Combination Therapy with Finerenone and Empagliflozin by Baseline Risk of Liver Fibrosis in the CONFIDENCE Trial

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BACKGROUND/OBJECTIVE

- The liver is an important organ in cardio-kidney-metabolic (CKM) disease
- We evaluated whether baseline liver fibrosis risk, estimated using the Fibrosis-4 (FIB-4) index, influenced treatment responses to established CKM therapies

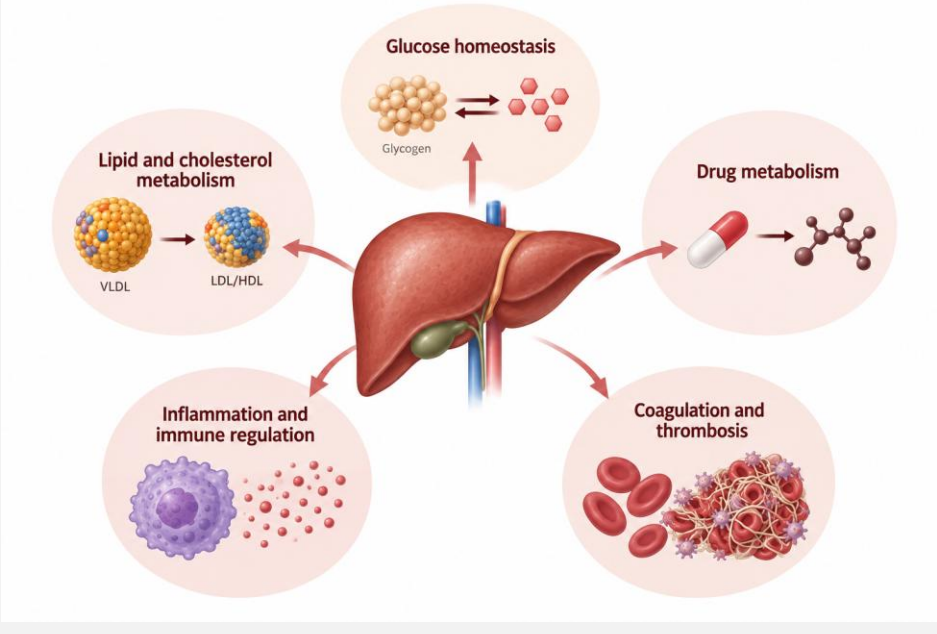


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Methods and Materials

CONFIDENCE

- Double-blind, randomized trial evaluating combination therapy with finerenone and empagliflozin in patients with chronic kidney disease (CKD) and type 2 diabetes [1]
- Randomization 1:1:1 to finerenone 10 or 20 mg/day, empagliflozin 10 mg/day, or combination therapy
- **Primary endpoint**: Relative change in log-transformed mean urinary albumin-to-creatinine ratio (UACR) (Baseline to Day 180)

FIB-4

- Age × AST / (platelets × √ALT)
- Low, intermediate, and high risk [2] for advanced liver fibrosis

Statistics

- Linear regression
- Covariates and stratification factors from the original trial

[1] Agarwal et al. Finerenone with Empagliflozin in Chronic Kidney Disease and Type 2 Diabetes. N Engl J Med 2025
[2] Low: FIB-4 <1.3 if age <65 years; <2.0 if age ≥65 years. Intermediate: FIB-4 1.3–2.67 if age <65 years; 2.0–2.67 if age ≥65 years. High: FIB-4 > 2.67

RESULTS

Among 755 participants with complete data

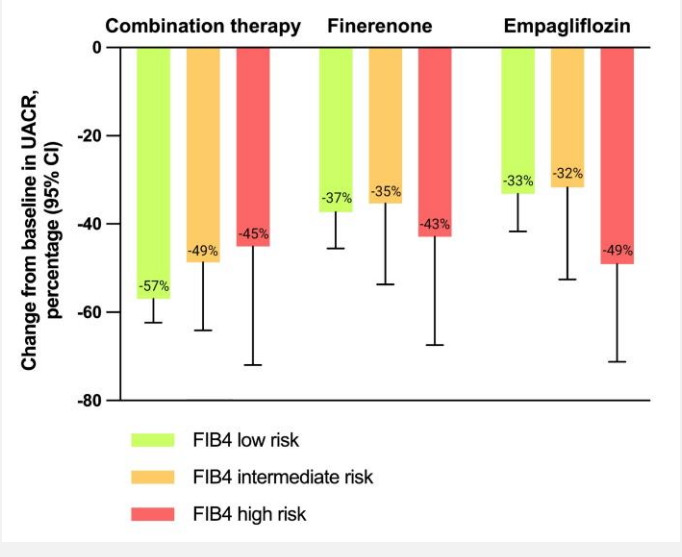
- Mean baseline FIB-4 index 1.53 (SD 0.86)

