Hypokalaemia in patients with type 2 diabetes and chronic kidney disease: The effect of finerenone – A FIDELITY analysis

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FInerenone in chronic kiDney diseasE and type 2 diabetes: Combined FIDELIO-DKD and FIGARO-DKD Trial programme analYsis

Disclosures

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Hypokalaemia is associated with CV events and mortality in patients with CKD

- Hypokalaemia (serum [K^+] <3.5 mmol/l) is a risk factor for increased adverse CV and kidney events[1–5]
- Occurrence of hypokalaemia (12–18%) has been shown to be at a similar rate to hyperkalaemia (14–20%) in patients with CKD[1]
  - In patients with CKD, the adverse CV and mortality outcomes are higher in those with serum [K^+] <4.0 mmol/l[2–4,7–9]
  - However, much attention is focused on hyperkalaemia in CKD, with hypokalaemia less recognised or effectively treated[1-5]

- MRAs, in combination with RAS inhibitors, have demonstrated cardiorenal benefits in patients with CKD,[10–13] and a reduced rate of hypokalaemia events was reported in patients with HF[14,15]
  - Finerenone, a nonsteroidal MRA, has shown a lower risk of treatment-emergent hyperkalaemia than steroidal MRAs in patients with HF and CKD[16]
  - Therefore, potassium management with MRAs may benefit some patients with CKD who are at risk of lower serum [K^+] levels

Objectives: This FIDELITY exploratory analysis examined the incidence and effect of hypokalaemia in patients with T2D and CKD treated with finerenone versus placebo

CKD, chronic kidney disease; CV, cardiovascular; HF, heart failure; [K^+], potassium concentration; MRA, mineralocorticoid receptor antagonist; RAS, renin–angiotensin system; T2D, type 2 diabetes

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The FIDELITY[1] prespecified pooled analysis of FIDELIO-DKD[2] and FIGARO-DKD[3] showed significant risk reductions in CV and kidney outcomes with finerenone

FIDELIO-DKD N=5674*

FIDELITY Prespecified pooled analysis N=13,026*

FIGARO-DKD N=7352*

3 years' median follow-up

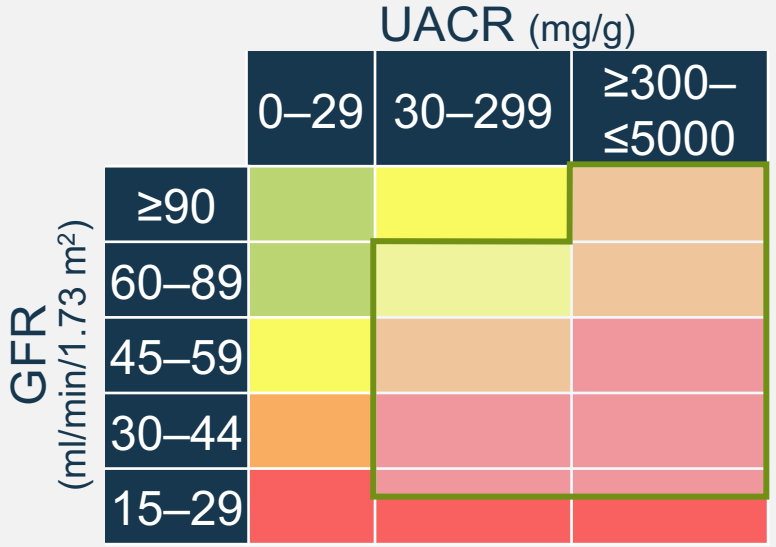
R → Finerenone 10 or 20 mg od (n=6519)

R → Placebo (n=6507)

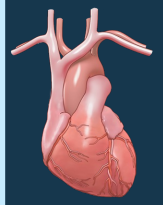
FIDELITY key eligibility criteria

- T2D
- CKD
- On maximum tolerated dose of a single RASi
- Serum [K^+] ≤4.8 mmol/l#

