FOUNTAIN

How can RWE support clinical decisions?

Adapted from:

Clinical outcomes in US patients initiating finerenone – a report from the FOUNTAIN platform

Kovesdy C et al., ERA 2024; poster (abstract #2022)

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Information Disclaimer

- This presentation may contain information regarding indications and/or instructions which differ from the approved use of products available in Canada.

- Currently, finerenone is approved by Health Canada. The complete product monograph can be found at https://pdf.hres.ca/dpd_pm/00067806.PDF [accessed 03 June 2024].

- Statements of fact and opinions expressed are those of the speaker and do not necessarily reflect the opinions or position of the sponsor (Bayer Inc).

FOUNTAIN

FinerenOne mUlti-database Network for daTA generatIoN

A platform to produce RWE that can support decision-making among health authorities and inform clinical practice to improve the care of patients with CKD and T2D

Aim

To provide comprehensive evidence regarding the effectiveness and safety of finerenone in clinical practice

Objectives

- Harmonise RWE generation across different research partners and data sources and build long-term research partnerships
- Describe utilisation of different treatment options and event rates of clinical and laboratory outcomes
- Assess the real-world effectiveness and safety of finerenone

Patient population

- Nine research partner collaborations
- Eight CDM-mapped data sources
- Seven countries

FOUNTAIN research programmes

- Multi-country description of SoC in patients with CKD and T2D
- Assessment of safety and effectiveness of finerenone in clinical practice across different countries and regions

CDM, common data model; CKD, chronic kidney disease; RWE, real-world evidence; SoC, standard of care; T2D, type 2 diabetes

1. Bayer. Data on file

Rationale for FOUNTAIN

FIDELITY

Prespecified pooled analysis (N=13,026)[1]

Kidney composite

23% **risk reduction of kidney composite outcome**

(HR=0.77; 95% CI 0.67–0.88; *p*=0.0002)

Time to kidney failure, sustained ≥57% decrease in eGFR from baseline or renal death

CV composite

14% **risk reduction of CV composite outcome**

(HR=0.86; 95% CI 0.78–0.95; *p*=0.002)

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

All-cause mortality

11% **Risk reduction of death from any cause**

(HR=0.89; 95% CI 0.79–1.00; *p*=0.051)

Hospitalisation for heart failure

22% **risk reduction of first HHF***

(HR=0.78; 95% CI 0.66–0.92; *p*=0.003)

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- As the demand for robust RWE increases across a multitude of stakeholders, the scientific community needs to find efficient ways of improving the consistency and generalisability of the evidence being generated
- Compared with more traditional clinical research settings, standards for RWE generation are more multifaceted, thus requiring a heterogeneous, portfolio-like approach to generate comprehensive and actionable evidence
- To improve the impact of RWE on clinical practice, decision processes and, ultimately, patient care, approaches to RWE generation must continually evolve

