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# Outcomes with finerenone in patients with stage 4 CKD and T2D: A FIDELITY subgroup analysis

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**on behalf of the FIDELIO-DKD and FIGARO-DKD Investigators**

**Disclosures for PS**: Advisor to AstraZeneca, Elpen, Genesis Pharma, Innovis Pharma, Menarini and Win Medica; speaker for Amgen, Bayer, Boehringer Ingelheim, Genesis, Menarini and Win Medica; received research support from AstraZeneca, Boehringer Ingelheim and Elpen; member of steering committees and endpoint adjudication committees for Bayer trials; Associate Editor for the *Journal of Human Hypertension* and Theme Editor for *Nephrology Dialysis and Transplantation*

# Subanalysis compared the efficacy and safety of finerenone versus placebo in patients with stage 4 CKD and T2D

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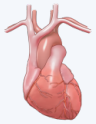
## FIDELITY*

**A prespecified, individual patient-level pooled efficacy and safety analysis of:**

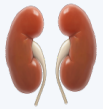
## FIDELIO-DKD and FIGARO-DKD

Phase III trials of patients with CKD and T2D, randomised 1:1 to receive finerenone or placebo

## Key endpoints:



CV composite: Time to CV death, non-fatal MI, non-fatal stroke or HHF



Kidney composite: Time to kidney failure, a sustained ≥57% decrease in eGFR from baseline over ≥4 weeks, or renal death

## Secondary endpoints:

- Change in eGFR
- Change in UACR

## Key baseline characteristics#

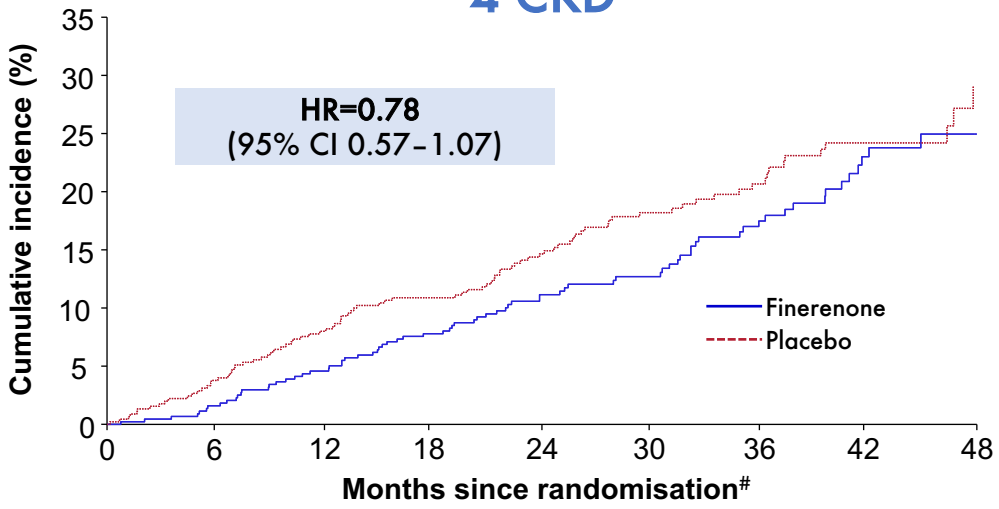
| | Total study population N=13,026 | |
|---|---|---|
| | Stage 4 CKD (n=890) | Stage 1–3 CKD (n=12,133) |
| Age, years | 67 | 65 |
| Male, % | 64 | 70 |
| HbA1c, % | 7.6 | 7.7 |
| SBP/DBP, mmHg | 136/73 | 137/77 |
| History of CV disease, % | 50 | 45 |
| eGFR,‡ ml/min/1.73 $m^2$ | 27 | 60 |
| UACR, mg/g, median | 720 | 503 |
| Medication use, % | | |
| ACEi | 32.5 | 39.5 |
| ARB | 67.3 | 60.5 |
| Insulin and analogues | 69 | 57.8 |
| SGLT-2i | 2 | 7 |
| GLP-1RA | 6 | 7 |

