Combination of Finerenone with Empagliflozin According to Frailty Status Among Participants with Type 2 Diabetes and CKD in the CONFIDENCE Trial

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American Heart Association. Scientific Sessions

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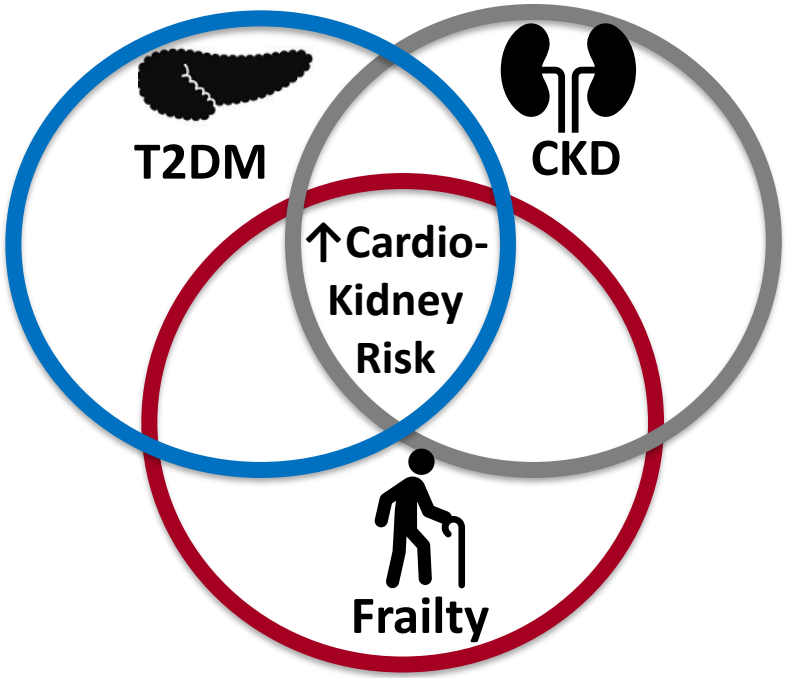
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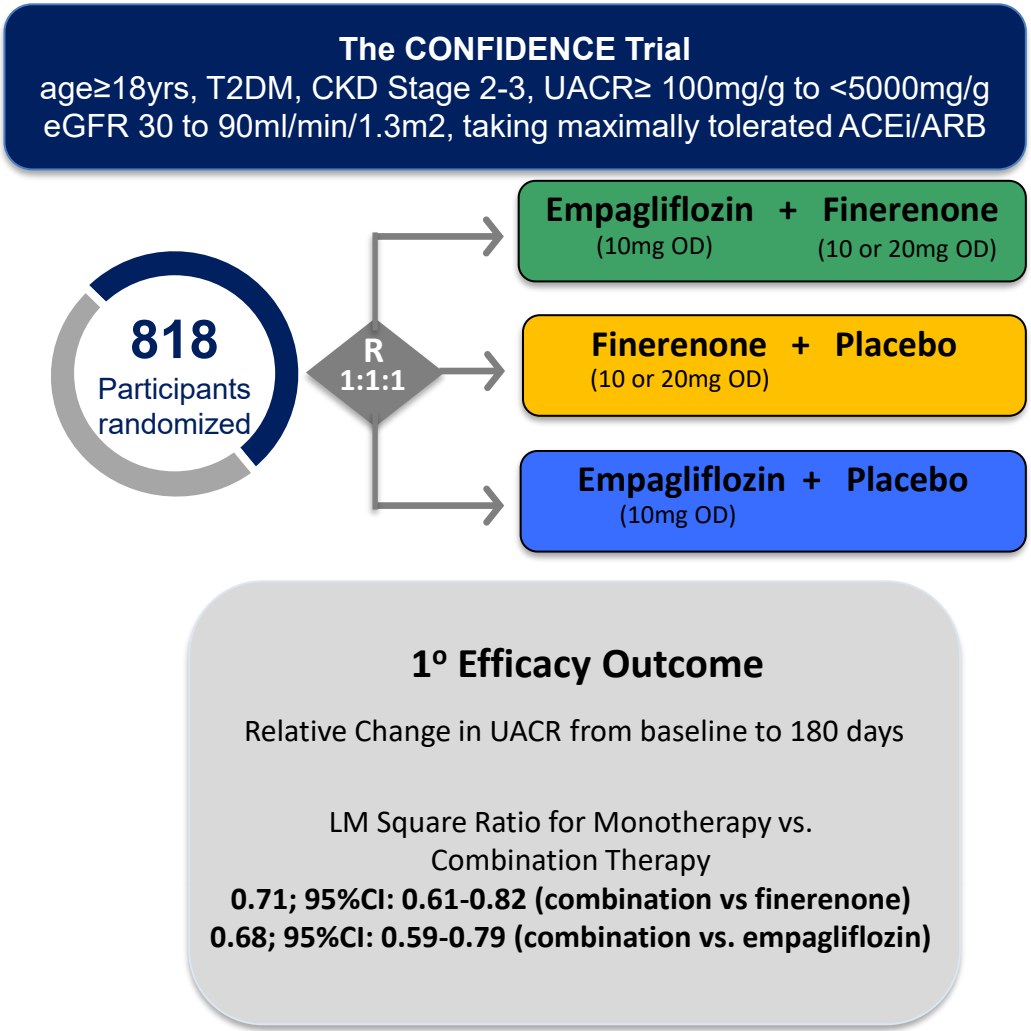
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Background and Rationale

