Design and rationale of FINE-REAL: A prospective study providing insights into the use of finerenone in routine clinical settings

Poster number INFO10

Susanne B. Nicholas,[1] Nihar R. Desai,[2] Sankar D. Navaneethan,[3] Kevin M. Pantalone,[4] Christoph Wanner,[5] Stefanie Hamacher,[6] Alain Gay,[7] and David C. Wheeler[8]

[1]David Geffen School of Medicine at UCLA, Los Angeles, California, USA; [2]Section of Cardiovascular Medicine, Yale School of Medicine, Yale New Haven Hospital, New Haven, Connecticut, USA; [3]Section of Nephrology, Baylor College of Medicine, Houston, Texas, USA; [4]Endocrinology and Metabolism Institute Cleveland Clinic, Cleveland, Ohio, USA; [5]University Hospital Würzburg, Department of Medicine, Division of Nephrology, Würzburg, Germany; [6]ClinStat GmbH, Cologne, Germany; [7]Medical Affairs & Pharmacovigilance, Pharmaceuticals, Bayer AG, Berlin, Germany; [8]Department of Renal Medicine, University College London, London, UK

Introduction

- Finerenone, a selective, nonsteroidal, mineralocorticoid receptor antagonist (MRA), has been recently approved for the treatment of chronic kidney disease (CKD) associated with type 2 diabetes (T2D) in the United States (US), European Union, and several other countries including China, India, and Japan[1–3]
  - The approvals were based on demonstrated efficacy in either the FIDELIO-DKD (NCT02540993) study alone, or in both the FIDELIO-DKD and FIGARO-DKD (NCT02545049) studies where finerenone reduced the risk of adverse cardiovascular and kidney outcomes compared with placebo in patients treated with maximum tolerated renin–angiotensin system inhibition[4–6]
- Finerenone is now included as a recommended treatment for CKD associated with T2D in the most recent guidance from the American Diabetes Association (ADA), the American Association of Clinical Endocrinologists, and in the ADA-Kidney Disease: Improving Global Outcomes consensus report on diabetes management in CKD[7–9]
  - Patients enrolled in randomized clinical trials may differ from those encountered in routine clinical practice
- Long-term efficacy and safety data from patients treated in clinical care are needed to inform clinicians and public health organizations on the most appropriate treatment pathway for patients and the management of adverse events
- The FINE-REAL study (NCT05348733; a non-interventional study providing insights into the use of finerenone in a routine clinical setting) aims to address this clinical need and will provide insights on the characteristics, treatment patterns, and clinical outcomes of patients with CKD and T2D treated with finerenone in routine clinical practice

Methods

Study design

- FINE-REAL is an international, prospective, observational, multicenter, single-arm study
- Details of the study design are presented in **Figure 1**

Figure 1. Design of the FINE-REAL study

CDB, clean database; CKD, chronic kidney disease; CSR, clinical study report; FPFV, first patient first visit; LPFV, last patient first visit; LPLV, last patient last visit; T2D, type 2 diabetes.

- FINE-REAL will be conducted in approximately 20 countries with a planned enrollment of approximately 4000 participants (**Figure 2**)
- Patients initiated on finerenone (10 or 20 mg) in accordance with the country/region-specific marketing authorization as part of their standard of care will be enrolled

Study participants and data collection

- Eligible individuals will be:

1. ≥18 years of age
2. Diagnosed with CKD associated with T2D
3. Initiating treatment with finerenone in accordance with the local label

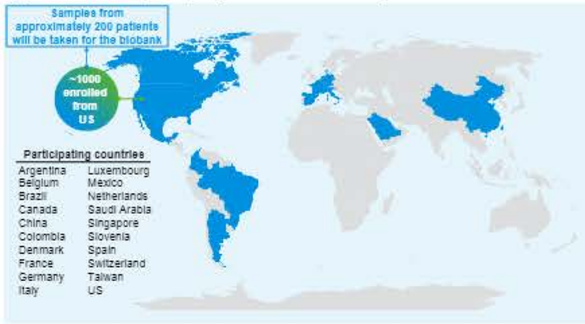
- A summary of data to be captured at all visits is shown in **Table 1**
- Patients will be followed up until 30 days after permanent discontinuation of finerenone