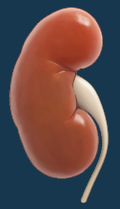
- Symptomatic HFrEF‡



FIDELITY key endpoint outcomes



CV composite§ vs placebo
HR=0.86 (95% CI 0.78–0.95)
p=0.0018
14%



Kidney composite¶ vs placebo
HR=0.77 (95% CI 0.67–0.88)
p=0.0002
23%

*Patients analysed; #at run-in or screening visit; ‡run-in only; § time to CV death, non-fatal myocardial infarction, non-fatal stroke or HHF; ¶time to kidney failure, sustained ≥57% eGFR from baseline over ≥4 weeks decline or kidney-related death

eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; HFrEF, heart failure with reduced ejection fraction; HHF, hospitalisation for heart failure; od, once daily; R, randomisation; RASi, renin–angiotensin system inhibitor; UACR, urine albumin-to-creatinine ratio

1. Bakris GB, *et al. N Engl J Med* 2020;383:2219–2229; 2. Pitt B, *et al. N Engl J Med* 2021;385:2252–2263; 3. Agarwal R, *et al. Eur Heart J* 2022;43:474–484

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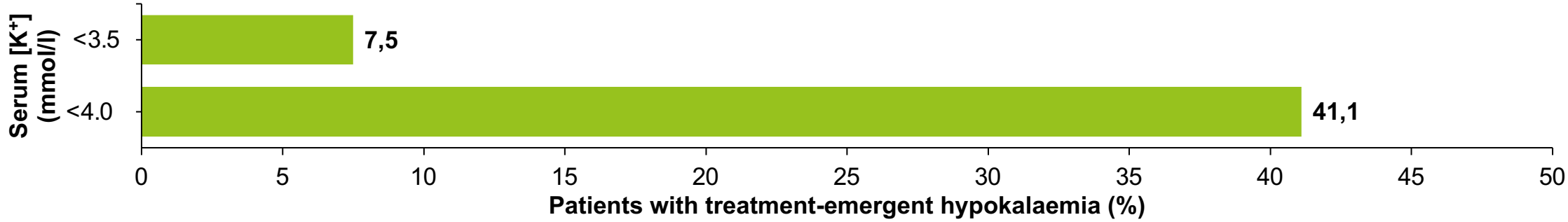
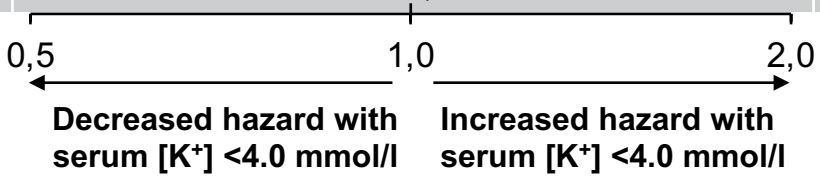
In FIDELITY, >40% of patients experienced treatment-emergent hypokalaemia and patients with serum [K^+] <4.0 mmol/l were at higher risk of adverse CV outcomes

Treatment-emergent hypokalaemia (n=12,859 patients with available data)



Safety outcomes (baseline serum [K^+] <4.0 mmol/l versus ≥4.0 mmol/l)

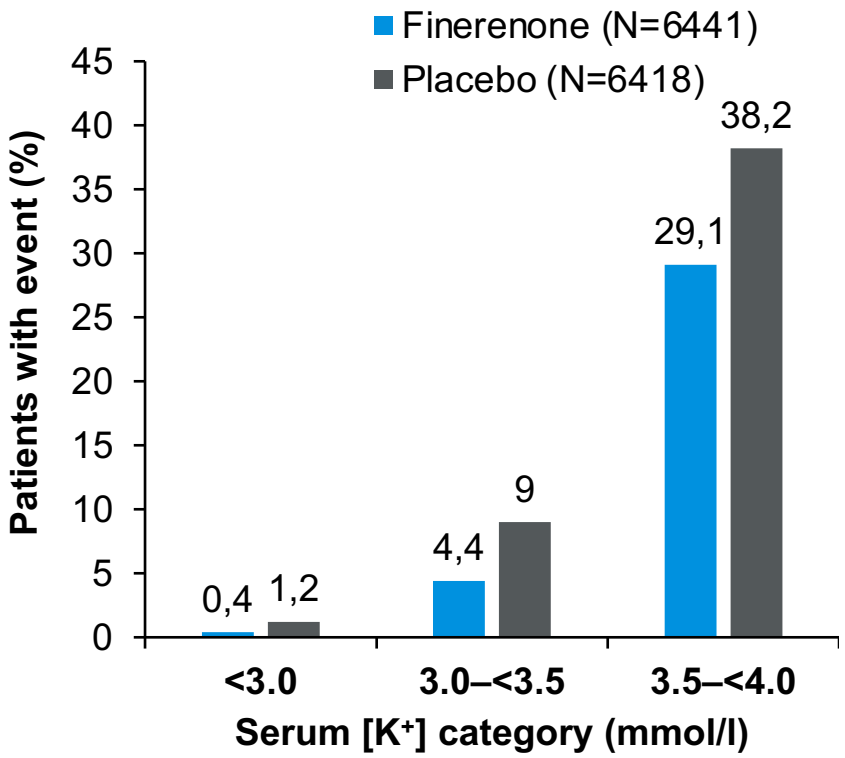
Endpoint	Hazard ratio* (95% CI)	Wald test *p*-value
CV composite#	1.18 (1.04–1.33)	0.008
Arrhythmia composite‡	1.21 (1.01–1.44)	0.034
All-cause mortality	1.03 (0.89–1.21)	0.671



