Abstract 254

# Impact of finerenone on chronic kidney disease progression in Black or African American patients with type 2 diabetes – analysis of the FIDELIO-DKD study

George L. Bakris,[1] Amer Joseph,[2] Stefan D. Anker,[3] Bertram Pitt,[4] Luis M. Ruilope,[5] Peter Rossing,[6] Sharon Adler,[7] Robert Toto,[8] Peter Kolkhof,[9] Charlie Scott,[10] Gerasimos Filippatos,[11] John M. Flack,[12] Kenneth Jamerson,[4] Rajiv Agarwal,[13] on behalf of the FIDELIO-DKD Investigators

## Background

- Over one-third of US patients receiving dialysis are Black or African American[1]
- Diabetes is the leading cause of kidney failure in African Americans[1]
- FIDELIO-DKD (Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease; NCT02540993) was a phase III, randomized, double-blind, placebo-controlled, multicenter clinical trial demonstrating that finerenone reduced the risk of chronic kidney disease (CKD) progression and cardiovascular (CV) events in patients with CKD and type 2 diabetes (T2D)[2]
- The aim of this subgroup analysis was to evaluate outcomes in Black/African American patients in FIDELIO-DKD compared with the non-Black/African American population

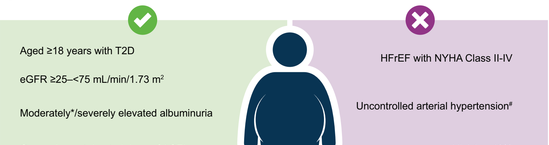
## Study design and methods

- The FIDELIO-DKD trial involved 5734 patients from 48 countries.[1] Patients aged ≥18 years with CKD (urine albumin-to-creatinine ratio 30–5000 mg/g and estimated glomerular filtration rate [eGFR] 25–<75 mL/min/1.73 m$^2$), T2D, and treated with optimized renin–angiotensin system blockade, were randomized (1:1) to finerenone or placebo (**Figure 1**)
- **Figure 2** presents the key inclusion/exclusion criteria for FIDELIO-DKD
- This analysis included patients who self-identified as Black or African American
- Outcomes:
  - Primary composite kidney outcome: time to kidney failure, sustained ≥40% decrease in eGFR from baseline, or renal death
  - Key secondary composite CV outcome: death from CV causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure
  - Other prespecified secondary outcomes included a composite of time to kidney failure, sustained ≥57% decrease in eGFR from baseline, or renal death

### Statistical analyses

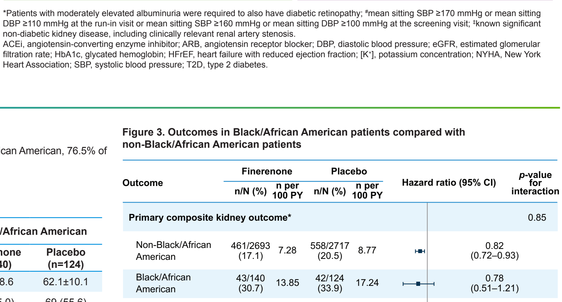
- Efficacy and safety analyses were performed in the full analysis set (all randomized patients without critical Good Clinical Practice violations)
- A statistical test for interaction was performed
- Time-to-event treatment outcomes were expressed as hazard ratios (HRs) with corresponding confidence intervals (CIs) from a stratified Cox regression model
- Events were reported from randomization up to the end-of-study visit. Patients without an event were censored at the date of their last contact, with complete information on all components of their respective outcomes

**Figure 1. FIDELIO-DKD: Study design[2]**




*10 mg if screening eGFR <60 mL/min/1.73 m$^2$; 20 mg if eGFR ≥60 mL/min/1.73 m$^2$, up-titration was encouraged from month 1 if serum potassium was ≤4.8 mmol/L and eGFR was stable.
eGFR, estimated glomerular filtration rate; od, once daily; R, randomization.