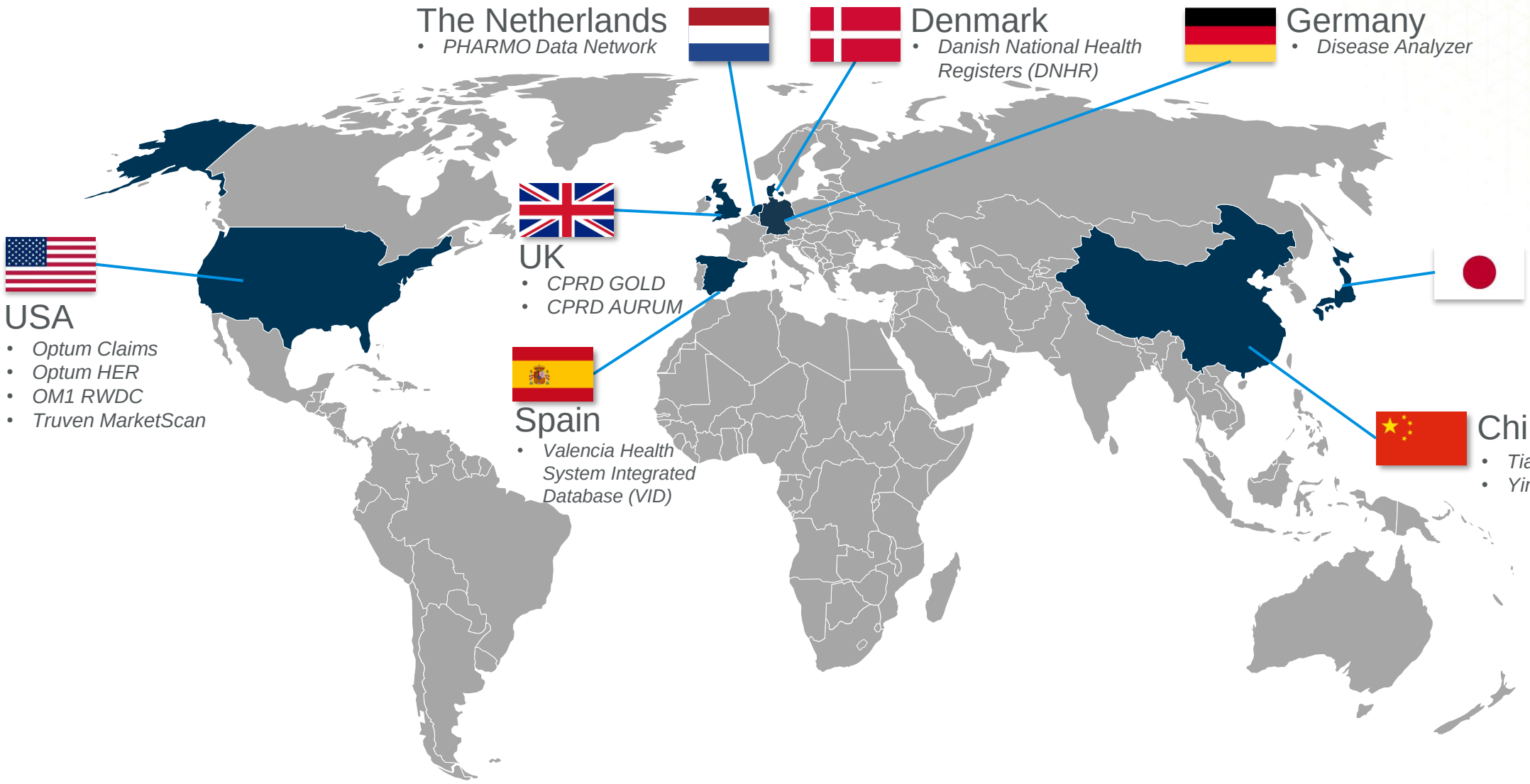
The objectives of FOUNTAIN are to: **harmonise RWE generation** across research and data partners through **complementary approaches**, and to build **long-term collaborations** with academic and commercial partners on a **global scale**

*First HHF defined as first event after randomisation

CI, confidence interval; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HHF, hospitalisation for heart failure; HR, hazard ratio; MI, myocardial infarction; RWE, real-world evidence

1. Agarwal R, *et al. Eur Heart J* 2022;43:474–484; 2. Nishioka K, *et al. Clin Pharmacol Ther* 2022;111:35–43; 3. Concato J & Corrigan-Curay J. *N Engl J Med* 2022;386:1680–1682; 4. Duke-Margolis Institute for Health Policy. 2022. https://healthpolicy.duke.edu/publications/aligning-shared-evidentiary-needs-among-payers-and-regulators-real-world-data; 5. ESMO public policy webinar: general data protection regulation and its impact on clinical research. 2021. https://www.esmo.org/content/download/439775/8425448/1/Sabine-Brosch-Orsolya-Eotvos-European-Medicines-Agency.pdf; 6. Wang SV, *et al. J Clin Epidemiol* 2022;151:161–70; 7. US Food and Drug Administration. Framework for FDA's real-world evidence program. 2018. https://www.fda.gov/media/120060/download; 8. National Institute for Health and Care Excellent (NICE). NICE real-world evidence framework. 2022. https://www.nice.org.uk/corporate/ecd9/resources/nice-realworld-evidence-framework-pdf-1124020816837 [all URLs accessed 13 May 2024]

Countries currently included in the FOUNTAIN platform



Local databases are listed in italics
UK, United Kingdom; USA, United States of America. Bayer. Data on file

Finerenone initiators in US clinical practice: A FOUNTAIN report

To describe patient characteristics and assess the early safety and effectiveness of finerenone used for the treatment of patients with CKD and T2D in routine clinical practice

Data sources	US database*	**Study period**	July 2021–August 2023
Patients	Adults with CKD[#] and T2D[‡] who initiated treatment with finerenone within the study period		
Design[1,2]	Observational, retrospective, longitudinal single-arm cohort study		

