Combination of Finerenone and Empagliflozin Across the Spectrum of Risk of Kidney Failure: The CONFIDENCE Trial

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@safchat

American Heart Association. Scientific Sessions

BAYER

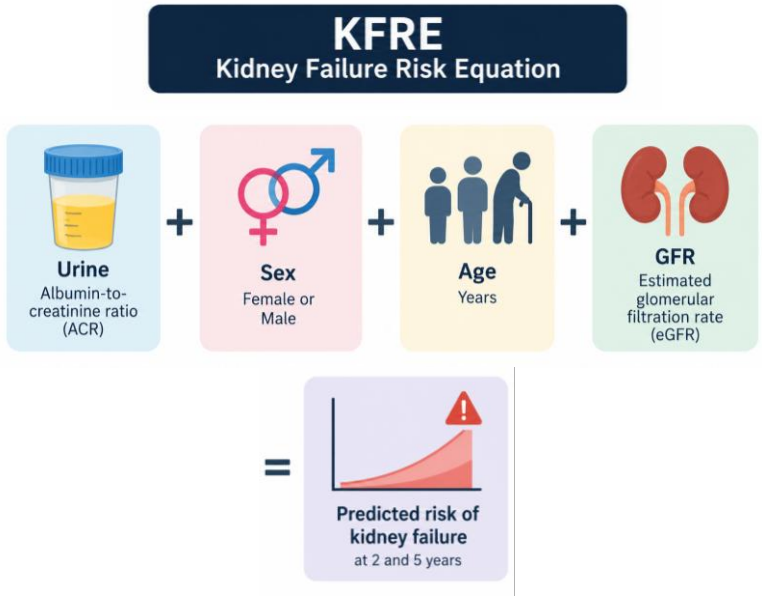
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Background and Rationale

- The CONFIDENCE trial demonstrated that **simultaneous initiation of finerenone and empagliflozin is safe and resulted ↑reduction in UACR** than either monotherapy alone in patients with T2D and CKD.
- **The Kidney Failure Risk Equation (KFRE)** is guideline recommended to predict near-term risk of adverse kidney outcomes in patients with CKD
- **KFRE** is a **4 variable score** which integrates eGFR, UACR, age and sex.
- Whether baseline KFRE risk may modify the safety and efficacy of empagliflozin, finerenone or the combination initiated simultaneously is not known



The CONFIDENCE Trial
age≥18yrs, T2DM, CKD Stage 2-3, UACR≥ 100mg/g to <5000mg/g
eGFR 30 to 90ml/min/1.3m2, taking maximally tolerated ACEi/ARB

818
Participants randomized

R
1:1:1

- **Empagliflozin** (10mg OD) + **Finerenone** (10 or 20mg OD)
- **Finerenone** (10 or 20mg OD) + **Placebo**
- **Empagliflozin** (10mg OD) + **Placebo**

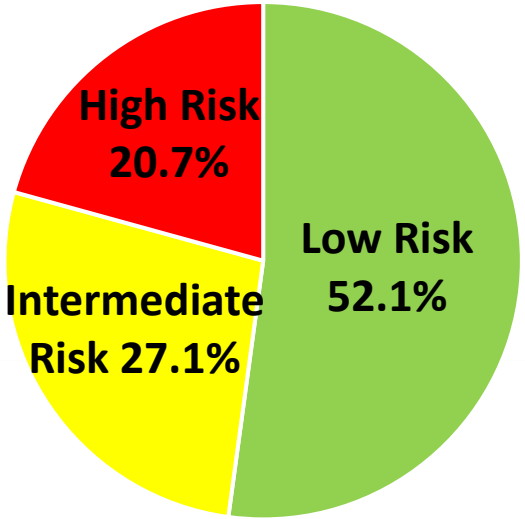
1º Efficacy Outcome

Relative Change in UACR from baseline to 180 days

LM Square Ratio for Monotherapy vs. Combination Therapy
0.71; 95%CI: 0.61-0.82 (combination vs finerenone)
0.68; 95%CI: 0.59-0.79 (combination vs. empagliflozin)

Key Objective: To evaluate the efficacy and safety of combination therapy with finerenone plus empagliflozin compared with either therapy alone according to baseline 5-year KFRE risk categories

