Temporal Changes in Biomarkers, Functional Status, and Quality of Life Prior to Adverse Clinical Outcomes in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

Henri Lu[1], Brian L. Claggett, Muthiah Vaduganathan, Akshay S. Desai, Pardeep S. Jhund, Adriaan A. Voors, Michele Senni, Faiez Zannad, Bertram Pitt, Sanjiv J. Shah, Carolyn S.P. Lam, Markus F. Scheerer, Andrea Scalise, Katharina Mueller, Mario Berger, Laura Goea, John J.V. McMurray, Scott D. Solomon

[1]*Division of Cardiology, Lausanne University Hospital (CHUV), University of Lausanne (UNIL), Lausanne, Switzerland. Division of Cardiovascular Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston MA, USA*

BACKGROUND

- Patients with heart failure with mildly reduced or preserved ejection fraction (HFmrEF/HFpEF) face a high risk of cardiovascular events.
- Mapping the temporal changes in readily available and routinely collected biomarkers, functional status, and patient-reported outcomes prior to adverse clinical events could inform surveillance strategies.

AIMS

In this *post hoc* analysis of the FINEARTS-HF trial, we assessed temporal patterns of 2 biomarkers (N-terminal pro B-type natriuretic peptide [NT-proBNP], estimated glomerular filtration rate [eGFR]), physician assigned functional status (New York Heart Association [NYHA]), and a patient reported outcome (Kansas City Cardiomyopathy Questionnaire Total Symptom Score [KCCQ-TSS]) leading up to a clinical event.

METHODS

- FINEARTS-HF: Multicenter, event-driven, randomized trial evaluating finerenone vs. placebo in heart failure (HF) patients with LVEF ≥40%.
- Key inclusion criteria: Age ≥40 years, NYHA class ≥II, elevated natriuretic peptides (NT-proBNP ≥300 pg/mL or BNP ≥100 pg/mL in sinus rhythm; higher thresholds in atrial fibrillation), evidence of structural heart disease and recent diuretic use.

- Parameters were assessed at randomization and regular intervals
- NT-proBNP: 3, 12 months.
- eGFR: 1, 3, 6, 9, 12 months, then every 4 months until 40 months.
- NYHA class: 1, 3, 6, 9, 12 months, then every 2 months until 42 months.
- KCCQ-TSS: 6, 9, 12, 16, 24, 32, 40 months.

- Analysis: Longitudinal trajectories of parameters of interest using repeated measures regression with cubic splines.
- Changes analyzed before primary endpoint (cardiovascular) death or first worsening HF event), and before/after a HF hospitalizations (HFH) event.
- Post-discharge trajectory assessed in HFH survivors.
- Event group compared to a control group (alive, no hospitalization during follow-up).

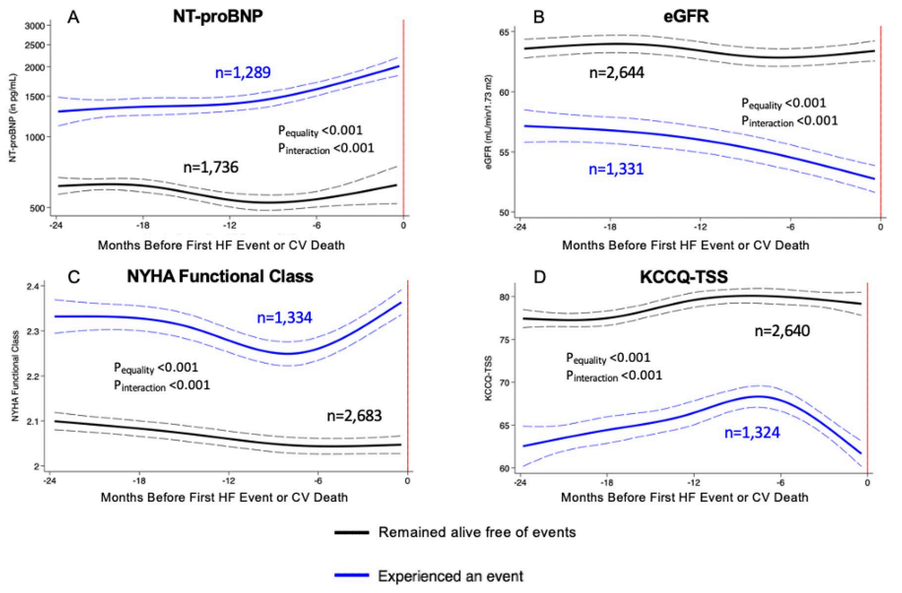
RESULTS

- Over 2.7 years median follow-up, 1,343 first primary events occurred.
- Participants who experienced a primary endpoint event had, at baseline, higher NT-proBNP values, lower eGFR, higher NYHA class and lower KCCQ-TSS, compared to the control group.

- NT-proBNP ↑ by ~ 70-80%, eGFR ↓ by about 5 ml/min/1.73m² over the 12-18 months preceding an event.
- NYHA class ↓ (worse) in the 6-9 months before an event. KCCQ-TSS ↓ by ~6 points during this period (greater symptom burden).
- These 4 variables remained stable in the control group (**Figure 1**).

Similar patterns were observed prior to a HFH for all 4 variables (**Figure 2**).