Key outcomes

- Baseline characteristics including demographics, comorbidities and comedications
- Incidence rates of hyperkalaemia
- Changes in UACR over time

The data shown here should not be compared with RCT data due to differences in study designs and patient populations

*OM1 RWDC; [#]defined as either having one diagnostic code for CKD stage 2–4 or unspecified stage, two eGFR measurements of 15–60 ml/min/1.73 m^2 separated by at least 90 days, or two UACR measurements >30 mg/g separated by at least 90 days; [‡]T2D was defined as having a diagnostic code for T2D

RWDC, Real-World Data Cloud™

1. Bayer. https://clinicaltrials.gov/study/NCT05703880 [accessed 5 Apr 2024]; 2. Kovesdy C, *et al*. ERA 2024; poster (abstract 2022)

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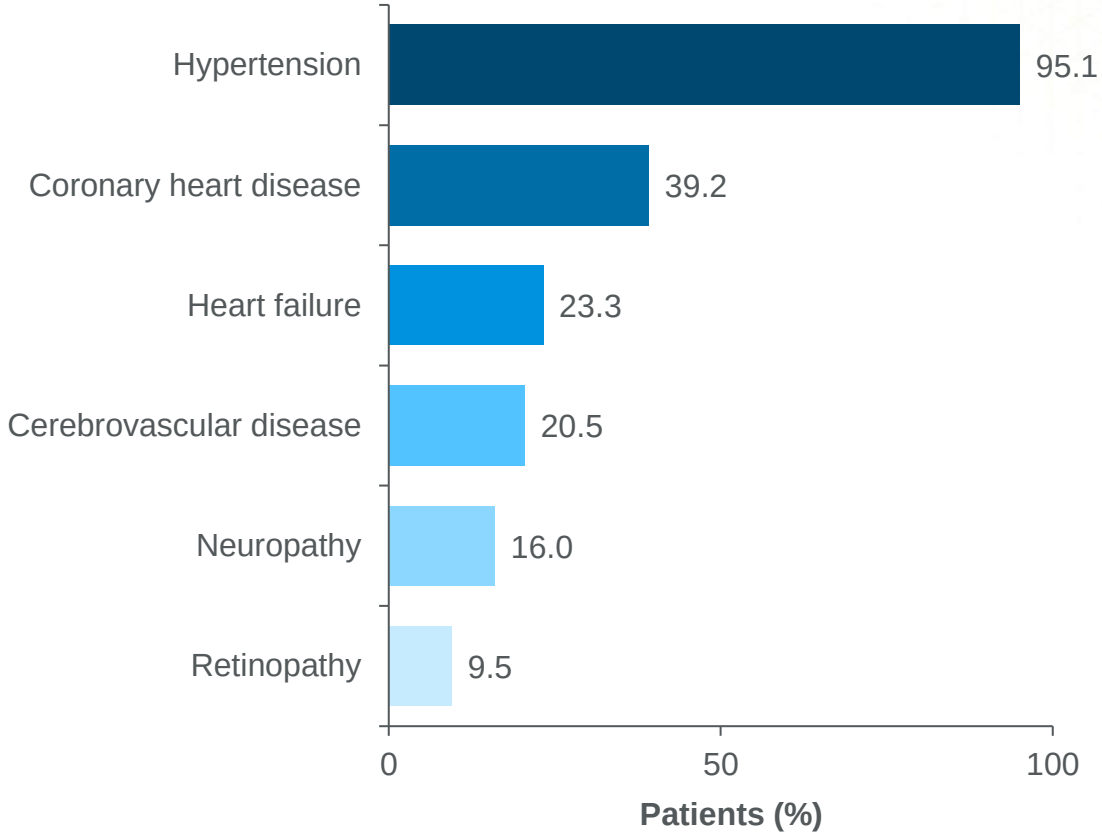
Nearly all patients with CKD and T2D initiating finerenone in US clinical practice had hypertension

Baseline demographics

Characteristic	Finerenone (N=15,948)
Female, n (%)	7036 (44.1)
Age, mean years ± SD	70.3 (10.1)
Race/Ethnic group*, n (%)	
White	3874 (69.5)
Black/African American	872 (15.6)
Asian	465 (8.3)
Other	365 (6.5)
Calendar year of index, n (%)	
2021 (July–December)	1061 (6.7)
2022	7888 (49.5)
2023 (January–August)	6999 (43.9)

Baseline comorbidities (N=15,948)



