Poster No.: 281

Finerenone in Black patients with type 2 diabetes and chronic kidney disease: A FIDELITY analysis

John M. Flack,[1*] Rajiv Agarwal,[2] Stefan D. Anker,[3] Bertram Pitt,[4] Luis M. Ruilope,[5–7] Peter Rossing,[8,9] Sharon G. Adler,[10] Linda Fried,[11] Kenneth Jamerson,[12] Robert Toto,[13] Meike Brinker,[14] Alfredo E. Farjat,[15] Peter Kolkhof,[16] Amer Joseph,[17] Robert Lawatscheck,[18] George L. Bakris,[19] on behalf of the FIDELIO-DKD and FIGARO-DKD Investigators

[1]Department of Medicine, Southern Illinois University School of Medicine, Illinois, IL, USA; [2]Richard L. Roudebush VA Medical Center and Indiana University, Indianapolis, IN, USA; [3]Department of Cardiology (CVK), and Berlin Institute of Health Center for Regenerative Therapies, German Centre for Cardiovascular Research Partner Site Berlin, Charité – Universitätsmedizin, Berlin, Germany; [4]Department of Medicine, University of Michigan School of Medicine, Ann Arbor, MI, USA; [5]Cardiorenal Translational Laboratory and Hypertension Unit, Institute of Research imas12, Madrid, Spain; [6]CIBER-CV, Hospital Universitario 12 de Octubre, Madrid, Spain; [7]Faculty of Sport Sciences, European University of Madrid, Madrid, Spain; [8]Steno Diabetes Center Copenhagen, Gentofte, Denmark; [9]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark; [10]Division of Nephrology and Hypertension, Harbor-UCLA Medical Center, Torrance, CA, USA; [11]Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA; [12]Cardiology Clinic, University of Michigan, Michigan, MI, USA; [13]Department of Internal Medicine, University of Texas Southwestern Medicine, Dallas, TX, USA; [14]Cardiology and Nephrology Clinical Development, Bayer AG, Wuppertal, Germany; [15]Research and Development, Statistics and Data Insights, Bayer PLC, Reading, United Kingdom; [16]Research and Development Cardiovascular Precision Medicines, Bayer AG, Wuppertal, Germany; [17]Cardiology and Nephrology Clinical Development, Bayer AG, Berlin, Germany; [18]Medical Affairs & Pharmacovigilance, Pharmaceuticals, Bayer AG, Berlin, Germany; [19]Department of Medicine, University of Chicago Medicine, Chicago, IL, USA

*John M. Flack; jflack47@siumed.edu

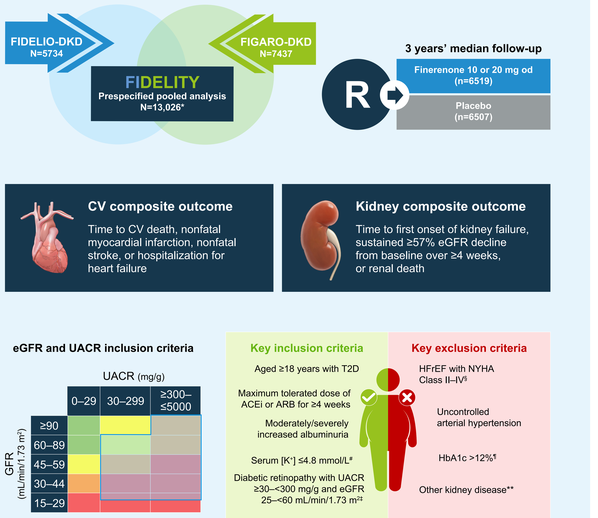
1. Background

- Chronic kidney disease (CKD) is a common complication of type 2 diabetes (T2D),[1] and Black or African American patients (herein referred to as Black) with T2D are at increased risk of kidney failure[2]
- In the FIDELITY prespecified pooled analysis of the FIDELIO-DKD and FIGARO-DKD trials, reduced risks of kidney and cardiovascular (CV) outcomes were demonstrated with finerenone versus placebo in patients with CKD and T2D[3]
- The aim of this FIDELITY subgroup analysis was to evaluate the kidney and CV benefits of finerenone in Black patients