- 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.
- **Guidelines increasingly support combination therapy** for patients with T2D with persistent albuminuria receiving background RASi therapy.
- **Frailty frequently co-exists with** chronic conditions including **CKD and T2D**
- **Frail patients face ↑ cardio-kidney risk**; however, clinicians may be reluctant to initiate combination therapy due to concerns of tolerability and uncertain risk-benefit profile.



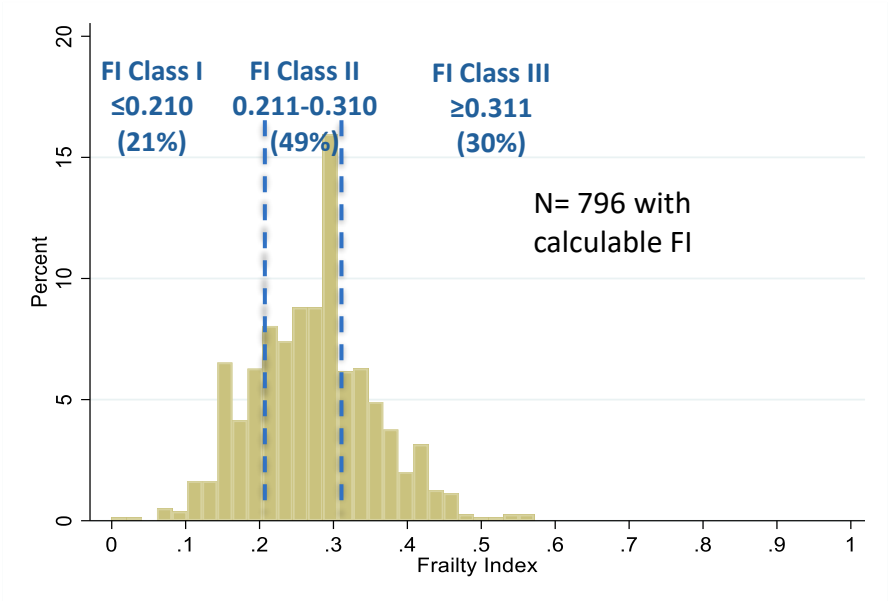


Key Objective: To evaluate the efficacy and safety of combination therapy with finerenone plus empagliflozin compared with either therapy alone according to baseline frailty status.

Frailty Classification

- Frailty was assessed using the Rockwood cumulative deficit approach
- 28 clinical variables were identified for inclusion in the FI across medical history, vital signs, laboratory values and medication use