**Figure 2. FIDELIO-DKD: Key inclusion and exclusion criteria**




*Patients with moderately elevated albuminuria were required to also have diabetic retinopathy; #mean sitting SBP ≥170 mmHg or mean sitting DBP ≥110 mmHg at the run-in visit or mean sitting SBP ≥160 mmHg or mean sitting DBP ≥100 mmHg at the screening visit; ‡known significant non-diabetic kidney disease, including clinically relevant renal artery stenosis.
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; HFrEF, heart failure with reduced ejection fraction; [K+], potassium concentration; NYHA, New York Heart Association; SBP, systolic blood pressure; T2D, type 2 diabetes.

## Results

### Baseline characteristics

- A total of 264/5674 (4.7%) patients analyzed in the trial were Black/African American, 76.5% of whom were from North America. The median follow-up was 2.6 years
- Baseline characteristics and medications are presented in **Table 1**

**Table 1. Baseline characteristics and medications**

| | Non-Black/African American | | Black/African American | |
|---|---|---|---|---|
| | Finerenone (n=2693) | Placebo (n=2717) | Finerenone (n=140) | Placebo (n=124) |
| Age, years | 65.6±8.9 | 65.8±9.1 | 61.9±8.6 | 62.1±10.1 |
| Sex, male | 1876 (69.7) | 1961 (72.2) | 77 (55.0) | 69 (55.6) |
| Duration of diabetes, years | 16.6±8.8 | 16.5±8.8 | 16.5±8.6 | 17.8±9.0 |
| Glycated hemoglobin, % | 7.7±1.3 | 7.7±1.4 | 7.9±1.4 | 7.9±1.4 |
| SBP, mmHg | 137.9±14.2 | 138.0±14.3 | 141.6±16.1 | 139.0±16.4 |
| History of CV disease, yes | 1238 (46.0) | 1248 (45.9) | 65 (46.4) | 54 (43.5) |
| Current smoker | 401 (14.9) | 385 (14.2) | 13 (9.3) | 7 (5.6) |
| eGFR, mL/min/1.73 m$^2$ | 44.5±12.6 | 44.3±12.6 | 42.6±12.2 | 44.3±13.2 |
| Median UACR (IQR), mg/g | 826 (440–1616) | 864 (448–1641) | 947 (467–1703) | 1011 (522–1718) |
| Serum potassium, mmol/L | 4.37±0.46 | 4.38±0.46 | 4.27±0.44 | 4.30±0.51 |
| **Baseline medications** | | | | |
| ACEi | 885 (32.9) | 937 (34.5) | 65 (46.4) | 55 (44.4) |
| ARB | 1803 (67.0) | 1777 (65.4) | 76 (54.3) | 69 (55.6) |
| Diuretic | 1487 (55.2) | 1549 (57.0) | 90 (64.3) | 88 (71.0) |
| Statin | 1992 (74.0) | 2014 (74.1) | 113 (80.7) | 96 (77.4) |
| Potassium-lowering agent* | 69 (2.6) | 66 (2.4) | 1 (0.7) | 0 (0) |
| Insulin | 1741 (64.6) | 1711 (63.0) | 102 (72.9) | 83 (66.9) |
| GLP-1RA | 179 (6.6) | 189 (7.0) | 10 (7.1) | 16 (12.9) |
| SGLT-2i | 123 (4.6) | 127 (4.7) | 1 (0.7) | 8 (6.5) |

Data are n (%) or mean ± SD unless stated otherwise.
*These agents included sodium polystyrene sulfonate, calcium polystyrene sulfonate, and potassium-binding agents.
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CV, cardiovascular; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide-1 receptor agonist; IQR, interquartile range; SBP, systolic blood pressure; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; UACR, urine albumin-to-creatinine ratio.