Distribution of 5-Year KFRE Risk In the CONFIDENCE Trial
(calculated among 704 patients)

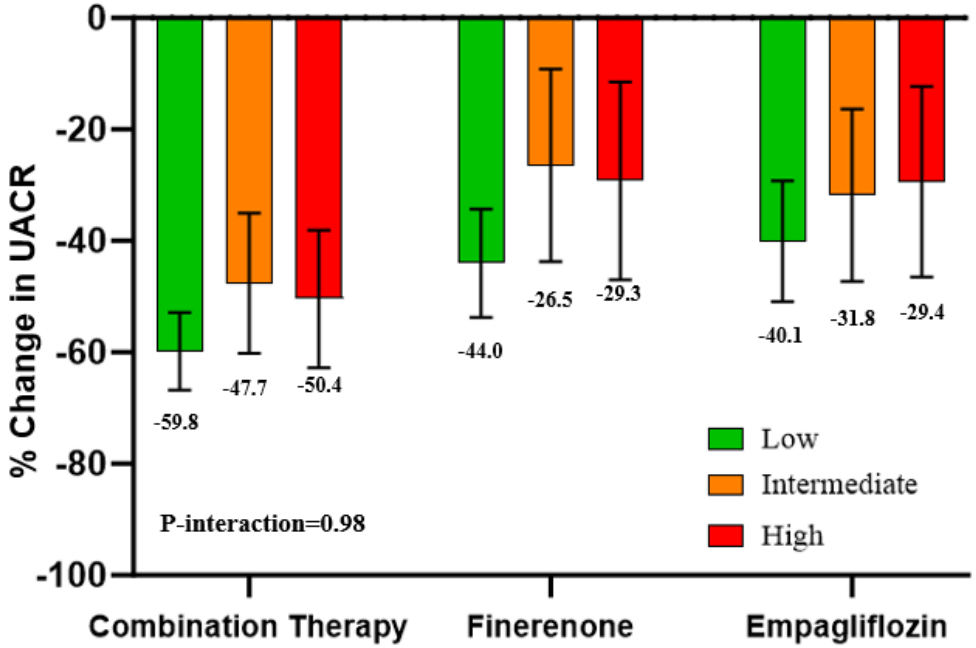


Low <3%
Intermediate 3-10%
High >10%

Selected Baseline Characteristics

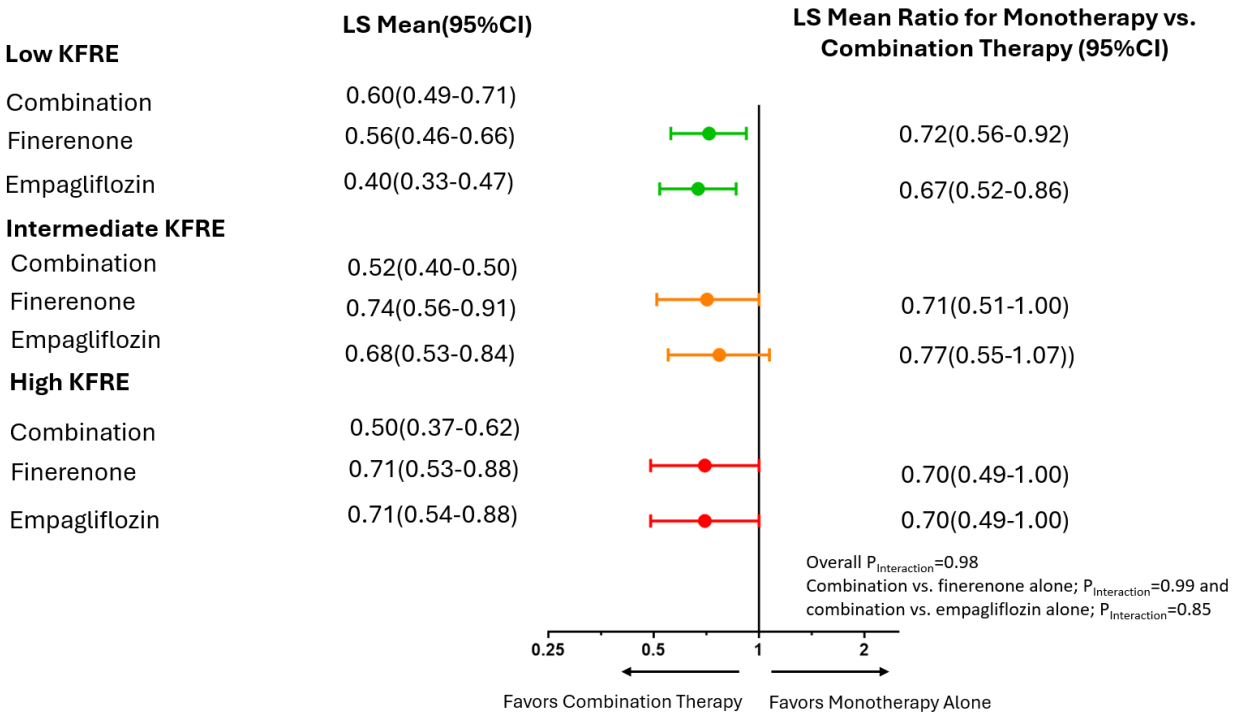
	Low KFRE (N=367)	Intermediate KFRE (n=191)	High KFRE (N=146)	P-Value
Age	66 ± 10	67 ± 10	64 ± 11	0.09
Male Sex	267(72.8%)	136(71.2%)	122(83.6%)	0.031
eGFR, mL/min/1.73 m²	67 ± 14	44 ± 6	35 ± 6	<0.001
UACR, mg/g	442 [248, 875]	574 [292, 1185]	955 [557, 2033]	<0.001
HbA1c, %	7.3 ± 1.2	7.3 ± 1.2	7.3 ± 1.4	0.90
History of ASCVD	89(24.3%)	63(33.0%)	46(31.5%)	0.043
History of HF	11(3.0 %)	7(3.7 %)	6(4.1 %)	0.51
History of hypertension	318(86.6%)	176(92.1%)	119(81.5%)	0.35