2. Study design and methods

- This analysis combines individual patient-level data from the FIDELIO-DKD (NCT02540993) and FIGARO-DKD (NCT02545049) phase III clinical trials. The designs and results of these studies have been published previously[4,5]
- Study design, efficacy outcomes, and inclusion/exclusion criteria are shown in **Figure 1**

Figure 1. Study design, efficacy outcomes, and patient population



*Prospective exclusion of 145 patients; #at run-in or screening visit; ‡FIDELIO-DKD only; §run-in only; ¶at the run-in or screening visit; **known significant nondiabetic kidney disease, including clinically relevant renal artery stenosis
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CV, cardiovascular; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; HbA1c, glycated hemoglobin; HFrEF, heart failure with reduced ejection fraction; [K+], potassium concentration; NYHA, New York Heart Association; od, once daily; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio

3. Results

- Of 13,026 patients, 522 (4.0%) self-identified as Black, of whom 72.2% were from North America
- Baseline characteristics and medication use at baseline were generally similar between Black and non-Black patients (**Table 1**)

Table 1. Baseline characteristics and medication use in Black and non-Black patients

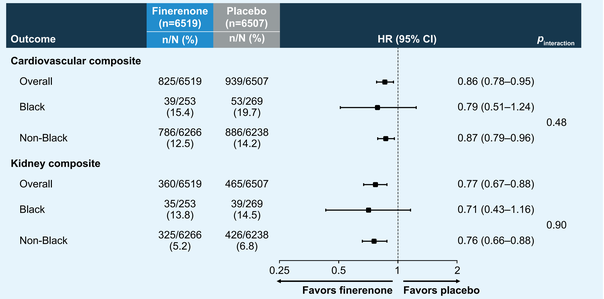
Characteristic	Black (n=522)	Non-Black (n=12,504)
Age, years, mean ± SD	61.8±10.0	64.9±9.5
Male, n (%)	284 (54.4)	8804 (70.4)
Duration of diabetes, years, mean ± SD	16.2±8.8	15.4±8.7
HbA1c, %, mean ± SD	7.9±1.4	7.7±1.4
BMI, kg/m², mean ± SD	34.1±7.4	31.2±5.9
Systolic blood pressure, mmHg, mean ± SD	138.6±15.7	136.7±14.1
History of cardiovascular disease, n (%)	233 (44.6)	5702 (45.6)
eGFR, mL/min/1.73 m², mean ± SD	53.8±21.8	57.7±21.7
UACR, mg/g, median (IQR)	529 (229–1175)	514 (196–1146)
Serum potassium, mmol/L, mean ± SD	4.25±0.46	4.35±0.44
Baseline medications, n (%)		
Angiotensin-converting enzyme inhibitors	255 (48.9)	5389 (43.1)
Angiotensin receptor blockers	302 (57.9)	8135 (65.1)
Beta blockers	356 (68.2)	7394 (59.1)
Diuretics	393 (75.3)	8268 (66.1)
Statins	443 (84.9)	9905 (79.2)
Potassium supplements	69 (13.2)	1167 (9.3)
Potassium-lowering agents	23 (4.4)	849 (6.8)
Glucose-lowering therapies		
Insulin and analogues	394 (75.5)	8347 (66.8)
Biguanides	239 (45.8)	7856 (62.8)
Sulfonamides	167 (32.0)	3729 (29.8)
DPP-4 inhibitors	112 (21.5)	4338 (34.7)
GLP-1RAs	76 (14.6)	1801 (14.4)
SGLT-2 inhibitors	41 (7.9)	2118 (16.9)

BMI, body mass index; DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated hemoglobin; IQR, interquartile range; SD, standard deviation; SGLT-2, sodium-glucose co-transporter-2; UACR, urine albumin-to-creatinine ratio

