Finerenone, Liver Biomarkers and Heart Failure With Mildly Reduced or Preserved Ejection Fraction: An Analysis of the FINEARTS-HF Trial

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Background

- Liver biomarkers are often abnormal in patients with heart failure (HF) with reduced ejection fraction and are associated with worse clinical outcomes.
- The prevalence and prognostic significance of these biomarkers in HF with mildly reduced and preserved ejection fraction (HFmrEF/HFpEF) are uncertain, with both potential hemodynamic and metabolic contributions to liver dysfunction in these patients.

Purpose

- To evaluate the prevalence and prognostic value of liver biomarkers, and to assess the effects of the non-steroidal mineralocorticoid receptor antagonist, finerenone, on these biomarkers and clinical outcomes, in FINEARTS-HF.

Methods

- FINEARTS-HF was a randomized, double-blind, controlled trial in patients with HFmrEF/HFpEF, evaluating the efficacy and safety of finerenone compared with placebo.
- **Key inclusion criteria:** NYHA II-IV; LVEF ≥40%; structural heart disease; elevated natriuretic peptides.
- **Key exclusion criteria:** eGFR <25 mL/min/1.73m^2; potassium 5.0 mmol/L; history of primary pulmonary arterial hypertension or severe pulmonary disease requiring home oxygen or chronic oral steroid therapy.
- **Liver biomarkers:** Total bilirubin, alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) measured at baseline, 1 month, 3, months, 6 months, 9 months, and 12 months, and every fourth month hereafter.
- **Primary outcome:** Cardiovascular death and total worsening HF events (HF hospitalization or urgent HF visit requiring intravenous diuretics).
- **Statistics:**
  Total events: Semiparametric proportional-rates models.
  Time-to-event outcomes: Cox proportional hazard models.
  Change in liver biomarkers: Mixed-effects models.

Results

Table 1. Markers of liver function at baseline

Baseline	Total bilirubin Mg/dL	ALP U/L	ALT U/L	AST U/L
Available measurement , %	97.9	97.6	96.9	95.4
Level, median (IQR)	0.5 (0.4-0.8)	79 (65-98)	20 (17-26)	17 (13-24)

Figure 2. Proportion of patients with elevated levels of liver function markers

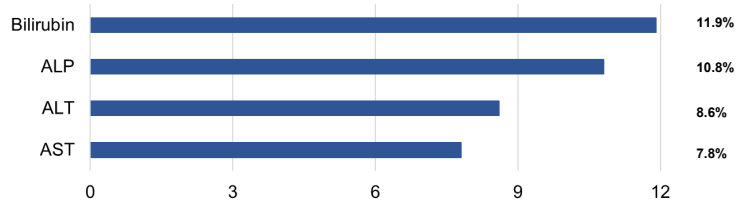
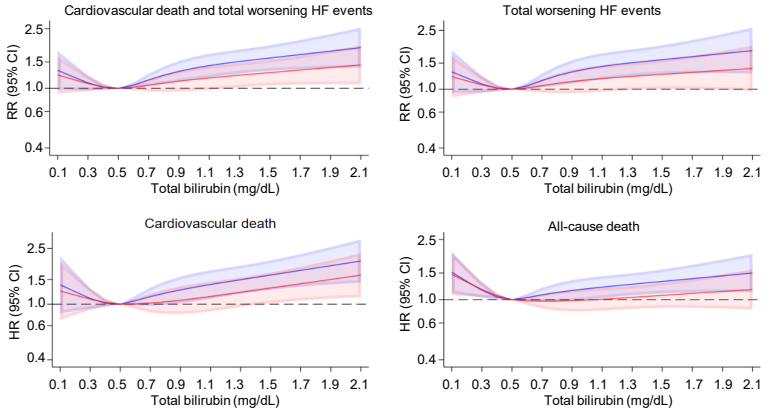


Figure 2. Outcomes according to continuous bilirubin



The blue spline is stratified for geographic region and LVEF stratification and adjusted for treatment assignment.
The red spline is stratified by geographic region and LVEF stratification and adjusted for treatment assignment, age, sex, systolic blood pressure, heart rate, BMI, eGFR, LVEF, NYHA functional class, log of NT-proBNP, log of high-sensitivity troponin T, prior HF hospitalization, type 2 diabetes, myocardial infarction or coronary revascularization, and atrial fibrillation/flutter.

Figure 3. Effect of finerenone compared with placebo on clinical outcomes according to bilirubin level at baseline

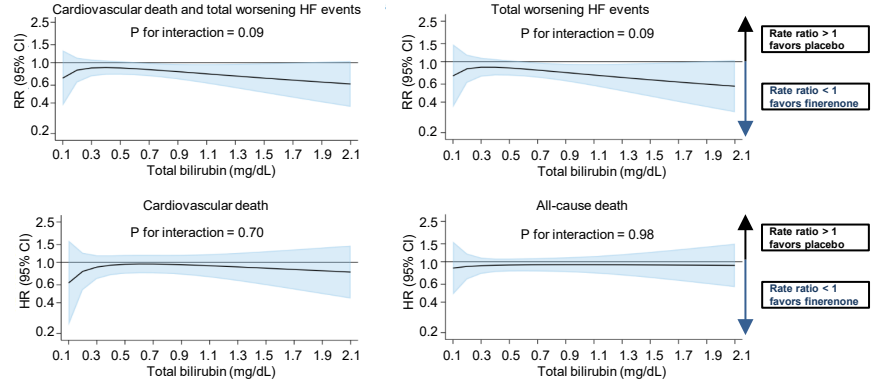
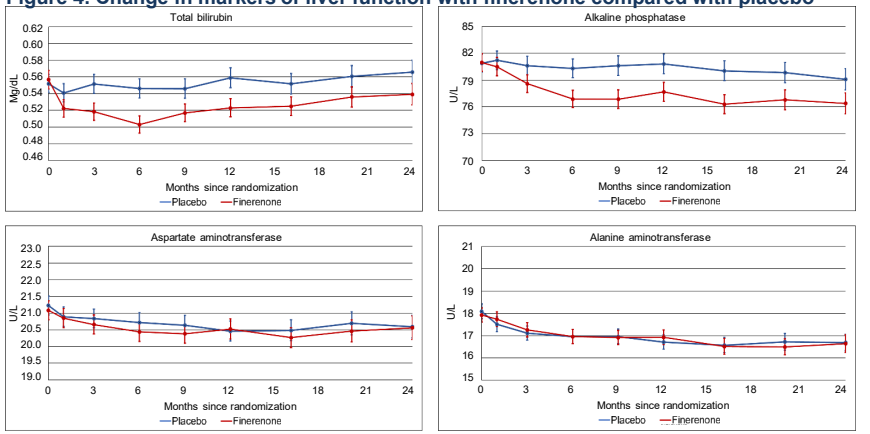


Figure 4. Change in markers of liver function with finerenone compared with placebo



Conclusions

In patients with HFmrEF/HFpEF, baseline bilirubin concentration was an independent predictor of worse outcomes, but it did not modify the benefits of finerenone on morbidity and mortality. Finerenone led to a rapid and sustained reduction in levels of bilirubin and ALP.