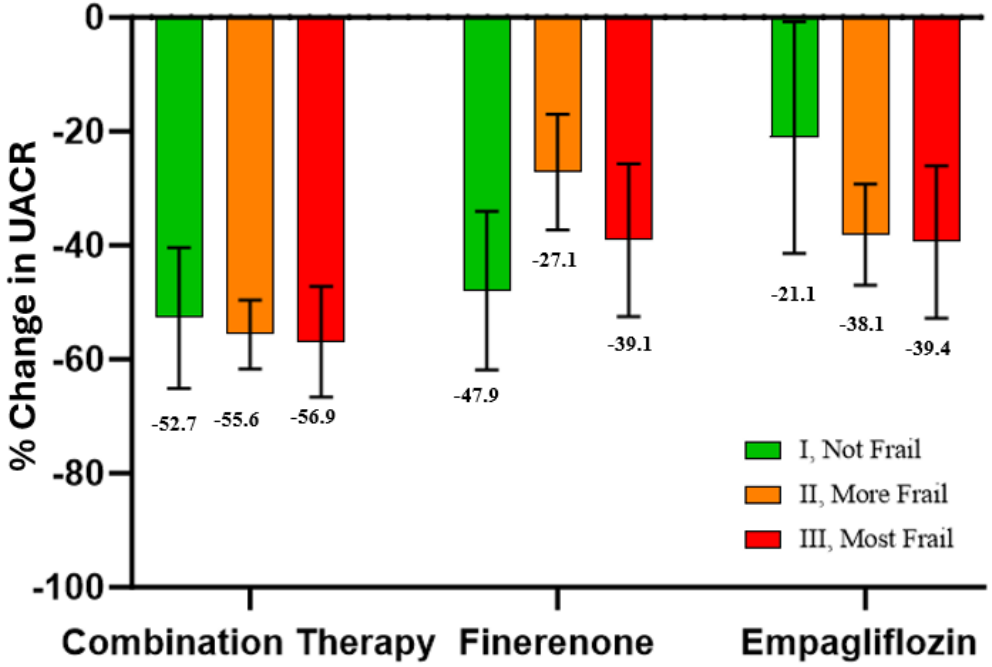
Distribution of Frailty in CONFIDENCE



Selected Baseline Characteristics

	Not Frail (I) (N=171)	More Frail (II) (n=389)	Most Frail (III) (N=236)
Age	64 ± 11	66 ± 10	69 ± 9
Male Sex	131 (76.6%)	294 (75.6%)	174 (73.7%)
eGFR, mL/min/1.73 m²	60 ± 18	55 ± 17	49 ± 16
UACR, mg/g	451 [267, 875]	548 [265, 1034]	655 [398, 1417]
HbA1c, %	7.0 ± 1.1	7.2 ± 1.2	7.6 ± 1.2
History of ASCVD	15 (8.8%)	84 (21.6%)	124 (52.5%)
History of HF	1 (0.6%)	6 (1.5%)	23 (9.7%)
History of hypertension	131 (76.6%)	342 (87.9%)	225 (95.3%)
Diuretic	30 (17.5%)	129 (33.2%)	130 (55.1%)

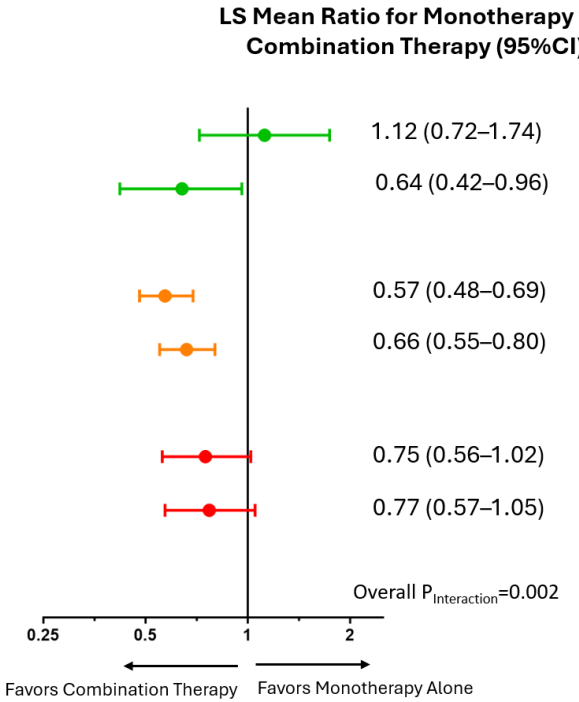
Relative Change in UACR From Baseline to Day 180 By Frailty Status