Figure 1. Trajectory of (A) NT-proBNP, (B) eGFR, (C) NYHA Functional Class, (D) KCCQ-TSS before a first HF event or cardiovascular death event



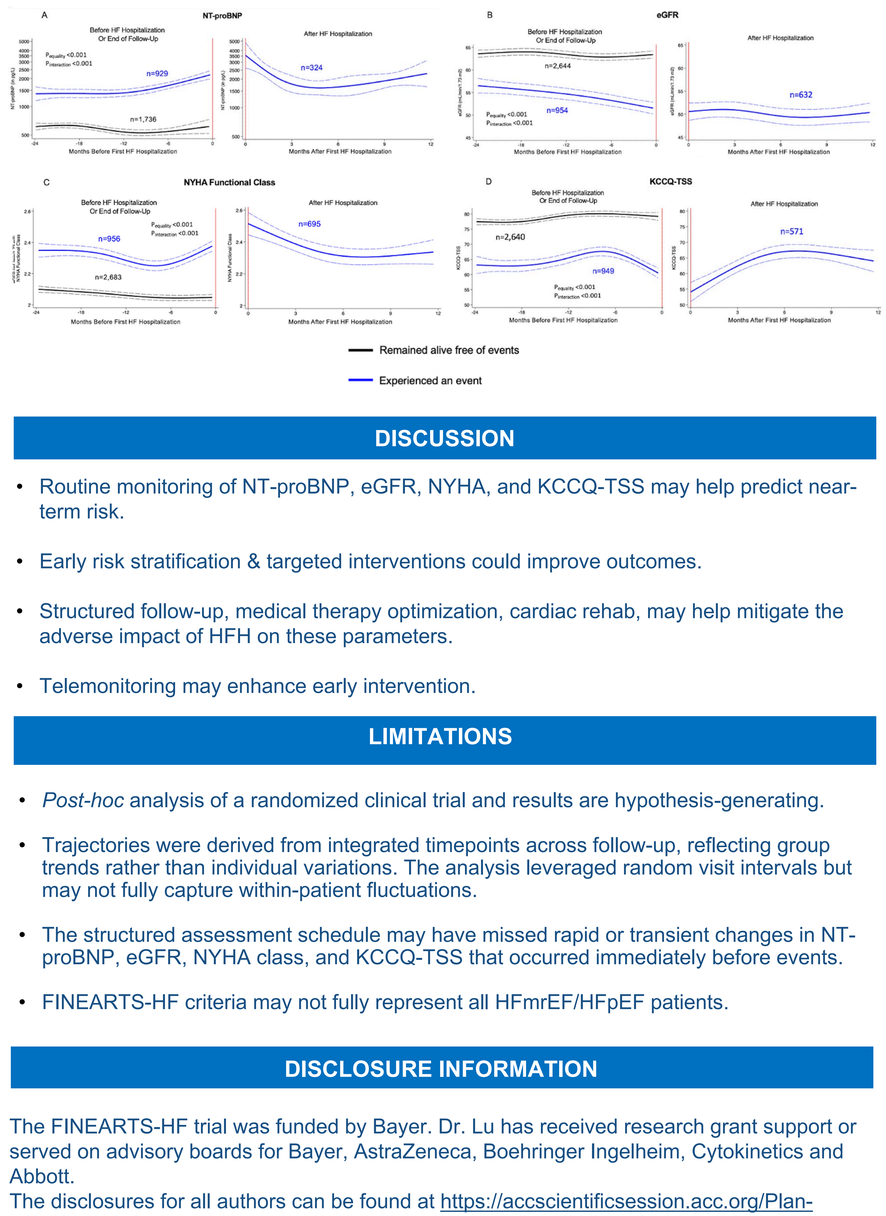
In this *post hoc* analysis of the FINEARTS-HF trial including a large, contemporary HFmrEF/HFpEF population, significant changes in readily available biomarkers, functional status, and patient-reported health status were observed in the months leading up to cardiovascular events.

Monitoring these parameters may help identify patients at high risk for near-term adverse clinical events.

For more information, email *henri.lu@chuv.ch, or follow @LuHenri8 on X.*

ACC.25

Figure 2. Trajectory of (A) NT-proBNP, (B) eGFR, (C) NYHA Functional Class, (D) KCCQ-TSS before and after a HF hospitalization event



DISCUSSION

- Routine monitoring of NT-proBNP, eGFR, NYHA, and KCCQ-TSS may help predict near-term risk.
- Early risk stratification & targeted interventions could improve outcomes.
- Structured follow-up, medical therapy optimization, cardiac rehab, may help mitigate the adverse impact of HFH on these parameters.
- Telemonitoring may enhance early intervention.

LIMITATIONS

- *Post-hoc* analysis of a randomized clinical trial and results are hypothesis-generating.
- Trajectories were derived from integrated timepoints across follow-up, reflecting group trends rather than individual variations. The analysis leveraged random visit intervals but may not fully capture within-patient fluctuations.
- The structured assessment schedule may have missed rapid or transient changes in NT-proBNP, eGFR, NYHA class, and KCCQ-TSS that occurred immediately before events.
- FINEARTS-HF criteria may not fully represent all HFmrEF/HFpEF patients.

DISCLOSURE INFORMATION

The FINEARTS-HF trial was funded by Bayer. Dr. Lu has received research grant support or served on advisory boards for Bayer, AstraZeneca, Boehringer Ingelheim, Cytokinetics and Abbott.
The disclosures for all authors can be found at https://accscientificsession.acc.org/Plan-Your%20Program/Presenter-Disclosures

FINEARTS-HF
FINerenone trial to investigate Efficacy and sAfety superioR to placebo in paTientS with Heart Failure

BRIGHAM HEALTH
BRIGHAM AND WOMEN'S HOSPITAL

HARVARD MEDICAL SCHOOL