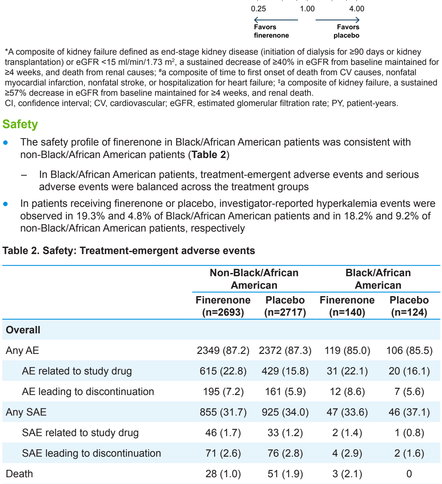
### Primary and key secondary outcomes

- There was no significant difference in the effect of finerenone on the incidence of the primary composite kidney outcome based on whether patients were Black/African American or not (*p*-value for interaction=0.85; **Figure 3**)
  - In Black/African American patients, the incidence of the primary kidney outcome was lower with finerenone (13.85/100 patient-years [PY]) vs placebo (17.24/100 PY; HR=0.78; 95% CI 0.51–1.21). The outcome was similar in non-Black/African American patients: finerenone (7.28/100 PY) vs placebo (8.77/100 PY; HR=0.82; 95% CI 0.72–0.93; **Figure 3**)
  - The risk of kidney failure was higher in Black/African American patients (7.58/100 PY and 6.21/100 PY for finerenone and placebo, respectively) compared with non-Black/African American patients (2.76/100 PY and 3.27/100 PY for finerenone and placebo, respectively)
- The effect of finerenone on the incidence of the key secondary composite CV outcome was similar, irrespective of race (*p*-value for interaction=0.51)
  - Among Black/African American patients, the incidence was 7.08/100 PY with finerenone vs 6.57/100 PY with placebo (HR=1.05; 95% CI 0.58–1.90). In non-Black/African American patients, the incidence was 5.01/100 PY with finerenone vs 5.89/100 PY with placebo (HR=0.85; 95% CI 0.74–0.98; **Figure 3**)

### Secondary outcomes

- Similarly, no race-related differences were observed in the effect of finerenone on the incidence of the secondary composite kidney outcome (*p*-value for interaction=0.90). In the Black/African American population, the incidence of the secondary composite kidney outcome was also lower with finerenone (9.24/100 PY) vs placebo (10.89/100 PY; HR=0.77; 95% CI 0.46–1.29)
  - The incidence was lower in non-Black/African American patients; 3.37/100 PY with finerenone vs 4.49/100 PY with placebo (HR=0.75; 95% CI 0.63–0.89; **Figure 3**)

**Figure 3. Outcomes in Black/African American patients compared with non-Black/African American patients**




*A composite of kidney failure defined as end-stage kidney disease (initiation of dialysis for ≥90 days or kidney transplantation) or eGFR <15 ml/min/1.73 m$^2$, a sustained decrease of ≥40% in eGFR from baseline maintained for ≥4 weeks, and death from renal causes; #a composite of time to first onset of death from CV causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure; ‡a composite of kidney failure, a sustained ≥57% decrease in eGFR from baseline maintained for ≥4 weeks, and renal death.
CI, confidence interval; CV, cardiovascular; eGFR, estimated glomerular filtration rate; PY, patient-years.

### Safety

- The safety profile of finerenone in Black/African American patients was consistent with non-Black/African American patients (**Table 2**)
  - In Black/African American patients, treatment-emergent adverse events and serious adverse events were balanced across the treatment groups
- In patients receiving finerenone or placebo, investigator-reported hyperkalemia events were observed in 19.3% and 4.8% of Black/African American patients and in 18.2% and 9.2% of non-Black/African American patients, respectively

