HARVARD MEDICAL SCHOOL

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Scientific Sessions

Time in High-Normal Potassium Range and Cardiovascular Outcomes Across the Cardio-Kidney-Metabolic Spectrum

A FINE-HEART participant-level analysis

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#ScientificSessions26

DISCLOSURES

Presenter: Henri Lu

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Background & Rationale

- Dyskalemia is common in HF and CKD, with both low and high serum potassium associated with adverse outcomes.
- Most prior studies relied on potassium levels at a single time point, rather than longitudinal exposure.
- POTCAST showed that targeting K 4.5–5.0 mmol/L reduced arrhythmic and clinical events in patients at high risk for ventricular arrhythmias.
- Whether sustained high-normal potassium exposure has prognostic relevance across the broader CKM spectrum is uncertain.

TIME IN TARGET RANGE

% of the first year with estimated serum K within 4.5–5.0 mmol/L.

OBJECTIVE

Assess TIR and subsequent CV outcomes, and explore whether potassium TIR accounts for the treatment benefit of finerenone.

Methods

Pooled individual-participant analysis of three randomized, placebo-controlled trials

FIDELIO-DKD

UACR 30–299 + eGFR 25–59
+ diabetic retinopathy
UACR ≥300 + eGFR 25–74

FIGARO-DKD

UACR 30–299 + eGFR 25–90
UACR ≥300 + eGFR ≥60

FINEARTS-HF

Symptomatic HF; LVEF ≥40%

- **TIR:** Daily serum K values were interpolated between protocolized visits during the first year. TIR within 4.5–5.0 mmol/L was calculated and analyzed continuously and by categories (<25, 25–<50, 50–<75, ≥75%).

- **Statistical analysis:** Cox models at a 1-year landmark, using linear splines and categories, adjusted for baseline potassium, CV and renal risk factors, and randomized treatment; stratified by trial.

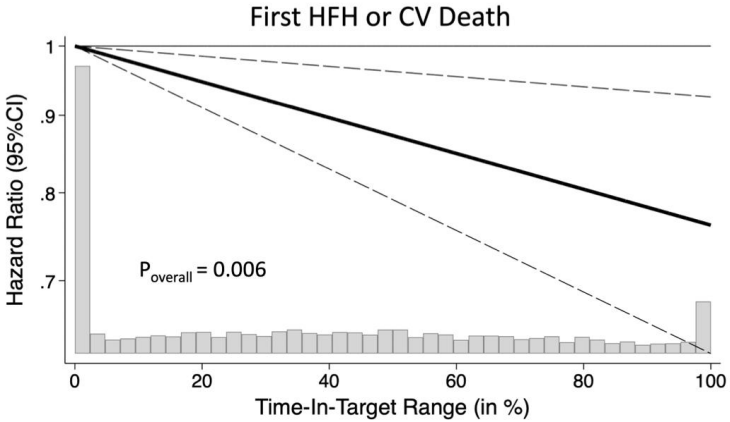
- **Outcomes:** First HF hospitalization or CV death (primary), individual components of the primary outcome.

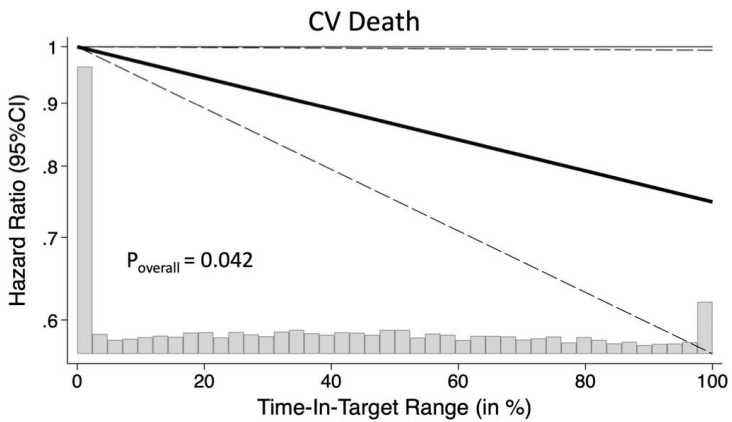
Baseline Characteristics by Potassium TIR Category

Selected characteristics | N=18,345 | Median subsequent follow-up: 1.9 years

Characteristic	TIR <25%	25–<50%	50–<75%	≥75%	P trend
Participants, n	8,137	3,940	3,311	2,957	—
Age, years	66.4 ± 10.5	66.9 ± 9.9	67.3 ± 9.8	67.7 ± 9.6	<0.001
Women, %	33.7	36.3	37.5	34.7	0.020
Baseline K, mmol/L	4.2 ± 0.5	4.4 ± 0.4	4.5 ± 0.4	4.6 ± 0.3	<0.001
eGFR, mL/min/1.73 m²	61 ± 22	59 ± 21	58 ± 21	57 ± 20	<0.001
UACR, mg/g	313 [51, 872]	299 [46, 868]	258 [42, 820]	261 [45, 783]	<0.001
Diuretic use, %	67.4	64.9	65.5	63.8	<0.001
SGLT2 inhibitor, %	9.9	8.3	7.9	7.5	<0.001
Finerenone assigned, %	42.3	55.8	57.7	55.5	<0.001

