FINE-REAL: Prospective Phase IV Study of Finerenone in Clinical Practice—Interim US Results[a]

Sankar D. Navaneethan,[1] David C. Wheeler,[2] Kevin M. Pantalone,[3] Lixin Guo,[4] Nihar R. Desai,[5] Ricardo Correa-Rotter,[6] Susanne B. Nicholas,[7] Nan Hee Kim,[8] Jon Mares,[9] Zihe Zheng,[9] Charlie Scott,[10] Andrea Horvat-Broecker,[11] Martin Merz,[12] Christoph Wanner[13]

[1]Baylor College of Medicine, Houston, TX, USA; [2]University College London, London, UK; [3]Cleveland Clinic, Cleveland, OH, USA; [4]Department of Endocrinology, Beijing Hospital, National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Sciences, Beijing, China; [5]Yale School of Medicine, New Haven, CT, USA; [6]Instituto Nacional de Ciencias Médicas y Nutricion Salvador Zubiran, Ciudad de Mexico, Mexico; [7]David Geffen School of Medicine, University of California, Los Angeles, CA, USA; [8]Division of Endocrinology and Metabolism, Department of Internal Medicine, Korea University College of Medicine, Seoul, South Korea; [9]Bayer US LLC, Whippany, NJ, USA; [10]Bayer Public Limited Company, Reading, UK; [11]Bayer AG, Wuppertal, Germany; [12]Bayer AG, Berlin, Germany; [13]Hospital Würzburg, Würzburg, Germany

Introduction

- Finerenone, a selective non-steroidal mineralocorticoid receptor antagonist (nsMRA), is indicated to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end-stage kidney disease, cardiovascular death, non-fatal myocardial infarction, and hospitalization for heart failure in adults with chronic kidney disease (CKD) associated with type 2 diabetes (T2D).[1–7]
- FINE-REAL (NCT05348733) is a global, prospective, single-arm, non-interventional study of finerenone to describe clinical characteristics of, and treatment patterns in, participants with CKD and T2D treated with finerenone in routine clinical practice.[8]
- This interim analysis of the FINE-REAL study describes the United States (US) cohort with a focus on dosing, treatment patterns, and safety.

Methods

- Inclusion criteria[8]:
  - At least 18 years of age.
  - Diagnosis of CKD associated with T2D based on physician assessment.
  - Receiving finerenone (10 or 20 mg) in accordance with the local marketing authorization.
    - Enrollment was allowed after the decision to initiate finerenone treatment had been made by the treating physician.
- The data cut-off for this interim analysis was June 13, 2024.
- Study endpoints are shown in **Table 1**.

Results

- 834 US participants were enrolled; 774 were included in the full analysis set.
  - 60 participants were excluded because participation was not possible (n=37) or finerenone was not being taken at the time of cut-off for this interim analysis (n=23).
- At baseline, mean (standard deviation [SD]) age was 66 (11) years and 54% of participants were male; median (interquartile range [IQR]) urine albumin:creatinine ratio was 198.3 (54.0–609.8) mg/g and mean (SD) eGFR was 53.8 (25.1) mL/min/1.73 m^2 (**Table 2**).
- 158 (20.4%) participants were Hispanic or Latino and 154 (19.9%) were Black/African American.
- Sodium-glucose cotransporter-2 inhibitors (SGLT-2is) and glucagon-like peptide-1 receptor agonists (GLP1-RAs) were used by 49.0% and 38.9% of participants, respectively (**Figure 1**).
- Median (IQR) follow-up time was 341 (206–367) days.
- At baseline, 216 (27.9%) participants had eGFR ≥60 mL/min/1.73 m^2 (**Figure 2**); 18 (2.3%), 119 (15.4%), 142 (18.3%), and 189 (24.4%) participants were at low, moderate, high, or very high eGFR Kidney Disease Improving Global Outcomes (KDIGO) risk, respectively; eGFR KDIGO risk was unknown for 306 (39.5%) participants.
- A total of 664 (85.8%) and 109 (14.1%) participants initiated finerenone at doses of 10 and 20 mg, respectively.
  - In 145 (21.8%) participants starting on 10 mg, the dose was up-titrated.
  - In 6 (5.5%) participants starting on 20 mg, the dose was down-titrated.
  - Most participants started on 10 mg despite 27.9% having eGFR ≥60 mL/min/1.73 m^2.
- Cumulative incidence based on Aalen–Johansen estimates for time to first treatment-emergent Medical Dictionary for Regulatory Activities labeling groupings hyperkalemia was 8.7% (95% confidence interval: 6.6–11.2%) at 12 months (**Figure 3**).