*Patients with unknown or missing information were removed from this analysis

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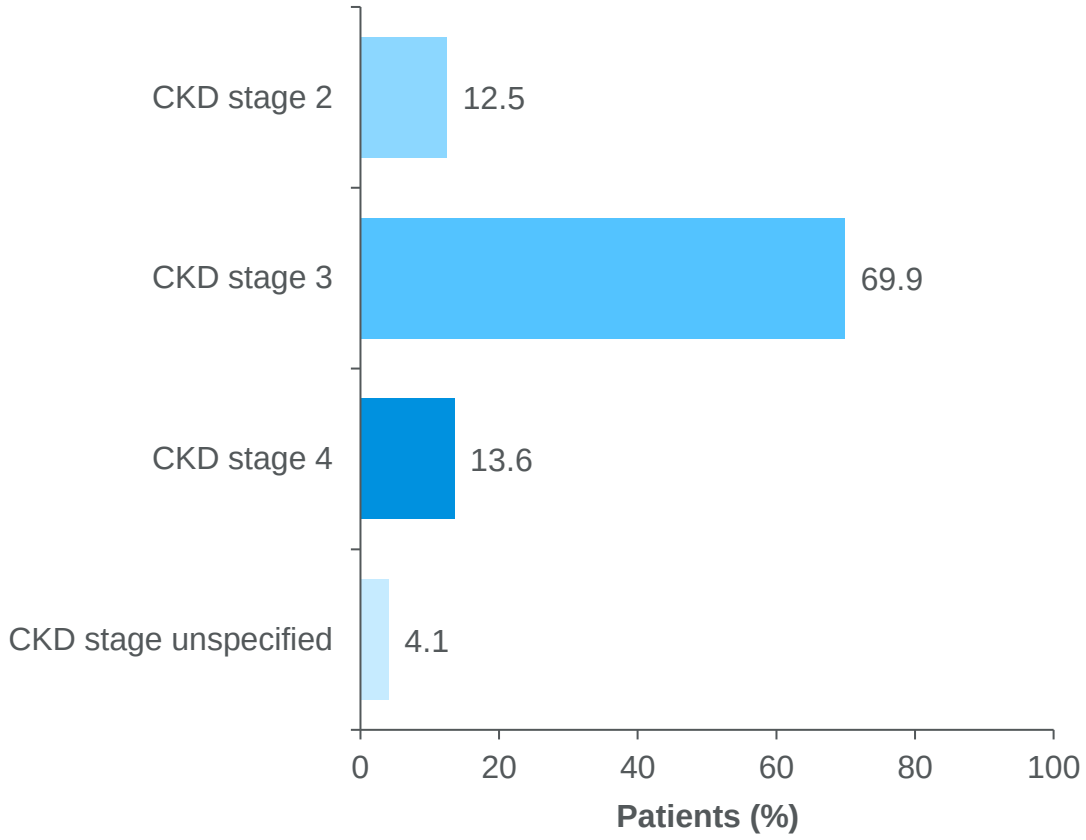
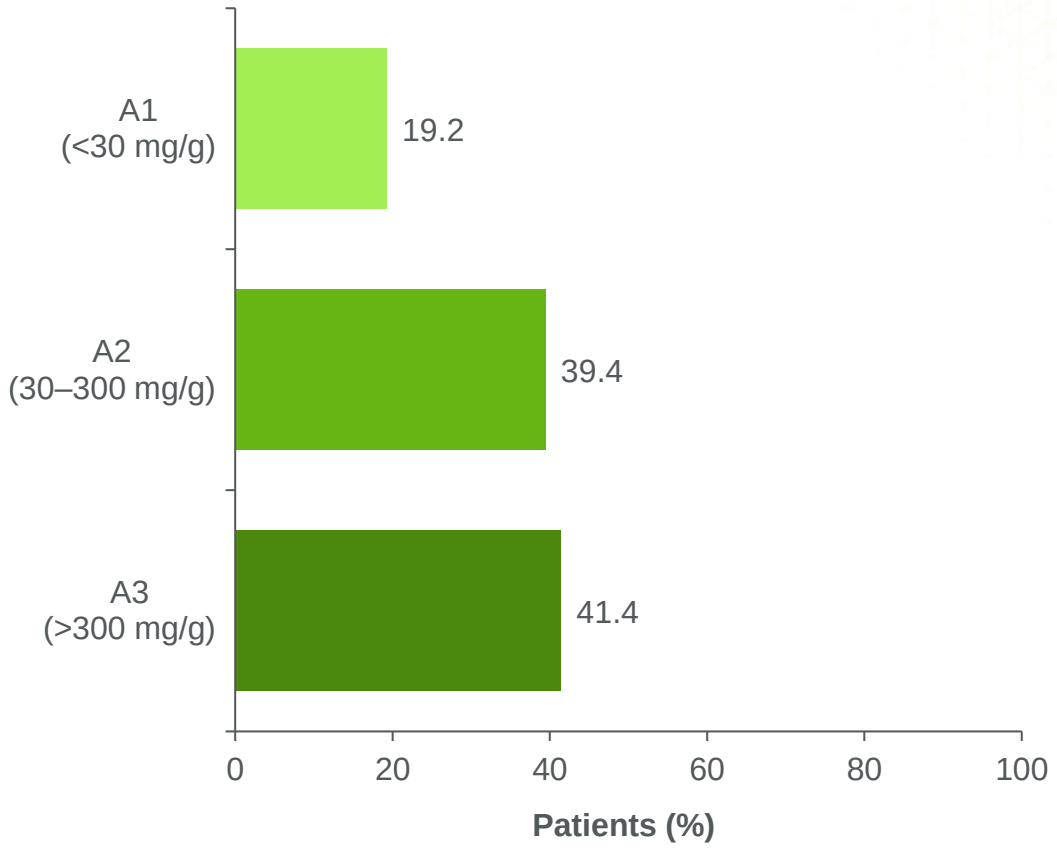
In clinical practice, finerenone is predominantly used in CKD stage 3 and albuminuria categories A2 and A3