Potassium TIR and Cardiovascular Outcomes





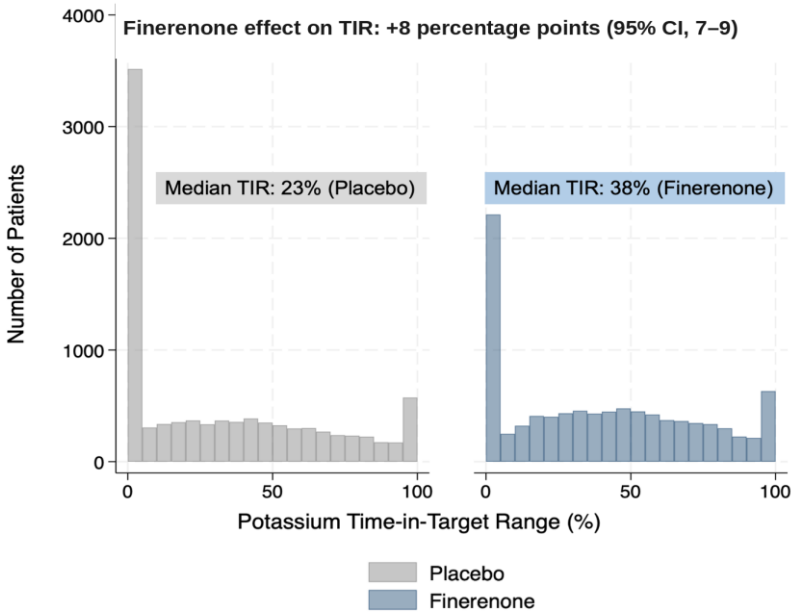
Adjusted HR (95% CI) by K TIR category

Outcome	<25%	25–<50%	50–<75%	≥75%
HFH / CV death	1.00 (ref)	1.10 (0.95–1.28)	0.79 (0.67–0.94)	0.81 (0.67–0.97)
CV death	1.00 (ref)	1.13 (0.91–1.40)	0.79 (0.61–1.02)	0.82 (0.63–1.07)

Figures: adjusted linear-spline models (HR vs K TIR); shaded = 95% CI.
Analyses adjusted for age, sex, BMI, eGFR, potassium level, UACR, SBP, history of HF, AF on ECG, history of diabetes, history of MI, region, use of ACEi/ARB/ARNI, beta blocker, loop diuretics, thiazide diuretics, SGLT2 inhibitors, GLP-1RA, trial, randomized treatment arm.

Finerenone, Potassium TIR, and Treatment Effects

Distribution of first-year potassium TIR by treatment assignment



Median TIR 38% vs 23%; mean difference +8 pts (95% CI 7–9).

Treatment effects on first HFH or CV death

Trial	Unadjusted HR	Adjusted HR*
FINE-HEART	0.85	0.88
FIDELIO-DKD	0.87	0.90
FIGARO-DKD	0.75	0.75
FINEARTS-HF	0.89	0.93

**Adjusted for first-year K TIR.*

The benefit of finerenone was not explained by its effect on potassium: treatment effects were consistent with or without adjustment for K TIR.

Limitations

Post hoc analysis

Hypothesis-generating association within randomized trials; not randomization to potassium targets.

Potassium measurement

Interpolation between scheduled visits may miss short-term fluctuations or transient dyskalemia.

Residual confounding

Disease severity, renal function and treatment tolerance may influence both achieved TIR and prognosis.

Landmark selection

Patients who died during the first year were excluded (n=640), potentially introducing selection bias.

Concomitant treatment changes

Changes in diuretics or RAAS inhibitors during follow-up may have influenced potassium TIR.

Conclusions

In 18,345 participants across the cardio-kidney-metabolic spectrum, greater time spent with serum potassium at 4.5–5.0 mmol/L during the first year was associated with lower subsequent cardiovascular risk.

- The association was mainly driven by cardiovascular death, without a significant association with first HF hospitalization alone.
- Finerenone increased K TIR, but **its benefit on the primary outcome was not explained by changes in potassium** and remained consistent after adjustment for K TIR.
- Potassium TIR may be a clinically informative longitudinal risk marker, rather than an established therapeutic target.

Prospective trials are needed to establish whether targeting high-normal potassium improves outcomes.