3.1. Efficacy outcomes

- The effect of finerenone on CV and kidney composite outcomes was not modified in Black and non-Black patients ($p_{interaction}$=0.48 and 0.90, respectively) (**Figure 2**)
  - Despite a small sample size with reduced power, finerenone numerically reduced the risk of the CV and kidney composite outcomes in Black patients compared with placebo (hazard ratio [HR]=0.79; 95% confidence interval [CI] 0.51–1.24 and HR=0.71; 95% CI 0.43–1.16, respectively) (**Figure 2**)

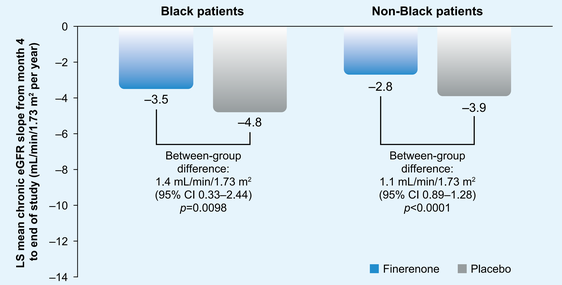
Figure 2. Cardiovascular and kidney outcomes in Black and non-Black patients



CI, confidence interval; HR, hazard ratio

- In Black patients, finerenone significantly reduced the urine albumin-to-creatinine ratio (UACR) by 40% at month 4 (least-squares [LS] mean treatment ratio 0.60; 95% CI 0.52–0.69; p<0.0001) compared with placebo
- In Black patients, LS mean change in estimated glomerular filtration rate (eGFR) from baseline to month 4 was –4.3 mL/min/1.73 m² (95% CI –5.5 to –3.2) with finerenone and –1.1 mL/min/1.73 m² (95% CI –2.4 to –0.1) with placebo (difference of LS means –3.2; 95% CI –4.9 to –1.5; p=0.0002)
  - LS mean change in chronic eGFR slope from month 4 to end of study was lower with finerenone compared with placebo in Black patients (–3.5 mL/min/1.73 m² with finerenone and –4.8 mL/min/1.73 m² with placebo; between group difference: 1.4 mL/min/1.73 m²; 95% CI 0.33–2.44; p=0.0098) (**Figure 3**)

Figure 3. Chronic eGFR slope from month 4 to end of study in Black and non-Black patients

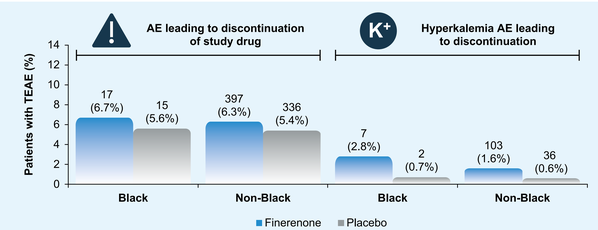


CI, confidence interval; eGFR, estimated glomerular filtration rate; LS, least-squares

3.2. Safety outcomes

- In Black patients, the overall incidence of treatment-emergent adverse events was similar between the finerenone and placebo groups
  - Adverse events leading to discontinuation of study drug were similar between Black and non-Black patients in the finerenone and placebo groups (**Figure 4**)
  - Incidence of investigator-reported treatment-emergent hyperkalemia was higher in patients treated with finerenone compared with placebo; however, the incidence of hyperkalemia leading to discontinuation of study drug was low in both treatment groups and across the Black and non-Black patient groups (**Figure 4**)

Figure 4. Safety outcomes in Black and non-Black patients



AE, adverse event; [K+], potassium concentration; TEAE, treatment-emergent adverse event

4. Conclusions

- Overall, finerenone appeared to have a similar impact in reducing albuminuria and eGFR slope with a comparable safety profile between Black and non-Black patients. The benefits of finerenone on the kidney and CV outcomes appeared consistent across the Black and non-Black subgroups; however, a larger sample size would be needed to reduce uncertainty around treatment effect estimates

Acknowledgments

Funded by Bayer AG; FIDELIO-DKD and FIGARO-DKD clinicaltrials.gov number NCT02540993 and NCT02545049, respectively. Medical writing assistance was provided by Chameleon Communications International and was funded by Bayer AG.