*Hazard ratios are based on stratified cox models including treatment and baseline serum [K+] category
#Time to CV death, non-fatal MI, non-fatal stroke or HHF;
‡new diagnosis of AF, hospitalisation due to arrhythmia, or sudden cardiac death
AF, atrial fibrillation/atrial flutter; CI, confidence intervals; MI, myocardial infarction

Finerenone reduced the incidence of treatment-emergent hypokalaemia and lowered the risk of CV and arrhythmia outcomes versus placebo irrespective of baseline serum [K+]

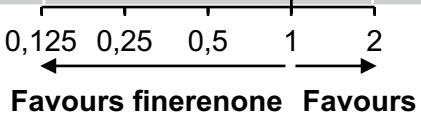
Incidence of treatment-emergent hypokalaemia



*Time to CV death, non-fatal MI, non-fatal stroke or HHF; #One patient per treatment group was not included in the dataset due to missing baseline serum [K+] measurement; ‡new diagnosis of AF, hospitalisation due to arrhythmia, or sudden cardiac death
PY, patient-years

Outcomes by baseline serum [K+]

Endpoint	Finerenone n of events (n/100 PY)	Placebo n of events (n/100 PY)	Hazard ratio (95% CI)	*p*-value for interaction
CV composite outcome*				
Overall	825 (4.34)	939 (5.01)	0.86 (0.78–0.95)	
Serum [K+] at baseline (mmol/l)#				
<3.5	22 (5.53)	23 (5.57)	0.64 (0.33–1.26)	0.98
3.5–<4.0	135 (4.82)	151 (5.55)	0.86 (0.68–1.09)	
≥4.0	667 (4.22)	764 (4.90)	0.86 (0.77–0.95)	
Arrhythmia composite outcome‡				
Overall	385 (1.98)	440 (2.28)	0.87 (0.76–1.00)	
Serum [K+] at baseline (mmol/l)				
<3.5	8 (1.93)	13 (3.10)	0.49 (0.19–1.26)	0.64
3.5–<4.0	65 (2.26)	74 (2.65)	0.95 (0.67–1.33)	
≥4.0	312 (1.93)	353 (2.20)	0.89 (0.76–1.03)	
All-cause mortality				
Overall	552 (2.76)	614 (3.10)	0.89 (0.79–1.00)	
Serum [K+] at baseline (mmol/l)#				
<3.5	9 (2.08)	16 (3.66)	0.43 (0.16–1.12)	0.46
3.5–<4.0	81 (2.72)	90 (3.12)	0.90 (0.67–1.23)	
≥4.0	461 (2.78)	507 (3.07)	0.90 (0.80–1.03)	



Summary

In the FIDELITY dataset:

- Patients with CKD and T2D experienced treatment-emergent hypokalaemia (defined as serum [K^+] <3.5 and <4.0 mmol/l) despite optimal RASi treatment
- Patients with baseline serum [K^+] <4.0 mmol/l were at increased risk for adverse CVD outcomes compared to >4.0 mmol/l

In patients with T2D across a broad spectrum of CKD stages and severity, with well-controlled blood pressure and HbA1c, and treated with a RASi at the maximum tolerated dose:

- Finerenone reduced the incidence of hypokalaemia compared with placebo
- Finerenone offered protection against CV outcomes and a consistent positive trend for arrhythmia outcomes and all-cause mortality across baseline serum [K^+] subgroups

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Thank you

48 countries, 33,292 patients enrolled, 13,171 patients randomised

Executive committee
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