Low Risk	Intermediate Risk	High Risk
551 (73.0%)	145 (19.2%)	59 (7.8%)

- Virtually unchanged mean FIB-4 index from Baseline to Day 180: overall mean change 0.006 (SD 0.67)

Combination therapy reduced UACR across FIB-4 categories

- Reduction in UACR was independent of baseline FIB-4

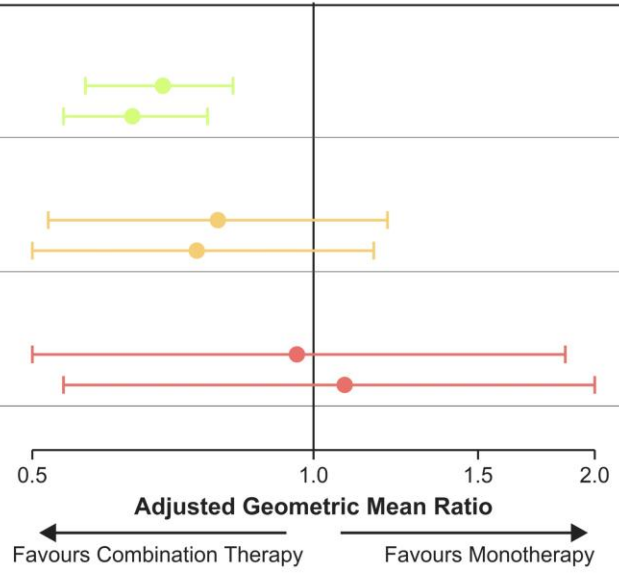


RESULTS

Consistent beneficial effect of combination vs monotherapy across FIB-4 categories

FIB-4 Category	Adjusted Geometric Mean Ratio*	95% CI	Adjusted Geometric Mean Ratio for Monotherapy vs Combination	95% CI
Low Risk				
Finerenone + Empagliflozin (n=182)	0.43	(0.38-0.48)		
Finerenone (n=179)	0.63	(0.54-0.71)	0.69	(0.57-0.82)
Empagliflozin (n=190)	0.67	(0.58-0.75)	0.64	(0.54-0.77)
Intermediate Risk				
Finerenone + Empagliflozin (n=53)	0.51	(0.36-0.67)		
Finerenone (n=49)	0.65	(0.46-0.83)	0.79	(0.52-1.20)
Empagliflozin (n=43)	0.68	(0.47-0.89)	0.75	(0.49-1.16)
High Risk				
Finerenone + Empagliflozin (n=17)	0.55	(0.28-0.82)		
Finerenone (n=19)	0.57	(0.33-0.82)	0.96	(0.50-1.86)
Empagliflozin (n=23)	0.51	(0.29-0.73)	1.08	(0.54-2.15)

*within each treatment group



Combination therapy vs finerenone: $P_{interaction} = 0.49$
Combination therapy vs empagliflozin: $P_{interaction} = 0.27$

Conclusion

- Approximately 1 in 4 patients with type 2 diabetes and CKD were at intermediate or high risk of liver fibrosis
- Combination therapy with finerenone and empagliflozin reduced levels of albuminuria across a range of liver fibrosis risk

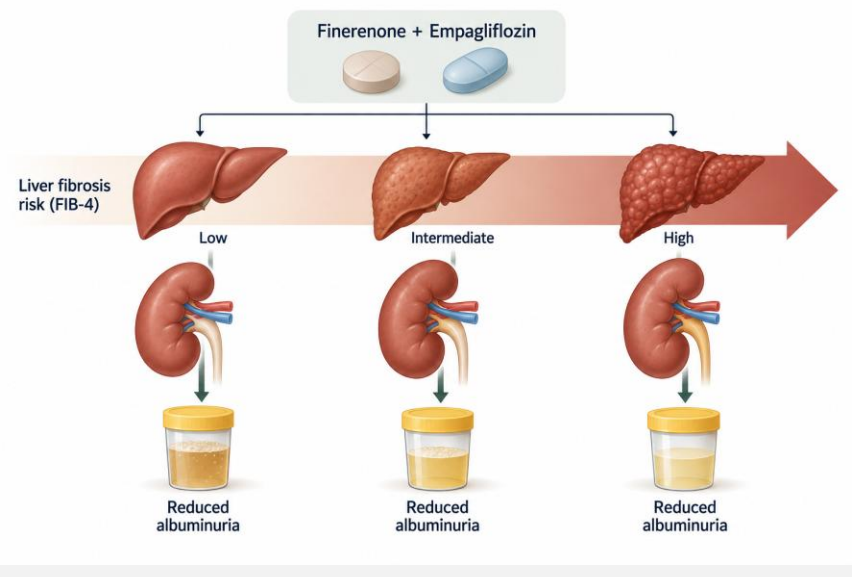


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