SIMULTANEOUS INITIATION OF FINERENONE AND EMPAGLIFLOZIN ACROSS THE GLYCEMIC SPECTRUM IN THE CONFIDENCE TRIAL

Poster number
1863-LB

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Introduction

- Several drugs reduce the risk of chronic kidney disease (CKD) progression and cardiovascular events in people with CKD and type 2 diabetes (T2D), including the selective non-steroidal mineralocorticoid receptor antagonist finerenone and sodium-glucose cotransporter 2 inhibitors.[1]
- In CONFIDENCE (NCT05254002 and EudraCT 2021-003037-11), initial combination therapy with finerenone and empagliflozin reduced albuminuria more than either treatment alone in people with CKD and T2D.[2]
- This secondary analysis assessed whether baseline glycated hemoglobin (HbA1c) influenced the efficacy of combination therapy in the CONFIDENCE trial.

Methods

- CONFIDENCE was a randomized, controlled, double-blind, double-dummy, multicenter clinical trial in adults with CKD, defined as having an estimated glomerular filtration rate (eGFR) of 30 to 90 mL/min/1.73 m^2 and a urinary albumin-to-creatinine ratio (UACR) ≥100 to <5000 mg/g, and T2D (as defined by the American Diabetes Association) with HbA1c at screening of <11%.
- Participants were randomized 1:1:1 to once daily finerenone (10 or 20 mg) plus placebo, empagliflozin (10 mg) plus placebo, or finerenone (10 or 20 mg) plus empagliflozin (10 mg).
- In this analysis, participants were categorized into quartiles based on HbA1c at baseline:
  - Change from baseline in HbA1c was analyzed.
  - The relative change in UACR from baseline at Day 180 was also assessed.

Results

- There were 818 participants randomized across 14 countries between June 2022 and August 2024. Of these, 800 participants were eligible for inclusion in the full analysis set.
- Mean eGFR (mL/min/1.73 m^2 [standard deviation {SD}]) was 54.2 (17.1). Median UACR (mg/g [interquartile range]) was 579 (292–1092).
- Mean HbA1c at baseline was available for 781 participants and was 7.3% (SD 1.2). Quartiles were defined as:
  - Quartile 1: HbA1c ≤6.4%,
  - Quartile 2: HbA1c >6.4 and ≤7.1%,
  - Quartile 3: HbA1c >7.1 and ≤7.9%, and
  - Quartile 4: HbA1c >7.9%.
  - There were 212, 190, 188, and 191 participants categorized to HbA1c quartiles 1, 2, 3 and 4, respectively.
- Baseline characteristics were mostly balanced across HbA1c quartiles, however, there were some notable differences including mean HbA1c, median UACR, prevalence of diabetic retinopathy, and insulin use (**Table 1**).
- Baseline characteristics were balanced across treatment arms within each Hb1Ac quartile.

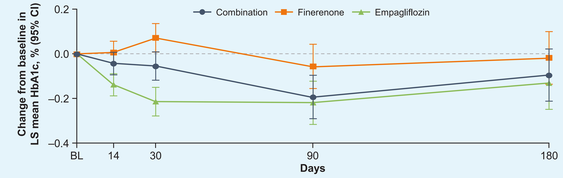
Table 1. Baseline demographic and clinical characteristics by Hb1Ac quartile

