Poster NKF25-G-301

Efficacy and safety of finerenone in patients with cancer: A FIDELITY subgroup analysis

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#At the time of analysis.

1. Background

- Globally, an estimated 12–53% of people with cancer have concurrent chronic kidney disease (CKD) at the time of diagnosis[1]
- Kidney function must be closely monitored to allow accurate dosing of chemotherapies[1]
- People with type 2 diabetes (T2D) have a 15–25% higher risk of cancer incidence and mortality compared with those without[2]
- The presence of CKD often leads to exclusion in clinical trials investigating cancer therapies,[1] limiting the data available on treatment options in patients with concurrent cancer, CKD, and T2D
- In the FIDELITY pooled analysis, finerenone was associated with a reduced risk of cardiovascular (CV) and kidney outcomes compared with placebo in people with CKD and T2D[3]
  - Albuminuria is an important indicator of kidney damage,[4,5] and a mediation analysis showed that 37% and 84% of the treatment effect of finerenone was attributed to the reduction in urine albumin-to-creatinine ratio (UACR) for the CV and kidney composite outcomes, respectively[6]
- This post hoc analysis of the FIDELITY cohort investigated the efficacy and safety of finerenone versus placebo in people with CKD and T2D according to baseline cancer status

2. Study design and methods

- Eligible participants[3,7,8]:
  - Were aged ≥18 years with CKD and T2D
  - Had a serum potassium level ≤4.8 mmol/L at screening
  - Had either a UACR ≥30–<300 mg/g and an estimated glomerular filtration rate (eGFR) ≥25–≤90 mL/min/1.73 m^2, or UACR ≥300–≤5000 mg/g and eGFR ≥25 mL/min/1.73 m^2
  - Were treated with the maximum tolerated dose of a renin–angiotensin system inhibitor
  - Were randomly assigned to receive oral finerenone at titrated doses of 10 or 20 mg once daily or matching placebo (1:1)
- Participants were classified as having cancer at baseline if cancer was reported in their medical history within the last 6 months or cancer was ongoing at the time of informed consent

Procedures and outcomes

- The main efficacy outcome was change from baseline in UACR across the study period
- Safety outcomes were measured by the incidence of treatment-emergent adverse events (AEs), including the incidence of hyperkalemia, hyponatremia, and acute kidney injury (AKI)
- All efficacy and safety outcomes were analyzed by baseline cancer status

Statistical analyses

- Baseline characteristics and UACR analyses were reported for the full analysis set
- Safety analyses were performed on the safety analysis set (participants who took ≥1 dose of study drug)
- Least-squares mean ratio to baseline in UACR across the study period was calculated using a mixed model analysis with stratification factors of treatment group, region, eGFR category at screening, type of albuminuria at screening, CV disease history, study, time, treatment*time, baseline value nested within eGFR category at screening, baseline value*time and treatment*study interaction as covariates

3. Results

3.1 Baseline characteristics

- Of the 12,990 participants included in this analysis, 289 (2.2%) had cancer at baseline
  - In participants with cancer at baseline, 243 (84.1%) had a T2D diagnosis before their cancer diagnosis
- Baseline characteristics, stratified by cancer status, are presented in **Table 1**

Table 1. Baseline characteristics stratified by cancer status

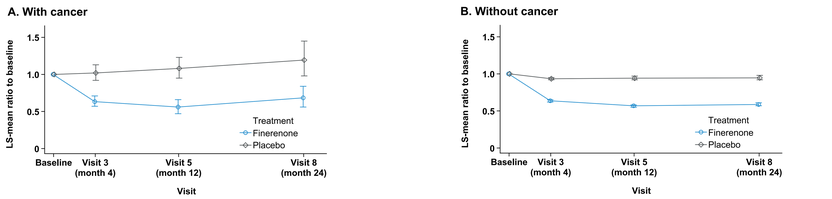
	With cancer (n=289)		Without cancer (n=12,701)	
Characteristic at baseline	**Finerenone (n=141)**	**Placebo (n=148)**	**Finerenone (n=6357)**	**Placebo (n=6344)**
Sex, male, n (%)	106 (75.2)	110 (74.3)	4357 (68.5)	4485 (70.7)
Age, years, mean ± SD	70.0 ± 7.5	69.8 ± 7.9	64.6 ± 9.4	64.7 ± 9.7
Race, n (%)				
Asian	25 (17.7)	33 (22.3)	1388 (21.8)	1414 (22.3)
Black or African American	5 (3.5)	9 (6.1)	246 (3.9)	260 (4.1)
White	110 (78.0)	101 (68.2)	4339 (68.3)	4319 (68.1)
BMI, kg/m^2, mean ± SD	30.3 ± 5.8	30.4 ± 5.2	31.4 ± 6.1	31.3 ± 6.0
Current smoker, n (%)	18 (12.8)	26 (17.6)	1041 (16.4)	997 (15.7)
UACR, mg/g, median (Q1–Q3)	493.0 (146.0–1204.6)	420.7 (164.3–1035.1)	515.4 (197.9–1131.2)	516.7 (201.9–1165.6)
eGFR, mL/min/1.73 m^2, mean ± SD	50.5 ± 18.7	51.3 ± 17.9	57.7 ± 21.6	57.8 ± 21.8
Serum potassium, mmol/L, mean ± SD	4.3 ± 0.5	4.4 ± 0.5	4.4 ± 0.4	4.4 ± 0.4
Serum albumin, g/dL, mean ± SD	4.2 ± 0.3	4.2 ± 0.4	4.2 ± 0.3	4.2 ± 0.3
C-reactive protein, mg/L, mean ± SD	4.4 ± 10.7	3.8 ± 5.3	4.9 ± 10.5	4.7 ± 9.3
HbA1c, %, mean ± SD	7.4 ± 1.1	7.5 ± 1.3	7.7 ± 1.4	7.7 ± 1.4
History of CV disease, n (%)	77 (54.6)	81 (54.7)	2896 (45.6)	2874 (45.3)
History of hypertension, n (%)	134 (95.0)	147 (99.3)	6126 (96.4)	6124 (96.5)
History of MI, n (%)	30 (21.3)	22 (14.9)	986 (15.5)	982 (15.5)
History of atrial fibrillation and atrial flutter, n (%)	23 (16.3)	21 (14.2)	543 (8.5)	517 (8.1)
History of heart failure, n (%)	15 (10.6)	11 (7.4)	470 (7.4)	511 (8.1)

