Diabetes Ther (2024) 15:1861–1864
https://doi.org/10.1007/s13300-024-01591-w

SUMMARY OF RESEARCH

Summary of Research: Cardiovascular and Kidney Outcomes with Finerenone in Patients with Type 2 Diabetes and Chronic Kidney Disease—The FIDELITY Pooled Analysis

Karin Humle · Boris Klanger · Peter Kolkhof · Sylvia E. Rosas · Peter Rossing · Eugene Wright · Nichole Jefferson

Received: February 23, 2024 / Accepted: April 16, 2024 / Published online: July 19, 2024

ABSTRACT

People living with type 2 diabetes (T2D) and chronic kidney disease (CKD) are at risk of CKD progression and kidney failure. This is a summary of the FIDELITY pooled analysis where two clinical trials (FIDELIO-DKD and FIGARO-DKD) were performed to investigate the safety and efficacy of finerenone in people with T2D and CKD. The data from these two studies were combined and analyzed and it was found that those who took finerenone on top of standard-of-care medicine had a 14% reduced risk of having a cardiovascular event and 23% reduced risk of having a kidney event versus those who took placebo. Those who took finerenone were also more likely to have high blood potassium, but this was mostly manageable.

A graphical abstract and translations of all content (Chinese, Japanese, German, Spanish, Brazilian-Portuguese, French) are available for this article.

Keywords: Cardiovascular disease; Chronic kidney disease; Finerenone; Type 2 diabetes

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13300-024-01591-w.

K. Humle
Patient Author, Vallensbæk Strand, Denmark

B. Klanger (✉)
LäkarGruppen, Källgatan 10, 722 11 Västerås, Sweden
e-mail: boris.klanger@ptj.se

P. Kolkhof
Research and Early Development, Cardiovascular Precision Medicines, Bayer AG, Aprather Weg 18a, 42113 Wuppertal, Germany

S. E. Rosas
Joslin Diabetes Center, Boston, MA, USA

S. E. Rosas
Harvard Medical School, Boston, MA, USA

P. Rossing
Steno Diabetes Center Copenhagen, Borgmester Ib Juuls Vej 83, 2730 Herlev, Denmark

P. Rossing
Department of Clinical Medicine, University of Copenhagen, Blegdamsvej 3b 33.5, 2200 Copenhagen, Denmark

E. Wright
South Piedmont Area Health Education Center, Charlotte, NC, USA

N. Jefferson
Patient Author, Dallas, TX, USA

Key Summary Points

The FIDELITY pooled analysis combined and analyzed the efficacy and safety data from two similar placebo-controlled phase 3 clinical trials of the drug finerenone in people with chronic kidney disease (CKD) and type 2 diabetes (T2D).

Finerenone, in addition to standard-of-care medicine, significantly reduced the risk of clinically significant kidney and cardiovascular outcomes in people with T2D and a broad range of CKD severities.

Hyperkalemia was more frequent with finerenone than with placebo, but in most cases it was manageable without discontinuing treatment.

DIGITAL FEATURES

This article is published with digital features, including a graphical abstract and translations of all content (Chinese, Japanese, German, Spanish, Brazilian-Portuguese, French), to facilitate understanding of the article. To view digital features for this article, go to https://doi.org/10.6084/m9.figshare.25610169.

BACKGROUND

This article summarizes the results of the FIDELITY pooled analysis [1]. People with chronic kidney disease (CKD) and type 2 diabetes (T2D) are at risk of kidney failure, cardiovascular (CV) events, and dying from kidney and CV causes. Increased activity at the mineralocorticoid receptor (MR) in the kidneys, heart, and blood vessels can cause excessive inflammation and fibrosis that drives CKD and CV disease progression. MRs are blocked by a nonsteroidal MR antagonist called finerenone. The FIDELITY analysis pooled data from two randomized clinical trials to obtain more robust evidence of finerenone's safety and effect on kidney and CV outcomes in people with T2D and CKD.