	Quartile 1 (n=212)	Quartile 2 (n=190)	Quartile 3 (n=188)	Quartile 4 (n=191)
Age, years	66.7±10.6	67.6±9.9	67.7±10.3	64.3±10.0
Female sex, n (%)	52 (24.5)	44 (23.2)	41 (21.8)	55 (28.8)
Race, n (%)				
White	95 (44.8)	89 (46.8)	84 (44.7)	76 (39.8)
Asian	101 (47.6)	86 (45.3)	81 (43.1)	92 (48.2)
Black/African American	14 (6.6)	14 (7.4)	18 (9.6)	20 (10.5)
Other†	1 (0.5)	0	3 (1.6)	1 (0.5)
Region, n (%)				
Europe	60 (28.3)	53 (27.9)	54 (28.7)	43 (22.5)
North America	54 (25.5)	54 (28.4)	53 (28.2)	60 (31.4)
Asia	98 (46.2)	83 (43.7)	81 (43.1)	88 (46.1)
HbA1c, %	6.0±0.4	6.8±0.2	7.5±0.2	9.0±0.8
Range, min–max	4.6–6.4	6.5–7.1	7.2–7.9	8.0–11.8
BMI, kg/m^2	28.6±5.8	28.6±5.7	30.1±6.7	30.1±5.9
eGFR, mL/min/1.73 m^2‡	52.5±16.7	54.7±16.9	54.6±16.5	54.5±17.9
Missing, n (%)	1 (0.5)	0	1 (0. 5)	0
Median UACR (IQR), mg/g	520 (0–5790)	504 (58–5145)	628 (44–9238)	649 (63–5375)
Missing, n (%)	4 (1.9)	5 (2.6)	4 (2.1)	2 (1.0)
SBP, mmHg	132.5±12.7	134.6±13.4	137.7±13.6	136.5±13.1
Serum potassium, mmol/L	4.4±0.4	4.5±0.4	4.5±0.4	4.5±0.5
Missing	1 (0.5)	1 (0.5)	1 (0.5)	0
Medical history, n (%)§				
Atherosclerotic cardiovascular disease‖	51 (24.1)	60 (31.6)	58 (30.9)	54 (28.3)
Diabetic retinopathy	23 (10.8)	25 (13.2)	38 (20.2)	40 (20.9)
Concomitant medications, n (%)				
ACEi/ARBs¶	208 (98.1)	187 (98.4)	184 (97.9)	189 (99.0)
Statins	150 (70.8)	148 (77.9)	144 (76.6)	145 (75.9)
Antiplatelets	87 (41.0)	75 (39.5)	78 (41.5)	75 (39.3)
Antihypertensives	209 (98.6)	188 (98.9)	185 (98.4)	190 (99.5)
Antihyperglycemic agents, n (%)				
DPP4 inhibitors	69 (32.5)	62 (32.6)	65 (34.6)	59 (30.9)
GLP-1 RAs	37 (17.5)	47 (24.7)	51 (27.1)	44 (23.0)
Insulin	43 (20.3)	62 (32.6)	86 (45.7)	120 (62.8)
Insulin secretagogues	40 (18.9)	44 (23.2)	59 (31.4)	62 (32.5)
Metformin	123 (58.0)	115 (60.5)	121 (64.4)	118 (61.8)

Note that values are means±SD unless otherwise stated.
†Includes American Indian, Alaska Native, Native Hawaiian, or other Pacific Islander. ‡Calculated by the CKD-EPI equation[3] with a modification to the equation for Japanese participants.[4] §Coded using the MedDRA dictionary. ‖Medical history of atherosclerotic cardiovascular disease is based on grouped MedDRA preferred terms for coronary artery disease, cerebral infarction, and stroke (a transient ischemic attack alone is not sufficient), as well as for peripheral artery disease and carotid revascularization. ¶According to the protocol, all patients were required to use an ACEi or ARB at the clinically maximum tolerated dose.
ACEi, angiotensin-converting–enzyme inhibitor; ARB, angiotensin-receptor blocker; BMI, body mass index; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; DPP4, dipeptidyl peptidase 4; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated hemoglobin; IQR, interquartile range; max, maximum; MedDRA, Medical Dictionary for Regulatory Activities; min, minimum; SBP, systolic blood pressure; SD, standard deviation; UACR, urinary albumin-to-creatinine ratio.

- There were no significant differences between treatment arms in change from baseline in HbA1c at Day 180 (**Figure 1**).

Figure 1. Change from baseline in HbA1c over time in the overall population

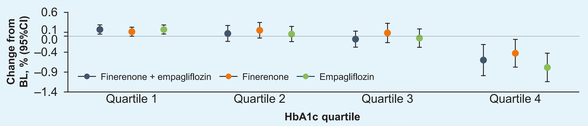


Combination	260	241	249	244	237
Finerenone	257	242	246	237	235
Empagliflozin	264	255	249	244	238

Mixed model for repeated measures including the factors treatment, time, treatment×time, UACR category at screening, eGFR category at screening, HbA1c baseline value, and HbA1c baseline value×time. Separate unstructured covariance patterns are estimated for each treatment group. BL, baseline; CI, confidence interval; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; LS, least squares; UACR, urinary albumin-to-creatinine ratio.