BMI, body mass index; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; MI, myocardial infarction; SD, standard deviation; UACR, urine albumin-to-creatinine ratio

3.2 Efficacy outcome

- Finerenone significantly reduced UACR relative to baseline in participants with and without cancer (**Figure 1**)
  - This effect was apparent as early as month 4 and was sustained until month 24 (p≤0.0001 at all visits)
  - At month 24, the least-squares mean treatment ratio between finerenone and placebo was 0.573 (95% confidence interval [CI] 0.433–0.757) in those with cancer, and 0.620 (95% CI 0.591–0.651) in those without cancer

Figure 1. Change in UACR from baseline according to baseline cancer status



No. of participants at visit			
Finerenone	136	123	91
Placebo	143	132	104
LS mean (95% CI)			
Finerenone ratio to baseline	0.633 (0.565–0.709)	0.560 (0.472–0.665)	0.684 (0.558–0.838)
Placebo ratio to baseline	1.020 (0.922–1.129)	1.081 (0.952–1.228)	1.194 (0.984–1.450)
Treatment ratio	0.620 (0.533–0.722)	0.518 (0.419–0.641)	0.573 (0.433–0.757)
p-value of treatment comparison	<0.0001	<0.0001	<0.0001

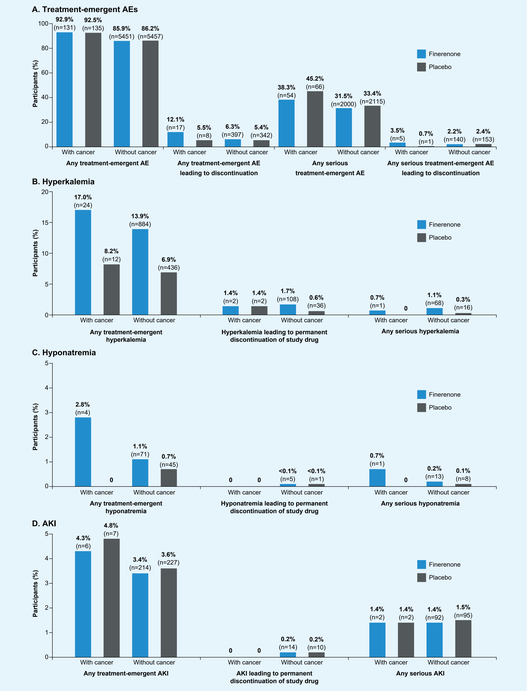
No. of participants at visit			
Finerenone	6116	5846	4757
Placebo	6081	5826	4711
LS mean (95% CI)			
Finerenone ratio to baseline	0.637 (0.624–0.650)	0.569 (0.553–0.585)	0.587 (0.566–0.608)
Placebo ratio to baseline	0.934 (0.916–0.953)	0.942 (0.918–0.967)	0.946 (0.915–0.978)
Treatment ratio	0.682 (0.662–0.702)	0.604 (0.581–0.627)	0.620 (0.591–0.651)
p-value of treatment comparison	<0.0001	<0.0001	<0.0001

CI, confidence interval; LS, least-squares; UACR, urine albumin-to-creatinine ratio

3.3 Safety outcomes

- The incidence of treatment-emergent AEs was higher in participants with cancer versus those without cancer; however, within each subgroup, the incidence rates were similar between treatment arms (**Figure 2A**)
  - The incidence rate of AEs leading to discontinuation in participants with cancer was 12.1% if treated with finerenone versus 5.5% if treated with placebo
  - The incidence of serious AEs in participants with cancer was lower in those treated with finerenone versus placebo
- Consistent with previous reports,[3] participants treated with finerenone had a twofold increased risk of treatment-emergent hyperkalemia compared with those treated with placebo, regardless of cancer status at baseline (**Figure 2B**)
  - The incidence of hyperkalemia leading to permanent discontinuation or serious hyperkalemia events were low across all participants in both treatment arms
  - There were no reported deaths due to hyperkalemia
- The incidence of any treatment-emergent hyponatremia event or any AKI event was low across both subgroups and treatment arms (**Figures 2C and 2D**)

Figure 2. Incidence rates of (A) treatment-emergent AEs, (B) hyperkalemia, (C) hyponatremia, and (D) AKI according to baseline cancer status



AE, adverse event; AKI, acute kidney injury

4. Conclusions

- This FIDELITY analysis is the first study to show the effects of the nonsteroidal mineralocorticoid receptor antagonist finerenone in patients with CKD, T2D, and cancer
- In participants with cancer treated with finerenone, there were significant sustained reductions in UACR up to month 24 compared with those treated with placebo
- The incidence rates of AEs were similar between treatment arms across both subgroups, and the incidence rates of hyponatremia, AKI, and serious hyperkalemia were low for all participants
- This suggests finerenone is effective and can be well managed in people with CKD, T2D, and cancer

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