*Median follow-up of 3.0 years; #Data are mean unless otherwise indicated; ‡analysis of 13,026 patients (data were missing in 3 patients (<0.1%)
ACEi, angiotensin-converting enyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; CV, cardiovascular; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated haemoglobin; HHF, hospitalisation for heart failure; MI, myocardial infarction; SBP, systolic blood pressure; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio

# Cardiovascular outcomes in eGFR subgroups

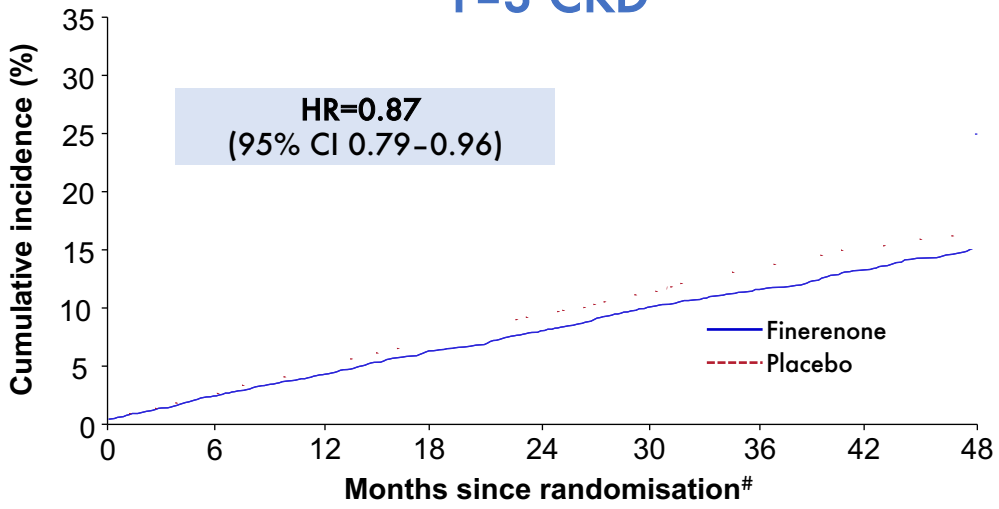


## CV composite endpoint in patients with stage 4 CKD




| No. of patients at risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| FIN | 440 | 428 | 413 | 394 | 301 | 242 | 167 | 98 | 41 |
| PBO | 450 | 432 | 412 | 393 | 304 | 226 | 162 | 107 | 33 |

## CV composite endpoint in patients with stage 1–3 CKD




| No. of patients at risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| FIN | 6078 | 5931 | 5788 | 5614 | 4971 | 3965 | 2898 | 2089 | 1046 |
| PBO | 6055 | 5896 | 5711 | 5543 | 4878 | 3920 | 2807 | 2028 | 1049 |