**Table 2. Safety: Treatment-emergent adverse events**

| | Non-Black/African American | | Black/African American | |
|---|---|---|---|---|
| | Finerenone (n=2693) | Placebo (n=2717) | Finerenone (n=140) | Placebo (n=124) |
| **Overall** | | | | |
| Any AE | 2349 (87.2) | 2372 (87.3) | 119 (85.0) | 106 (85.5) |
| AE related to study drug | 615 (22.8) | 429 (15.8) | 31 (22.1) | 20 (16.1) |
| AE leading to discontinuation | 195 (7.2) | 161 (5.9) | 12 (8.6) | 7 (5.6) |
| Any SAE | 855 (31.7) | 925 (34.0) | 47 (33.6) | 46 (37.1) |
| SAE related to study drug | 46 (1.7) | 33 (1.2) | 2 (1.4) | 1 (0.8) |
| SAE leading to discontinuation | 71 (2.6) | 76 (2.8) | 4 (2.9) | 2 (1.6) |
| Death | 28 (1.0) | 51 (1.9) | 3 (2.1) | 0 |
| **Hyperkalemia related** | | | | |
| Investigator-reported hyperkalemia* | 489 (18.2) | 249 (9.2) | 27 (19.3) | 6 (4.8) |
| Hyperkalemia related to study drug | 317 (11.8) | 132 (4.9) | 16 (11.4) | 3 (2.4) |
| Serious hyperkalemia | 39 (1.4) | 11 (0.4) | 5 (3.6) | 1 (0.8) |
| Hospitalization due to hyperkalemia | 35 (1.3) | 7 (0.3) | 5 (3.6) | 1 (0.8) |
| Permanent discontinuation due to hyperkalemia | 60 (2.2) | 25 (0.9) | 4 (2.9) | 0 |

Data are n (%); full analysis set.
*Shown are AEs that were reported by investigators with the use of the MedDRA-preferred terms "hyperkalemia" and "blood potassium increased".
AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event.

## Conclusions

- Findings from this subgroup analysis of FIDELIO-DKD demonstrate that the effects of finerenone on the key renal and CV outcomes do not differ between Black/African American and non-Black/African American subgroups
- The evaluation of Black/African American patients is based on low numbers, with just 4.7% of the participating patients self-identifying as Black or African American

[1]UChicago Medicine, Chicago, IN, USA; [2]Bayer AG, Berlin, Germany; [3]Charité Universitätsmedizin, Berlin, Germany; [4]Michigan Medicine, University of Michigan, Ann Arbor, MI, USA; [5]Research Institute Hospital 12 de Octubre (i+12), Madrid, Spain; [6]University of Copenhagen, Copenhagen, Denmark; [7]Harbor-UCLA Medical Center, Torrance, CA, USA; [8]UT Southwestern Medical Center, Dallas, TX, USA; [9]Bayer, Wuppertal, Germany; [10]Bayer PLC, Reading, United Kingdom; [11]National and Kapodistrian University of Athens, School of Medicine, Athens University Hospital Attikon, Greece; [12]Southern Illinois University School of Medicine, Springfield, IL, USA; [13]Indiana University, Indianapolis, IN, USA

**Contact information for corresponding author**

**Name:** George Bakris
**Email:** gbakris@gmail.com

**Acknowledgments**

The FIDELIO-DKD trial was funded by Bayer AG. Medical writing assistance was provided by Chameleon Communications International with funding from Bayer AG.