Table 1. Study endpoints[8]

Primary endpoint	Secondary endpoints
Describe clinical characteristics and treatment patterns in participants with CKD and T2D treated with finerenone	The occurrence of: • TEAEs • Serious TEAEs • Hyperkalemia TEAEs – Hyperkalemia leading to permanent study drug discontinuation – Hyperkalemia leading to dialysis – Hyperkalemia leading to hospitalization

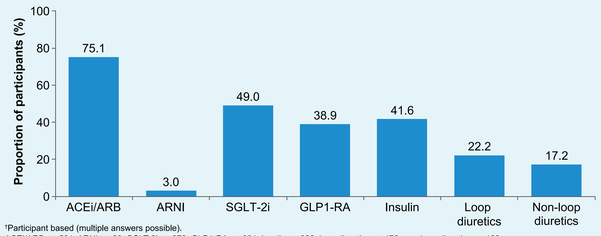
CKD, chronic kidney disease; T2D, type 2 diabetes; TEAE, treatment-emergent adverse event.

Table 2. Baseline demographics and disease characteristics

Characteristic	FAS (N=774)
Age, mean (SD), years	66.1 (11.3)
Sex, n (%)	
Male	416 (53.7)
Female	358 (46.3)
BMI, median (IQR), kg/m^2 (n=704)	32.3 (27.7–37.3)
Time from diagnosis of T2D, median (IQR), years (n=589)	13.0 (7.0–21.0)
Time from diagnosis of CKD, median (IQR), years (n=594)	3.5 (2.0–6.0)
UACR, median (IQR), mg/g (n=470)	198.3 (54.0–609.8)
eGFR, mean (SD), mL/min/1.73 m^2† (n=675)	53.8 (25.1)
Serum potassium, median (IQR), mmol/L (n=671)	4.4 (4.1–4.6)
Serum potassium, category, n (%) (n=671)	
≤3.6 mmol/L	31 (4.6)
>3.6–5.0 mmol/L	610 (90.9)
>5.0–5.5 mmol/L	25 (3.7)
>5.5–6.0 mmol/L	4 (0.6)
>6.0 mmol/L	1 (0.2)
HbA1c, mean (SD), % (n=493)	7.5 (1.7)
Seated systolic blood pressure, mean (SD), mmHg (n=737)	136.7 (20.3)
Seated diastolic blood pressure, mean (SD), mmHg (n=737)	76.9 (10.4)

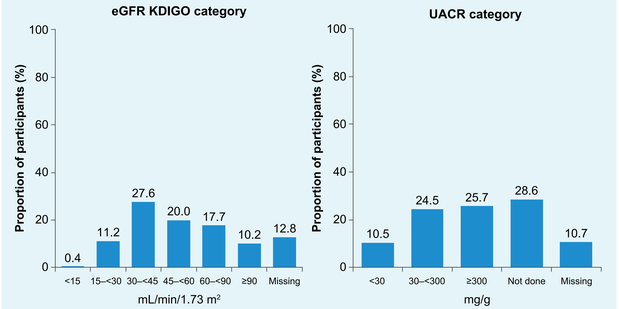
†Calculated using the CKD-EPI 2009 formula without adjustment for race.
BMI, body mass index; CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; FAS, full analysis set; HbA1c, hemoglobin A1c; IQR, interquartile range; SD, standard deviation; T2D, type 2 diabetes; UACR, urine albumin:creatinine ratio.

Figure 1. Concomitant medication at finerenone initiation† (N=774)



†Participant based (multiple answers possible).
ACEi/ARB, n=581; ARNI, n=23; SGLT-2i, n=379; GLP1-RA, n=301; insulin, n=322; loop diuretics, n=172; non-loop diuretics, n=133.
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; GLP1-RA, glucagon-like peptide-1 receptor agonist; SGLT-2i, sodium-glucose cotransporter-2 inhibitor.

Figure 2. eGFR and UACR at finerenone initiation (N=774)



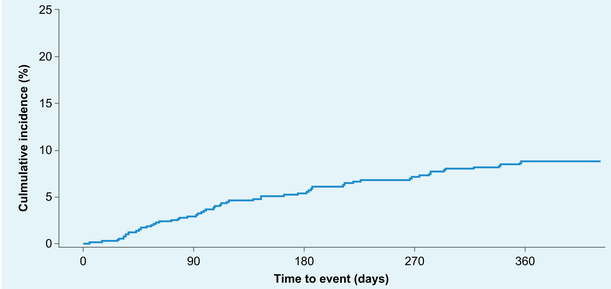
eGFR: <15, n=3; 15–<30, n=87; 30–<45, n=214; 45–<60, n=155; 60–<90, n=137; ≥90, n=79; missing, n=99. UACR: <30, n=81; 30–<300, n=190; ≥300, n=199; not done, n=221; missing, n=83.
eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease Improving Global Outcomes; UACR, urine albumin:creatinine ratio.