**Results indicate a benefit of finerenone vs placebo in stage 4 and stage 1–3 CKD*#**

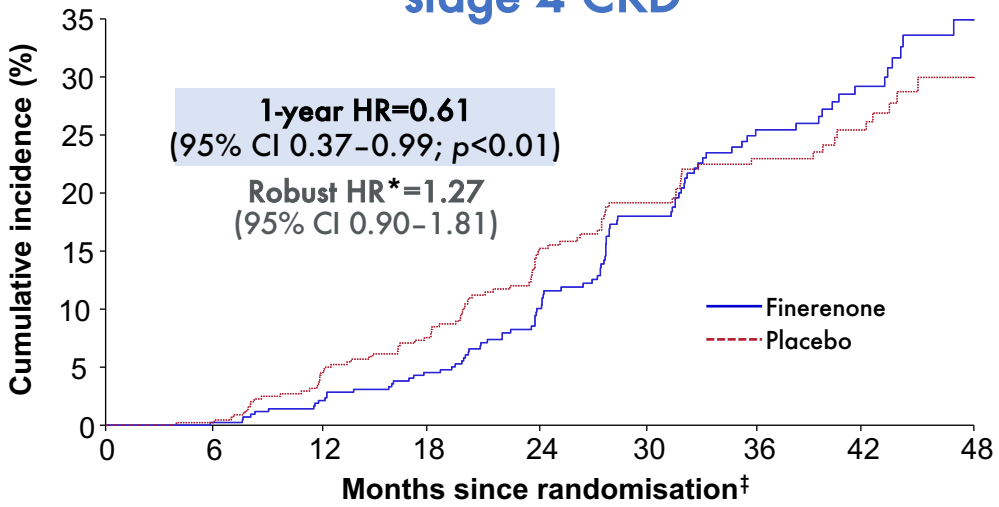
*$p_{interaction}$ between stage 1–3 versus stage 4 CKD = 0.67; #HR 95% CI is below 1 for stage 1-3 CKD and overlaps 1 for stage 4 CKD, however the sample size is low for stage 4 CKD; #The no. of patients for months 42 and 48 since randomisation is smaller than the previous months

CI, confidence interval; CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; FIN, finerenone; HR, hazard ratio; PBO, placebo; T2D, type 2 diabetes

# Kidney outcomes in eGFR subgroups

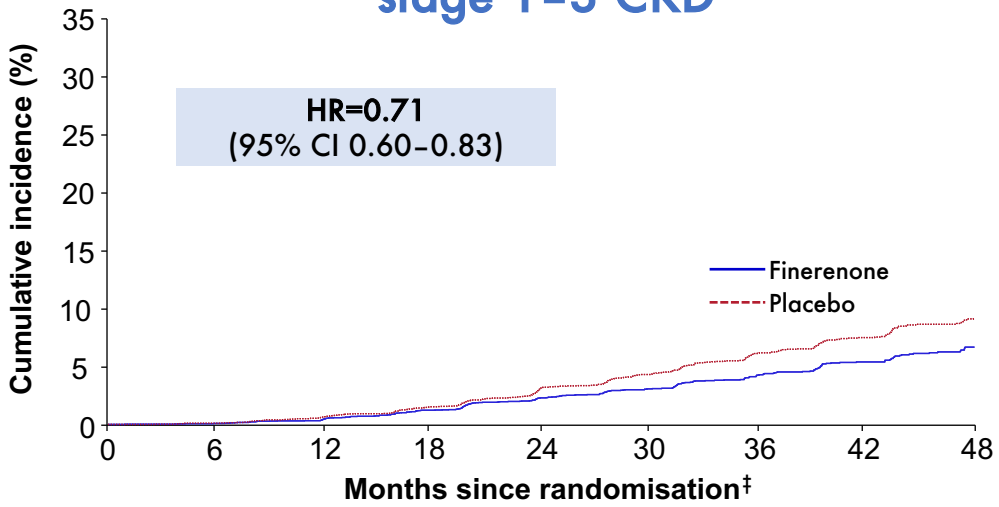


## Kidney composite endpoint in patients with stage 4 CKD




| No. of patients at risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| FIN | 440 | 421 | 401 | 373 | 277 | 203 | 130 | 85 | 31 |
| PBO | 450 | 432 | 398 | 367 | 258 | 189 | 130 | 87 | 24 |

## Kidney composite endpoint in patients with stage 1–3 CKD




| No. of patients at risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| FIN | 6078 | 5870 | 5706 | 5475 | 4750 | 3770 | 2685 | 1939 | 938 |
| PBO | 6055 | 5859 | 5672 | 5447 | 4690 | 3742 | 2668 | 1901 | 938 |

**The HR for the risk of a sustained ≥57% decrease in eGFR component# was 0.69 (95% CI 0.43–1.11) in patients with stage 4 CKD and 0.70 (95% CI 0.59–0.83) in patients with stage 1–3 CKD**