CKD stage (n=14,566)*



Albuminuria categories (n=3758)#



Patients with missing information were removed from this analysis
*Last available CKD diagnosis code or eGFR measurement prior to finerenone initiation; #last available UACR measurement prior to finerenone initiation
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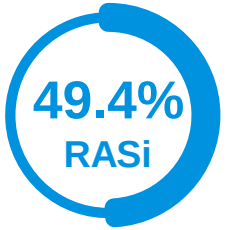
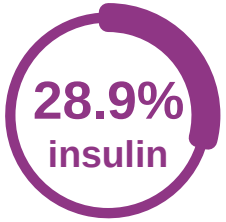
Finerenone is initiated in combination with other treatment options, including SGLT-2i and GLP-1RA



patients initiating finerenone used a RASi during the baseline period

patients initiating finerenone used an SGLT-2i during the baseline period

patients initiating finerenone used a GLP-1RA during the baseline period



patients initiating finerenone used insulin during the baseline period

Baseline comedications in the 180 days before and including the index date (N=15,948)
RASi, renin–angiotensin system inhibitor
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After 12 months, approximately 29% of patients were up-titrated to the target dose*

Prescription at index (N=15,948)

patients are prescribed **10 mg**

patients are prescribed **20 mg**

After 12 months (n=2212)

patients are prescribed **10 mg**

patients are prescribed **20 mg**

*The recommended target dose of finerenone is 20 mg once daily, and this is also the recommended starting dose for patients with eGFR ≥60 ml/min/1.73 m^2. For patients with eGFR ≥25–<60 ml/min/1.73 m^2, the recommended starting dose is 10 mg once daily[2]

1. Kovesdy C, *et al*. ERA 2024; poster (abstract 2022); 2. Bayer Inc. KERENDIA® (finerenone) Product Monograph. OCT 2022 https://pdf.hres.ca/dpd_pm/00067806.PDF [accessed 03 June 2024]

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In clinical practice, the observed incidence of hyperkalaemia after finerenone initiation appeared low

1.96
IR*

Among 15,948 initiators of finerenone, **1.32%** (n=210) had **hyperkalaemia**[#] during follow-up

0.07
IR*

Among 15,948 initiators of finerenone, **7** patients (0.04%) had **hyperkalaemia associated with a hospitalisation**[‡] during follow-up