Disclosures

JF reports research funding from Glaxo Smith Kline, Indorsia, Quantum Genomics, ReCor Medical, and Vascular Dynamics. **RA** reports personal fees and non-financial support from Bayer Healthcare Pharmaceuticals Inc. during the conduct of the study; he also reports personal fees and non-financial support from Akebia Therapeutics, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Fresenius, Janssen, Relypsa, Sanofi, and Vifor Pharma; he has received personal fees from Ironwood Pharmaceuticals, Lexicon, Merck & Co, and Reata, and non-financial support from E. R. Squibb & Sons, Opko Pharmaceuticals, and Otsuka America Pharmaceutical; 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; a member of adjudication committees for AbbVie, Bayer, Boehringer Ingelheim, and Janssen; he has served as associate editor of the *American Journal of Nephrology and Nephrology Dialysis and Transplantation* and has been an author for UpToDate; and he has received research grants from the U.S. Veterans Administration and the National Institutes of Health. **SDA** has received research support from Abbott Vascular and Vifor International, and personal fees from Abbott Vascular, Bayer, Boehringer Ingelheim, BRAHMS, Cardiac Dimensions, Impulse Dynamics, Novartis, Servier, and Vifor Pharma. **BP** reports consultant fees for AstraZeneca, Bayer, Boehringer Ingelheim, Brainstorm Medical, Cereno Scientific, G3 Pharmaceuticals, KBP Biosciences, PhaseBio, Proton Intel, Sanofi/Lexicon, Sarfez, scPharmaceuticals, SQ Innovation, Tricida, and Vifor/Relypsa; he has stock options for Brainstorm Medical, Cereno Scientific, G3 Pharmaceuticals, KBP Biosciences, Proton Intel, Sarfez, scPharmaceuticals, SQ Innovation, Tricida, Vifor/Relypsa; he also holds a patent for site-specific delivery of eplerenone to the myocardium (US patent #9031412) and a provisional patent for histone-acetylation-modulating agents for the treatment and prevention of organ injury (provisional patent US 63/045,784). **LMR** has received consultancy fees from Bayer. **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 Astellas, Boehringer Ingelheim, Eli Lilly, Gilead, Mundipharma, Sanofi, and Vifor; all fees are given to Steno Diabetes Center Copenhagen. **SGA** reports research grants from CureGN, the NephCure Accelerating Cures Network and Immune Tolerance Network, and the Nephrotic Syndrome Study Network (NEPTUNE); she also reports fees from Bayer, Bristol Myers Squibb, Calliditas, ChemoCentryx, MorphoSys, and Retrophin. **LF** reports consulting fees from Bayer and has received fees for serving as a member of data safety monitoring boards for CSL Behring and Novo Nordisk studies. **KJ** has received consulting fees from Elsevier and Medtronic. **RT** reports consultant work with Akebia, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Chinook Pharma, Medscape, Otsuka, Reata, and Vifor. **MB** is a full-time employee of Bayer AG, Division Pharmaceuticals, Germany. **AEF** is a full-time employee of Bayer PLC, Division Pharmaceuticals, Reading, UK. **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** was a full-time employee of Bayer AG, Division Pharmaceuticals, Germany, at the time of the studies and analysis; he is now a full-time employee of Chiesi S.p.A. Parma, Italy. **GLB** reports research funding, paid to the University of Chicago Medicine, from Bayer during the conduct of the study; he also reported 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 Alnylam, Merck, and Relypsa; he is an editor of the *American Journal of Nephrology, Nephrology,* and *Hypertension,* and section editor of UpToDate; and is an associate editor of *Diabetes Care* and *Hypertension Research.*

References

1. United States Renal Data System. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2017.
2. Peralta CA, *et al. J Am Soc Nephrol* 2011;22:1327–1334.
3. Agarwal R, *et al. Eur Heart J* 2022;43:474–484.
4. Ruilope LM, *et al. Am J Nephrol* 2019;50:345–356.
5. Bakris GL, *et al. Am J Nephrol* 2019;50:333–344.