*Calculated when the proportional hazard assumption was not met (based on robust proportional hazard estimators with conditionally independent censoring on treatment groups);
#Component of the kidney composite endpoint; ‡The no. of patients for months 42 and 48 since randomisation is smaller than the previous months
CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FIN, finerenone; HR, hazard ratio; PBO, placebo; T2D, type 2 diabetes

# Finerenone slowed eGFR decline and resulted in a 31% reduction in UACR by month 4 compared with placebo in patients with stage 4 CKD

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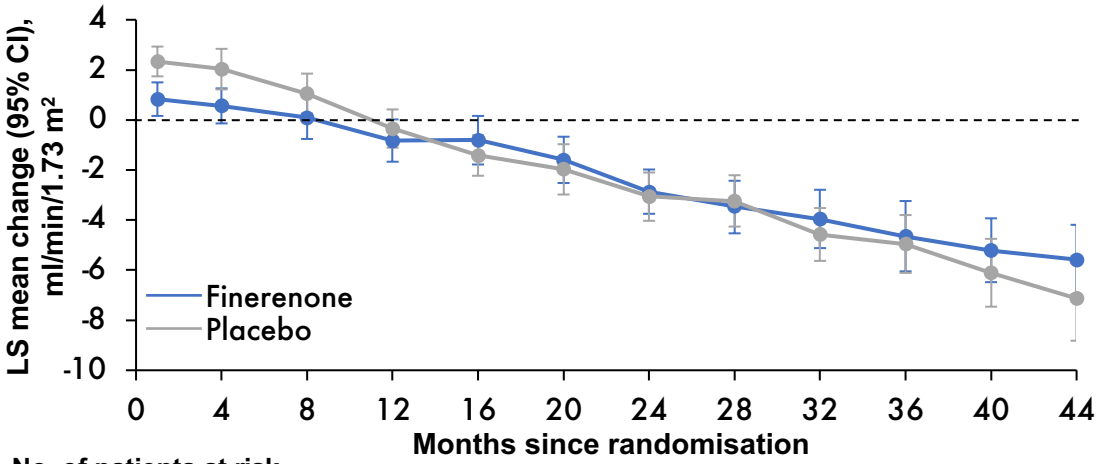
## Change from baseline eGFR



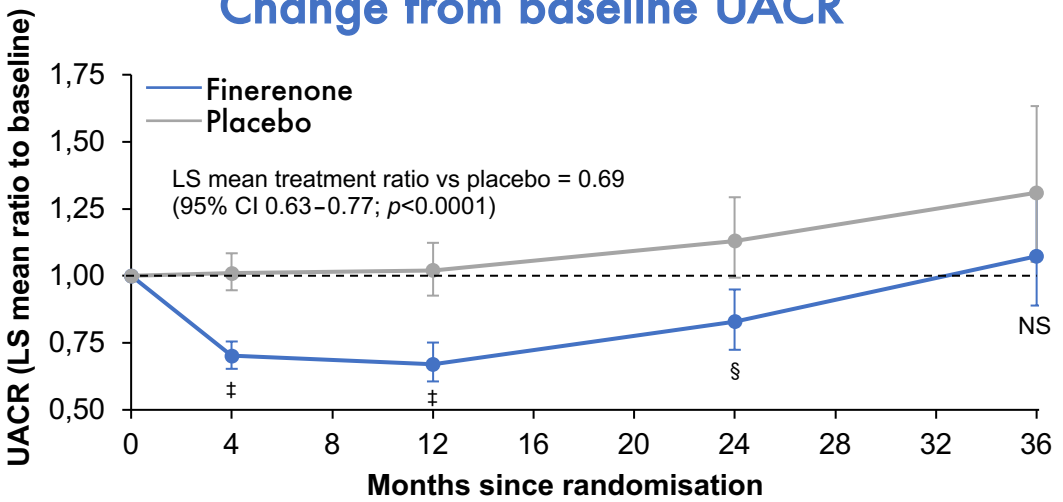

**No. of patients at risk**

| | | | | | | |
|---|---|---|---|---|---|---|
| **FIN** | 431 | 422 | 402 | 281 | 140 | 64 |
| **PBO** | 445 | 433 | 406 | 270 | 138 | 57 |