- Similarly, there were no differences between treatments within each quartile for change from baseline in HbA1c at Day 180 (**Figure 2**).

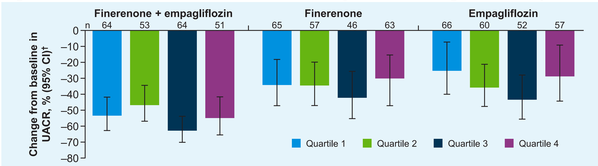
Figure 2. LS mean change from baseline in HbA1c (% [95% CI]) at Day 180



Mixed model for repeated measures including the factors treatment, time, treatment×time, UACR category at screening, eGFR category at screening, HbA1c baseline value, and HbA1c baseline value×time. Separate unstructured covariance patterns are estimated for each treatment group. Values presented to one decimal place.
BL, baseline; CI, confidence interval; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; LS, least squares; UACR, urinary albumin-to-creatinine ratio.

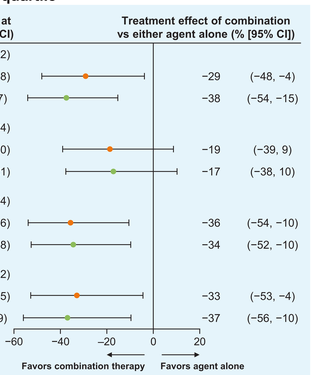
- Combination therapy reduced UACR consistently across HbA1c quartiles and to a greater extent than either monotherapy alone (**Figures 3** and **4**).

Figure 3. UACR reductions from baseline to Day 180 according to HbA1c quartile



Mixed model for repeated measures including the factors treatment, time, treatment×time, UACR category at screening, eGFR category at screening, HbA1c baseline value, and HbA1c baseline value×time. Separate unstructured covariance patterns are estimated for each treatment group.
†Percentage change calculation = (least-squares mean ratio to baseline − 1)×100.
CI, confidence interval; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; n, participants with evaluable UACR at Day 180; UACR, urinary albumin-to-creatinine ratio.

Figure 4. Percent change in UACR from baseline to Day 180 for combination therapy vs either agent alone according to HbA1c quartile



HbA1c quartile	Treatment group	Change from BL at Day 180, % (95% CI)		Treatment effect of combination vs either agent alone (% [95% CI])	
Quartile 1	Finerenone + empagliflozin	−53	(−63, −42)		
	Finerenone	−34	(−47, −18)	−29	(−48, −4)
	Empagliflozin	−25	(−40, −7)	−38	(−54, −15)
Quartile 2	Finerenone + empagliflozin	−47	(−57, −34)		
	Finerenone	−35	(−47, −20)	−19	(−39, 9)
	Empagliflozin	−36	(−48, −21)	−17	(−38, 10)
Quartile 3	Finerenone + empagliflozin	−63	(−70, −54)		
	Finerenone	−42	(−55, −26)	−36	(−54, −10)
	Empagliflozin	−43	(−56, −28)	−34	(−52, −10)
Quartile 4	Finerenone + empagliflozin	−55	(−65, −42)		
	Finerenone	−33	(−47, −15)	−33	(−53, −4)
	Empagliflozin	−29	(−44, −9)	−37	(−56, −10)

Mixed model for repeated measures including the factors treatment, time, treatment×time, UACR category at screening, eGFR category at screening, HbA1c baseline value, and HbA1c baseline value×time. Separate unstructured covariance patterns are estimated for each treatment group.
BL, baseline; CI, confidence interval; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; UACR, urinary albumin-to-creatinine ratio.

Conclusions

- Combination therapy with finerenone plus empagliflozin reduced UACR consistently across HbA1c quartiles and to a generally greater extent than either agent alone.
- Changes in HbA1c at Day 180 were greatest in quartile 4, but consistent across treatment arms in each quartile.
- Combination therapy reduced UACR more effectively than either agent alone irrespective of change in blood glucose control.

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