Table 3. Summary of TEAEs overall

Event, n (%)	FAS (N=774)
Any TEAE	259 (33.5)
Any serious TEAE	63 (8.1)
Any TEAE leading to death	1 (0.1)

FAS, full analysis set; TEAE, treatment-emergent adverse event.

Figure 3. Cumulative incidences based on Aalen–Johansen estimates for time to treatment-emergent MedDRA labeling groupings hyperkalemia†



†The term "hyperkalemia" refers to the combined MedDRA preferred terms "hyperkalemia" and "blood potassium increased."
Participants with events occurring throughout the study period (overall). Cumulative incidences calculated by Aalen–Johansen estimator using all-cause death as a competing risk. All interruptions were excluded from the person-time at risk and calculation of relative days, i.e. for participants with an interruption; events in the period of interruption start +3 days until the end of interruption were not considered.
MedDRA, Medical Dictionary for Regulatory Activities.

Table 4. Hyperkalemia† TEAEs

Outcome, n (%)	FAS (N=774)
Any event	53 (6.8)
Serious events	5 (0.6)
Study drug related	47 (6.1)
Leading to permanent study drug discontinuation	8 (1.0)
Leading to hospitalization	1 (0.1)

†The term "hyperkalemia" refers to the combined MedDRA preferred terms "hyperkalemia" and "blood potassium increased."
FAS, full analysis set; MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event.

- TEAEs were reported in 259 (33.5%) participants (**Table 3**).
- The most common TEAEs (≥1%) were hyperkalemia (6.8%) (for details see **Table 4** and **Figure 3**), urinary tract infection (4.0%), urogenital tract hemorrhage (3.7%), renal failure (2.2%), COVID-19 (1.3%), edema (1.0%), and hypotension (1.0%).
- There were no fatal events of hyperkalemia and no hyperkalemia requiring dialysis.
- Serious TEAEs were reported in 63 (8.1%) participants.
- The most frequently reported serious TEAE was renal failure (10 participants; 1.3%).
- Five (0.6%) participants died; one each from hepatic failure, congestive cardiac failure, cerebral hemorrhage, and road traffic accident, and one from unknown cause.

Conclusions

- FINE-REAL is the first global, prospective, observational study investigating the use of an nsMRA in routine clinical care in participants with CKD and T2D.
- Participants across a wide spectrum of KDIGO risk categories at baseline were observed in the US cohort of FINE-REAL.
- The FINE-REAL US cohort was at lower KDIGO risk than in the FIDELITY combined analysis of finerenone Phase III trials in CKD and T2D overall, and more often received SGLT-2is or GLP1-RAs.[9]
- Underdosing with finerenone was common at the time of initiation despite many participants having eGFR ≥60 mL/min/1.73 m^2.
- The incidence of hyperkalemia in the US FINE-REAL population was low.
- There were no fatal events of hyperkalemia and no hyperkalemia requiring dialysis.
- Finerenone demonstrated a favorable safety profile in this population.

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Acknowledgments

The authors would like to thank the participants, their families, and all US investigators (A. Abdellatif, D. Amberker, A. Arif, V. Bansal, K. Bartolomei, V. Bland, L. Blonde, V. Dawson, A. Del Priore, A. Elsharkawi, M. Gaffney, K. Gaurav, R. Graf, L. Hanson, N. Haq, V. Houchin, W. Kaye, S. Khurana, C. Kwoh, R. Minasian, L. Mulloy, A. Narayan, R. Neyra, G. Ortiz, L. Ovadje, A. Parsa, M. Quadrini, J. Ravid, R. Rosen, S. Rovner, C. Semakula, T. To, L. Tom, S. Udani, P. Velasquez-Mieyer, T. Wooldridge, T. Yacoub, and W. Yang) involved in this study. We thank Joe Largay, Mafaza Qaiser, and Juan Villafana for study support in the USA. Medical writing support was provided by Laura Chalmers, PhD, of Adelphi Communications Ltd (Bollington, UK), funded by Bayer AG in accordance with Good Publication Practice 2022 guidelines (https://www.acpjournals.org/doi/10.7326/M22-1460).

Disclosures

This study is sponsored by Bayer AG. The authors developed the poster with the assistance of a medical writer funded by the sponsor. The sponsor was involved in the study design and the writing of the report. SDN received research support from Bayer AG for the submitted work.

Contact details: Name: Sankar D. Navaneethan; Email: Sankar.Navaneethan@bcm.edu