STUDY METHODS

Participants were adults with CKD and T2D with an estimated glomerular filtration rate (eGFR: a marker of kidney function) of at least 25 ml/min/1.73 m^2, a urinary albumin-to-serum creatinine ratio (UACR: a marker of kidney damage) of at least 30 mg/g, and a maximum serum potassium concentration of 4.8 mmol/l. Most participants were taking the maximum tolerated labeled dose of either an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB).

Participants received either oral finerenone (10 or 20 mg, once daily) or placebo, plus standard-of-care medicine (ACEi or ARB). Sodium-glucose co-transporter-2 (SGLT2) inhibitors were taken by 6.7% of participants. Since the design of the FIDELIO and FIGARO clinical trials, SGLT2 inhibitors have become a therapeutic option for CKD and T2D.

Researchers analyzed the length of time until one of a combination (composite) of events first occurred. The CV composite outcome was CV death, non-fatal myocardial infarction (MI), non-fatal stroke, or hospitalization due to heart failure (HHF). The kidney composite outcome was onset of kidney failure, sustained decrease in eGFR of 57% or more from study start over 4 or more weeks, or death from kidney causes. Kidney failure was defined as end-stage kidney disease (ESKD) or a sustained decrease in eGFR to less than 15 ml/min/1.73 m^2, and ESKD was defined as a patient starting chronic dialysis (for 90 days or more) or having a kidney transplant. In the safety analysis, the researchers monitored side effects that occurred or worsened. The statistical analysis plan for this analysis was described before the data were analyzed (prespecified).

ANALYSIS RESULTS

Overall, 13,026 participants were followed up for a median of 3 years.

Cardiovascular Outcomes

Participants who received finerenone had a 14% reduced risk relative to participants who received placebo of experiencing a CV composite outcome. A CV event occurred in 12.7 and 14.4% of participants in the finerenone and placebo groups, respectively ($p = 0.0018$). Participants who received finerenone had a 22% reduced risk relative to participants who received placebo of HHF. HHF occurred in 3.9% of participants who received finerenone compared with 5% of participants who received placebo ($p = 0.003$) (Fig. 1).

Kidney Outcomes

Participants who received finerenone had a 23% reduced risk relative to participants who received placebo of experiencing a kidney composite outcome. A kidney event occurred in 5.5 vs. 7.1% of participants in the finerenone and placebo groups, respectively ($p = 0.0002$). Participants who received finerenone had a 30% reduced risk of a sustained decrease in eGFR of ≥ 57% for ≥ 4 weeks and a 20% reduced risk of ESKD relative to participants who received placebo ($p < 0.0001$ and $p = 0.040$, respectively; not prespecified). At 4 months, the mean change in UACR from the start of the study was 32% lower in patients who received finerenone compared with patients who received placebo.

Safety Analysis

Serious side effects occurred in 31.6% of patients who took finerenone compared with 33.7% of patients who took placebo. Hyperkalemia (serum potassium > 5.5 mmol/l) occurred in more participants with finerenone (14%) than with placebo (6.9%). Hyperkalemia leading to permanent treatment discontinuation occurred more frequently in patients receiving finerenone (1.7%) than placebo (0.6%). However, no cases were fatal, and 0.9% of cases led to hospitalization.