Table 1. Data collection at baseline, follow-up visits, and end of study

	Baseline visit	Follow-up visit(s) including the final visit
Date/type of visit	X	X
Eligibility/informed consent	X	
Demographics Year of birth, sex, ethnic group, race (black/non-black)†, smoking status, and alcohol consumption	X	
Vital signs Weight, height, and blood pressure	X	
Disease history	X	
Comorbidities (medical history, concomitant diseases)	X	
Concomitant medications Glucose-lowering agents, lipid-lowering treatment, RAS inhibitors, MRA‡, digoxin, β-blockers, diuretics, potassium supplements, potassium binders, herbal therapy, traditional Chinese medicine, anti-thrombotic treatment, vaccination against SARS-CoV-2, and NSAIDs	X	X
Exposure/treatment	X	X
Laboratory parameters Collected at baseline: eGFR, liver function (AST and ALT), hemoglobin, serum sodium, HbA1c, fasting blood glucose, and UACR Collected at baseline and post-baseline: serum creatinine, serum or plasma potassium, urine test results	X	X
AEs	(X)	X§
Hyperkalemia	X	X
Healthcare resource utilization (inpatient/outpatient/emergency visits)	X	X
Diabetic retinopathy	X	X
Sampling of blood and urine samples for biobanking (for patients in the US only)	X	X

†Assessment of race required for calculation of eGFR using the CKD-EPI 2009 formula.[10] ‡Another MRA should not be given together with finerenone, however, we are interested to know if a patient was exposed before the initiation of finerenone. §AEs up to 30 days after the last treatment with finerenone. AE, adverse event; ALT, alanine transaminase; AST, aspartate aminotransferase; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; MRA, mineralocorticoid receptor antagonist; NSAID, non-steroidal anti-inflammatory drug; RAS, renin–angiotensin system; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus-2; UACR, urinary albumin-to-creatinine ratio.

Figure 2. Countries participating in the FINE-REAL study



Study objectives

- The primary objective of the FINE-REAL study is to describe treatment patterns in patients with CKD and T2D treated with finerenone in routine clinical practice (**Table 2**)
- Details on the primary, secondary, further, and exploratory objectives are shown in **Table 2**
- A US-specific prespecified exploratory objective is to collect blood and urine samples to establish a biobank for future analyses; it is anticipated that up to a quarter of all enrolled participants will be from the US, of whom approximately 200 will have samples collected for the biobank (**Table 2**)

Table 2. List of primary, secondary, and exploratory study objectives and endpoints

Study objectives and endpoints
Primary objective: **To describe treatment patterns in patients with CKD and T2D treated with finerenone, based on:** Clinical characteristics of patients with CKD and T2D Reasons for introducing finerenone Reasons for discontinuation of finerenone Planned and actual duration of treatment with finerenone Dosing of finerenone Use of secondary therapies in patients with CKD and T2D
Secondary objective: **To evaluate overall reported safety of finerenone in treated patients and hyperkalemia, based on:** Reported AE/SAEs Reported hyperkalemia Reported hyperkalemia leading to study drug discontinuation Reported hyperkalemia leading to dialysis Reported hyperkalemia leading to hospitalization
Further objective: **To assess healthcare resource utilization and diabetic retinopathy, based on:** Reported visits with healthcare providers (reasons, duration, and outcomes) Outpatient visits (including but not limited to emergency room department visits), inpatient stays Reported diabetic retinopathy and its progression if existing at time of ICF signature
Exploratory objective† Establishment of a biobank to support future analyses

AE, adverse event; CKD, chronic kidney disease; ICF, informed consent form; SAE, serious adverse event; T2D, type 2 diabetes.
†US patients only.