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

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

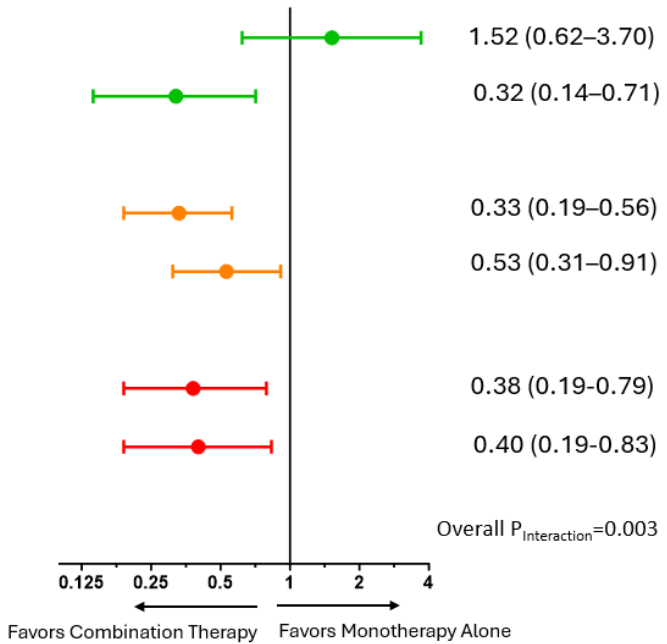
	LS Mean(95%CI)
FI I, Not Frail	
Combination	0.49 (0.34–0.64)
Finerenone	0.43 (0.29–0.58)
Empagliflozin	0.76 (0.54–0.98)
FI II, More Frail	
Combination	0.42 (0.37–0.48)
Finerenone	0.74 (0.64–0.84)
Empagliflozin	0.64 (0.56–0.73)
FI III, Most Frail	
Combination	0.47 (0.37–0.58)
Finerenone	0.63 (0.50–0.76)
Empagliflozin	0.62 (0.48–0.75)



Compared with either monotherapy, combination therapy resulted in similar or greater relative reductions UACR with increasing frailty risk

>30% Reduction In UACR from Baseline at Day 180 By Frailty Category

	Proportion with >30% UACR Decline from baseline, n(%)	OR(95%CI)
FI I, Not Frail		
Combination	33 (63.5%)	
Finerenone	33 (73.3%)	1.52 (0.62–3.70)
Empagliflozin	22 (38.6%)	0.32 (0.14–0.71)
FI II, More Frail		
Combination	89 (72.4%)	
Finerenone	56 (46.3%)	0.33 (0.19–0.56)
Empagliflozin	65 (58.0%)	0.53 (0.31–0.91)
FI III, Most Frail		
Combination	46 (70.8%)	
Finerenone	34 (46.6%)	0.38 (0.19-0.79)
Empagliflozin	35 (52.2%)	0.40 (0.19-0.83)



Relative to monotherapy combination therapy resulted in similar or greater odds of achieving >30% reduction in UACR with increasing frailty risk

Selected Adverse Events By Frailty Risk Category

Safety Outcome	Not Frail(I)	More Frail (II)	Most Frail (III)	P-Int
Any Adverse Event				0.49
Combination	17(30.4%)	76 (57.1%)	50(64.1%)	
Finerenone	15(30.0%)	66 (50.0%)	56(69.1%)	
Empagliflozin	24(37.5%)	62 (50.4%)	47(61.0%)	
Any Adverse Event Leading to Treatment Discontinuation				0.31
Combination	0 (0.0%)	7 (5.3%)	5 (6.4%)	
Finerenone	3 (6.0%)	3 (2.3%)	4 (4.9%)	
Empagliflozin	1 (1.6%)	2 (1.6%)	6 (7.8%)	
Serious Adverse Event				0.59
Combination	1 (1.8%)	8 (6.0%)	10 (12.8%)	
Finerenone	3 (6.0%)	6 (4.5%)	7 (8.6%)	
Empagliflozin	3 (4.7%)	4 (3.3%)	10 (13.0%)	
Serious Adverse Event Leading to Discontinuation				0.44
Combination	0 (0.0%)	2 (1.5%)	1 (1.3%)	
Finerenone	0 (0.0%)	1 (0.8%)	2 (2.5%)	
Empagliflozin	1 (1.6%)	0 (0.0%)	1 (1.3%)	
Investigator Reported Hyperkalemia				0.34
Combination	6 (10.7%)	12 (9.0%)	7 (9.0%)	
Finerenone	2 (4.0%)	18 (13.6%)	10 (12.3%)	
Empagliflozin	0 (0.0%)	5 (4.1%)	5 (6.5%)	

Conclusions

- In the CONFIDENCE trial **> three quarters** of participants with T2D and CKD were **classified as frail**.

- **Combination therapy** with empagliflozin and finerenone **achieved at least as much UACR lowering as either monotherapy** across the frailty spectrum

- **Safety and tolerability profile** of **combination therapy** relative to monotherapy **did not significantly vary across frailty categories** including among participants with the greatest frailty

Take Home Point: These findings support the efficacy and tolerability of simultaneous initiation of finerenone and empagliflozin across a broad spectrum of frailty.