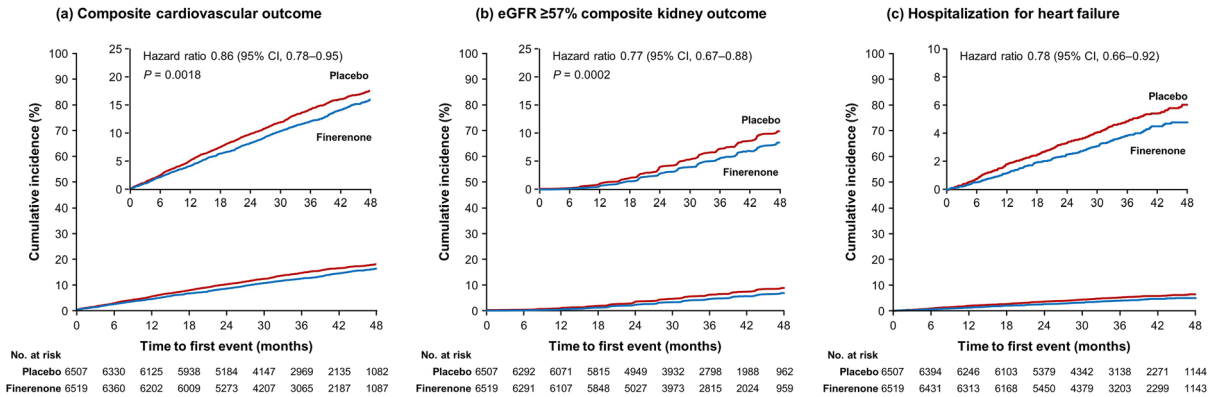

Fig. 1 Time to efficacy outcomes for a cardiovascular composite event (**a**), a kidney composite event (**b**), and hospitalization for heart failure (**c**). These graphs demonstrate the changing risk of an event (**a**, **b**, or **c**) taking place over time for patients in the finerenone and placebo treatment group. Cumulative incidence = number of new events divided by the total number of individuals in the treatment group. Time to first event = time (months) taken until first event took place. Hazard ratio (HR) = risk of experiencing an event. HR < 1 indicates a reduced risk experiencing an event, HR = 1 indicates same risk of experiencing an event in both groups, HR > 1 indicates an increased risk of experiencing an event (i.e., an HR of 0.86 corresponds to a 14% reduced risk in the finerenone group compared to the placebo group). Number at risk = number of individuals still at risk of experiencing an event. 95% confidence interval = 95% certainty that the HR lies within the specified HR range. Please see the original article for a full description of the cardiovascular and kidney composite outcomes. Graphs available for free re-use in publications under a CC-BY-NC license [1]

DISCUSSION

These results support finerenone's safety and efficacy in reducing CV events and kidney failure outcomes in patients with T2D and a broad range of CKD severity. Treatment with finerenone reduced the risk of a CV event by 14% and the risk of a kidney event by 23%, relative to treatment with placebo. Finerenone is indicated to reduce the risk of sustained eGFR decline, ESKD, CV death, non-fatal MI, and HHF in adults with CKD associated with T2D. The limitations of this analysis were excluding participants with CKD who did not have albuminuria and not including enough Black participants.

CONCLUSIONS

Finerenone, in addition to standard-of-care medicine, reduced the risk of clinically important CV and kidney outcomes compared with placebo in people with T2D and a broad range of CKD severity.

Medical Writing and Editorial Assistance. Medical writing assistance was provided by Charlotte Maddocks of Envision Pharma Group, funded by Bayer Corporation. Envision Pharma Group's services complied with international guidelines for Good Publication Practice (GPP4).

Author Contributions. Boris Klanger, Eugene Wright, Peter Rossing, Sylvia E. Rosas, Peter Kolkhof, Nichole Jefferson, and Karin Humle contributed to writing and reviewing the manuscript and take full responsibility for the integrity of the article content.

Funding. The journal's Rapid Service Fee was funded by Bayer Corporation. The authors did not receive any honoraria for this summary of research article.

Declarations

Conflict of interest. Boris Klanger: Received grants for cooperation with the following companies during the past 5 years: NovoNordisk, Boehringer Ingelheim, Bayer, AstraZeneca, Pfizer, Lilly, Abbott, Sanofi, Amgen, Amarin, Teva, Region Västmanland, Novartis. Eugene Wright: Bayer advisor, consultant, and speaker; Boehringer Ingelheim advisor, consultant, and speaker; GSK consultant and speaker. Sylvia Rosas: Received research funds from and on advisory boards for Bayer and AstraZeneca. Nichole Jefferson: Bayer consultant. Karin Humle: No conflicts of interest. The disclosure information for Peter Rossing and Peter Kolkhof have not changed compared to the original article—for their disclosure information, please see the original article.

Ethical Approval. This article is based on previously published studies and does not contain any new studies with human participants or animals performed by any of the authors. Please see the referenced article for ethics relating to the original study.

REFERENCE

1. Agarwal R, Filippatos G, Pitt B, et al. Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis. Eur Heart J. 2022;43(6):474–84. https://doi.org/10.1093/eurheartj/ehab777.