***E**vents per 100 PY; [#]hyperkalaemia is defined as i) a hospitalisation or emergency department visit with a diagnosis code for hyperkalaemia, or ii) at least 2 serum [K^+] laboratory values >5.5 mmol/l, as follows: two inpatient serum [K^+] values >5.5 mmol/l on the inpatient record within 7 days or one serum [K^+] value >5.5 mmol/l in a non-hospitalised setting and another value in any setting within 7 days, or iii) a serum [K^+] laboratory value >5.5 mmol/l in any setting and the occurrence of an inpatient or outpatient diagnosis code for hyperkalaemia within 3 days; [‡]hyperkalaemia associated with a hospitalisation: a medical diagnosis code or increased serum [K^+] (>5.5 mmol/l) 7 days prior to or after a hospitalisation record
IR, incidence rate; PY, patient-years
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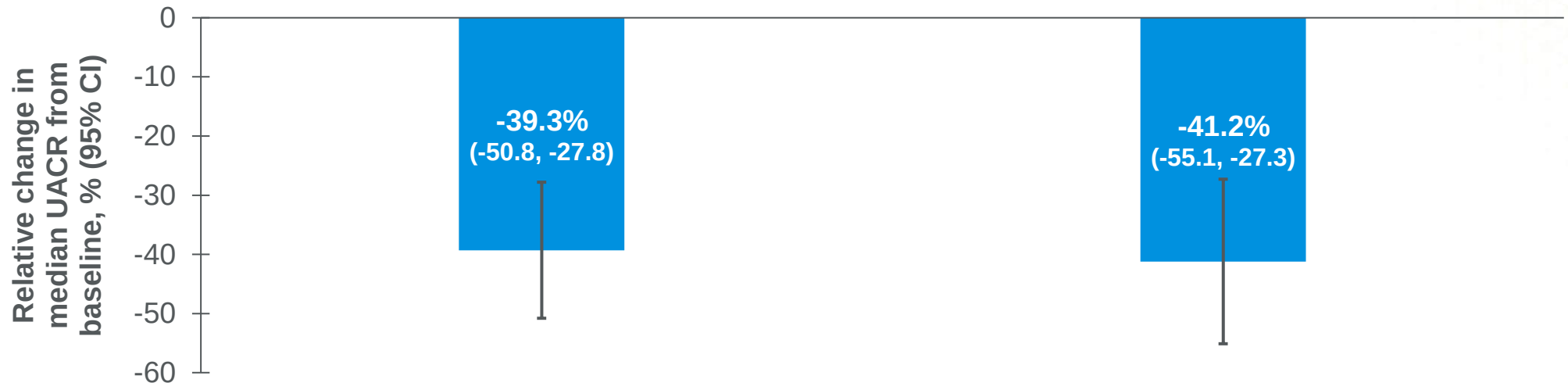
Finerenone was associated with a 39% relative reduction in UACR after 4 months, which was sustained at 12 months (41%)

Relative change in median UACR from baseline



	Baseline	Month 4	Month 12
Number of patients	2137	1617	900
UACR, mg/g, median (Q1–Q3)	211 (56–750)	128 (31–551)	124 (26–544)

Kovesdy C, *et al*. ERA 2024; poster (abstract 2022)

Summary

Recent data have provided valuable insights into the usage and effects of finerenone

Subanalyses from FIDELITY

- **Finerenone increased improvement** and **reduced worsening in KDIGO risk category** versus placebo[1]
- **Finerenone reduced CV risk*** compared with placebo **irrespective of CKD stage**[2]
- **Finerenone improved mortality outcomes** versus placebo **irrespective of baseline UACR**[3]

Finerenone in RWE

- **Finerenone** is used **alongside other drugs** indicated for kidney and CV risk reduction in patients with CKD and T2D[4,5]
- In real-world studies, the **incidence of hyperkalaemia with finerenone appeared low**[4,5]
- **Finerenone was associated with substantial reductions in UACR from baseline to month 4, which were sustained at month 12**[5]

In Canada, finerenone is indicated as an adjunct to standard of care therapy in adults with chronic kidney disease (CKD) and type 2 diabetes(T2D) to reduce the risk of: - End-stage kidney disease and a sustained decrease in estimated glomerular filtration rate, - Cardiovascular death, non-fatal myocardial infarction and hospitalization for heart failure.

*Risk of the composite CV outcome of time to CV death, non-fatal MI, non-fatal stroke, or hospitalisation for heart failure; #finerenone was associated with a 39% reduction from baseline in UACR after 4 months, which was sustained at 12 months (41%)

1. Inzucchi SE, *et al. EASD* 2023; oral presentation 698; 2. Sarafidis P, *et al. Clin J Am Soc Nephrol* 2023;18:602–612; 3. Filippatos G, *et al. Eur Heart J Cardiovasc Pharmacother* 2023;9:183–191; 4. Nicholas SB, *et al. ASN Kidney Week* 2023; poster (abstract SA-PO481); 5. Kovesdy C, *et al*. ERA 2024; poster (abstract 2022)