Relative Change in UACR From Baseline to Day 180 By KFRE Risk Category



At 180 days, combination therapy significantly reduced UACR levels across all KFRE risk categories

Least Squares Mean Ratios Of Change from Baseline in UACR For Combination Therapy vs. Monotherapy by KFRE Risk Category



Compared with finerenone or emapagliflozin monotherapy, combination therapy resulted in a greater relative reduction in UACR across KFRE risk categories

Selected Adverse Events By KFRE Risk Category

Safety Outcome	Low KFRE Risk	Intermediate KFRE Risk	High KFRE Risk	P-Int
Any Adverse Event				0.86
Combination	70 (55.6%)	34 (57.6%)	24 (52.2%)	
Finerenone	65 (52.0%)	35 (55.6%)	23 (46.9%)	
Empagliflozin	59 (51.8%)	34 (49.3%)	28 (54.9%)	
Serious Adverse Event				0.62
Combination	9 (7.1%)	6 (10.2%)	2 (4.3%)	
Finerenone	6 (4.8%)	6 (9.5%)	4 (8.2%)	
Empagliflozin	7 (6.1%)	3 (4.3%)	4 (7.8%)	
Hyperkalemia				0.91
Combination	9 (7.1%)	5 (8.5%)	10 (21.7%)	
Finerenone	9 (7.2%)	7 (11.1%)	11 (22.4%)	
Empagliflozin	3 (2.6%)	1 (1.4%)	5 (9.8%)	
Early eGFR Decline				0.51
Combination	10 (7.9%)	5 (8.5%)	1 (2.2%)	
Finerenone	7 (5.6%)	2 (3.2%)	0 (0.0%)	
Empagliflozin	2 (1.7%)	0 (0.0%)	1 (2.0%)	

Conclusions

- In the CONFIDENCE trial **52.1%, 27.1% and 20.7%** of participants with T2D and CKD were **classified as low, intermediate and high risk of kidney failure.**

- **Simultaneous initiation of finerenone and empagliflozin** produced **greater reductions in UACR** consistently **across the spectrum** of **baseline 5-year KFRE risk.**

- **Safety and tolerability profile** of **combination therapy** relative to monotherapy **was consistent across 5-year KFRE risk categories**

Take Home Point: These findings support a strategy of combination therapy across a broad range of CKD risk profiles including patients in the higher risk categories