Analysis

- Statistical analyses will be of an explorative and descriptive nature as the FINE-REAL study is not intended to test a pre-specified statistical hypothesis
- The primary objective will be analyzed using descriptive statistics
- Frequency tables for hyperkalemia-related events will be provided and cumulative incidences will be provided in the form of Aalen-Johansen estimates and curves
- For the diabetic retinopathy-related endpoints, frequency tables describing the severity will be presented
- All analyses will be performed for the overall population and separately for each participating country if patient numbers are sufficient and if required for local reasons. Where possible, data will be stratified by subgroups (e.g., age, sex, and other baseline characteristics)

Conclusions

- FINE-REAL will provide meaningful perceptions and insights into CKD associated with T2D treated with finerenone
- FINE-REAL will capture AEs, particularly hyperkalemia, and identify how these are managed in routine clinical care
- New onset and progression of microvascular complications, specifically diabetic retinopathy, is a prespecified endpoint due to the paucity of pharmacological treatments available for this complication
- The establishment of a biobank will support future analyses to better characterize the mechanisms of disease and mechanism of action of finerenone
- The FINE-REAL study will help to inform decision-making with respect to initiation of finerenone in patients with CKD and T2D
- FINE-REAL will provide insights into the dynamics of new therapy adoption across different geographies and health systems, a useful insight for international guidance and implementation

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Acknowledgements

The authors would like to thank the patients, their families and all investigators involved in this study. The authors would like to acknowledge Samuel Falcoba, PhD, of Bayer US LLC, Whippany, NJ, USA, and Marcel Schulz, PhD, of Bayer AG, Berlin, Germany, for their support with the study design and setup. Medical writing support was provided by Maureen Hammad, PhD, and editorial support, including formatting, proofreading and e-poster upload, was provided by George Chiapoli, MSc, both of Scion, London, UK, supported by Bayer according to Good Publication Practice guidelines (https://www.ecpcjournals.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. S.B.N. is supported by NIH research grants R01MD014712, RF01260-2022-0038, U2CCK128498 and P60MD017366, and CDC project number 75D301-21-R-12264, receives research support from Bayer AG for the submitted work, Goldfinch Bio, Travere and Terasaki Institute of Biomedical Innovation, and personal fees and other support from AstraZeneca, Bayer AG, Gilead, NovoNordisk and Boehringer Ingelheim/Lilly. N.R.D. works under contract with the Centers for Medicare and Medicaid Services to develop and maintain performance measures used for public reporting and pay for performance programs. He reports research grants and consulting for Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Cytokinetics, Merck, Novartis, BCPharmaceuticals, and Vifor. S.D.N. reports receipt of personal fees from AstraZeneca (DSMB), ACI clinical (EAC), Bayer, Boehringer-Ingelheim/Lilly, Vertex, Vifor and grants from Kenyx, outside the submitted work. K.M.P. discloses speaker bureau fees from AstraZeneca, Corcept Therapeutics, Merck, and Novo Nordisk; consulting fees from AstraZeneca, Bayer, Corcept Therapeutics, Diasome, Eli Lilly, Novo Nordisk, Merck, Sanofi and Theracrin; and research support from Bayer, Novo Nordisk, Merck, and Thirdhealth. C.W. reports steering committee and advisory board participation as well as lecturing honoraria from AstraZeneca, Bayer, Boehringer-Ingelheim, Eli Lilly, FMC, Gilead, GBK, MSD, Sanofi and Vifor. S.H. is an employee of ClinStat GmbH and reports consulting or advisory roles of her CRO with Bayer AG. A.G. is an employee of Bayer AG, Germany. D.C.W. has received honoraria from Astellas, AstraZeneca (ongoing consultancy agreement), Amgen, Bayer, Boehringer Ingelheim, Gilead, GBK, Janssen, Mundipharma, Merck Sharp and Dohme, Tricida, Vifor and Zydus.

Contact details: Name: Susanne B. Nicholas; Email: SuNicholas@mednet.ucla.edu