**Disclosures**

**SA** reports research grants from the Nephrotic Syndrome Study Network (NEPTUNE), CureGN, NephCure Accelerating Cures Network, and Immune Tolerance Network; she also reports fees from Bayer, Bristol Myers Squibb, Retrophin/Travere Therapeutics, ChemoCentryx, Calliditas, and MorphoSys. **RA** reports personal fees and nonfinancial support from Bayer Healthcare Pharmaceuticals Inc. during the conduct of the study; he also reports personal fees and nonfinancial support from Akebia Therapeutics, Janssen, Relypsa/Vifor Pharma, Boehringer Ingelheim, Sanofi, Eli Lilly and Company, AstraZeneca, and Fresenius; he has received personal fees from Ironwood Pharmaceuticals, Merck & Co., Lexicon, and Reata Pharmaceuticals, and nonfinancial support from Otsuka America Pharmaceutical, Inc., OPKO Health, and E.R. Squibb & Sons; he is a member of data safety monitoring committees for Amgen, AstraZeneca, and Celgene; a member of steering committees of randomized trials for Akebia Therapeutics, Bayer, Janssen, and Relypsa; he is a member of adjudication committees for AbbVie, Bayer, Boehringer Ingelheim, and Janssen; he has been an author for UpToDate and has served as associate editor of the *American Journal of Nephrology* and *Nephrology Dialysis Transplantation*; and he has received research grants from the U.S. Department of Veterans Affairs and the National Institutes of Health. **SDA** has received research support from Abbott Vascular and Vifor Pharma, and personal fees from Abbott Vascular, Boehringer Ingelheim, Bayer, BRAHMS, Novartis, Servier, Vifor Pharma, Impulse Dynamics, and Cardiac Dimensions. **GLB** reports research funding, paid to the University of Chicago Medicine from Bayer, during the conduct of the study; he also reports research funding, paid to the University of Chicago Medicine from Novo Nordisk and Vascular Dynamics; he acted as a consultant and received personal fees from for Merck, Relypsa, and Alnylam Pharmaceuticals; he is an editor of *American Journal of Nephrology*, *Nephrology*, and *Hypertension*, and section editor of UpToDate; and he is an associate editor of *Diabetes Care* and *Hypertension Research*. **GF** reports lectures fees and/or that he is a committee member of trials and registries sponsored by Bayer, Novartis, Vifor Pharma, Medtronic, Servier, Amgen, and Boehringer Ingelheim. He is a senior consulting editor for *JACC Heart Failure*, and he has received research support from the European Union. **JMF** reports research funding from Glaxo Smith Kline, Indorsia, Quantam Genomics, ReCor Medical, and Vascular Dynamics. **KJ** has no disclosures. **BP** reports consultant fees for Bayer, AstraZeneca, Sanofi/Lexicon, scPharmaceuticals, SQ Innovation, G3 Pharmaceuticals, Sarfez Pharmaceuticals, PhaseBio, Relypsa/Vifor Pharma, Cereno Scientific, Ardelyx, KBP Biosciences, Boehringer Ingelheim, Brainstorm Medical, and Tricida; he has stock options for Ardelyx, KBP Biosciences, SQ Innovation, Sarfez Pharmaceuticals, scPharmaceuticals, Cereno Scientific G3 Pharmaceuticals, Relypsa/Vifor Pharma, Brainstorm Medical, and Tricida; he also holds a patent for site-specific delivery of eplerenone to the myocardium (US patent #9931412) and a provisional patent for histone-acetylation-modulating agents for the treatment and prevention of organ injury (provisional patent US 63/045,784). **PR** reports personal fees from Bayer, during the conduct of the study; he has received research support and personal fees from AstraZeneca and Novo Nordisk, and personal fees from Eli Lilly and Company, Boehringer Ingelheim, Astellas, Gilead, Mundipharma, Sanofi, and Vifor Pharma. All fees are given to Steno Diabetes Center Copenhagen. He has an equity interest in Novo Nordisk. **LMR** has no disclosures. **RT** reports funding from AstraZeneca, Boehringer Ingelheim, Bayer, Otsuka, Medscape, Reata Pharmaceuticals, Relypsa. **PK** is a full-time employee of Bayer AG, Division Pharmaceuticals, Germany. He is the co-inventor of finerenone and holds US and European patents relating to finerenone (US8436180B2 and EP2132206B1). **AJ** is a full-time employee of Bayer AG, Division Pharmaceuticals, Germany. **CS** is a full-time employee of Bayer PLC, United Kingdom.

**References:**

1. National Kidney Foundation. 2016. *https://www.kidney.org/news/newsroom/factsheets/African-Americans-and-CKD* [accessed 17 Mar 2021]
2. Bakris GL, et al. *N Engl J Med* 2020;383:2219–2229

Abstract 254 presented at the National Kidney Foundation Spring Clinical Meeting, April 6–10, 2021