**Total slope***: LS mean change (95% CI), ml/min/1.73 m²/year
Finerenone: −0.74 (−1.32 to −0.16); placebo: −1.58 (−2.16 to −1.00)
Difference of LS means (95% CI): 0.84 (0.02–1.67), *p*=0.22

**Chronic slope#**: LS mean change (95% CI), ml/min/1.73 m²/year
Finerenone: −1.77 (−2.41 to −1.12); placebo: −3.15 (−3.80 to −2.51)
Difference of LS means (95% CI): 1.39 (0.48–2.30), *p*=0.04

## Change from baseline UACR




**No. of patients at risk**

| | | | | | |
|---|---|---|---|---|---|
| **FIN** | 440 | 419 | 391 | 274 | 139 |
| **PBO** | 450 | 431 | 398 | 268 | 134 |

**Ratio of LS means**

| | | | | |
|---|---|---|---|---|
| Ref | 0.69 (0.63–0.77) | 0.66 (0.57–0.76) | 0.73 (0.61–0.88) | 0.82 (0.62–1.09) |

**Mean change from baseline**

| | | | | | |
|---|---|---|---|---|---|
| **FIN** | Ref | −30 | −33 | −17 | 7 |
| **PBO** | Ref | 1 | 2 | 13 | 31 |

*Total slope assessed as annualised LS mean change in eGFR from baseline to permanent discontinuation or end-of-study visit based on ANCOVA model;
#Chronic slope assessed as annualised LS mean change in eGFR from month 4 to permanent discontinuation or end-of-study visit based on ANCOVA model; ‡$p<0.0001$; §$p=0.0012$
ANCOVA, analysis of covariance; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FIN, finerenone; LS, least-squares; NS, not significant; PBO, placebo; UACR, urine albumin-to-creatinine ratio

# Safety outcomes and summary



## Safety

| % | Stage 4 | | Stage 1–3 | |
|---|---|---|---|---|
| | FIN | PBO | FIN | PBO |
| Any TEAE | 90 | 91 | 86 | 86 |
| Led to discontinuation | 10 | 9 | 6 | 5 |
| Any serious TEAE | 34 | 42 | 32 | 33 |
| Renal/urinary disorders* | 20 | 23 | 15 | 17 |
| AKI | 6 | 7 | 3 | 3 |
| Hyperkalaemia# | 26 | 13 | 13 | 7 |
| Led to discontinuation | 3 | 2 | 2 | 1 |
| Led to hospitalisation | 3 | 1 | 1 | <1 |

## Conclusions

CV effects of finerenone vs placebo are consistent with results in patients with stage 1–3 CKD

Finerenone consistently reduced the risk of sustained ≥57% eGFR decline and showed improvements in eGFR slope and UACR vs placebo in patients with stage 4 CKD

The safety profile of finerenone in patients with stage 4 CKD was generally consistent with that in patients who had stage 1–3 CKD and T2D at baseline

*Including AKI, azotaemia, CKD, ESKD, haematuria, nephropathy toxic, nocturia, pollakiuria, renal artery stenosis, renal cyst, renal failure, renal impairment, urinary hesitation, urinary incompetence, urinary retention; #Defined as serum [K+] ≥5.5 mmol/l, and investigator-reported using the terms 'hyperkalaemia' and 'blood potassium increased'
AKI, acute kidney injury; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FIN, finerenone; PBO, placebo; TEAE, treatment-emergent adverse event; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio