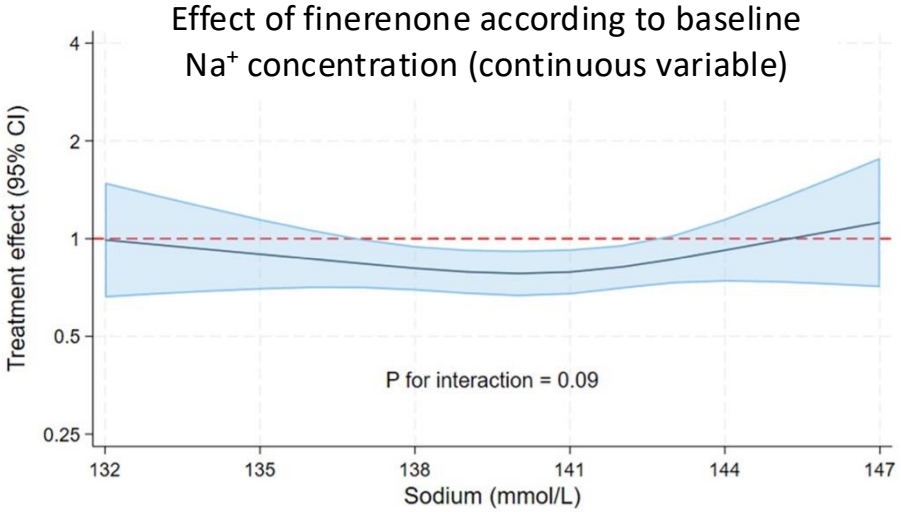


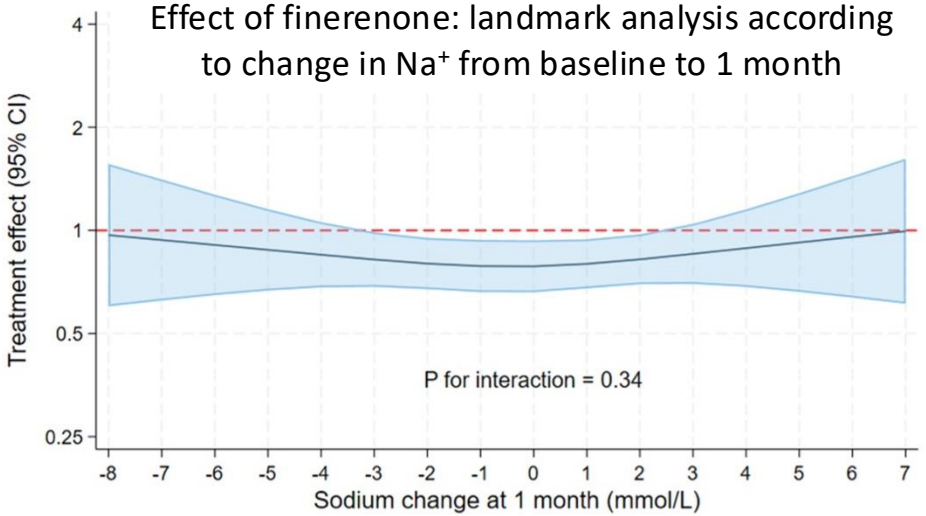
Effect of finerenone on serum sodium during follow-up



Effect of finerenone on CV death and HF events according to Na^+ level

	Tertile 1 (Na^+ 117-140 mmol/L) (n = 2,632)		Tertile 2 (Na^+ 141-142 mmol/L) (n = 1,773)		Tertile 3 (Na^+ 143-154 mmol/L) (n = 1,450)		Interaction P value
	Finerenone (n = 1,295)	Placebo (n = 1,337)	Finerenone (n = 896)	Placebo (n = 877)	Finerenone (n = 739)	Placebo (n = 711)	
Total HF events and cardiovascular death							
Total No. of events	495	628	310	352	253	272	
Event rate (95% CI)	16.2 (14.2-18.5)	19.9 (17.6-22.5)	14.0 (11.7-16.8)	16.1 (13.6-19.2)	13.6 (10.9-17.0)	15.5 (12.9-18.5)	
Rate ratio (95% CI)	0.82 (0.68-0.98)		0.85 (0.66-1.09)		0.91 (0.68-1.21)		0.87





Conclusions: Serum sodium in FINEARTS-HF

- Hyponatraemia (≤135 mmol/L) was uncommon (4.6%) at baseline in FINEARTS-HF.
- Treatment with finerenone led to only a small (approximately 1 mmol/L) reduction in serum sodium concentration during follow-up.
- The benefits of finerenone were consistent across the range of baseline sodium concentrations and were not modified by early changes in serum sodium concentration.