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RESEARCH LETTER

Increases in Natriuretic Peptides Precede Heart Failure Hospitalization in Patients With a Recent Coronary Event and Type 2 Diabetes Mellitus

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with type 2 diabetes mellitus and an acute coronary syndrome (index event) occurring within 180 days of randomization were enrolled. The trial was designed to assess the efficacy and safety of lixisenatide, a glucagon-like peptide-1 receptor agonist, with respect to cardiovascular morbidity and mortality.⁵ Sampling of BNP and NT-proBNP occurred at baseline and at weeks 24, 76, and 108 after randomization, yielding 19 585 samples. Samples were collected and analyzed at a core laboratory (Covance Central Laboratory Services, Meyrin, Switzerland). ELIXA was approved by appropriate institutional or central review boards. All participants provided written informed consent.

For our analyses, patients with both a baseline and a week 24 NP sample without an intervening HFH were included. This yielded 5450 patients (90% of randomized patients) for analysis, of whom 22% reported a history of HF before randomization. To describe the temporal trajectory of NP levels before HFH, a retrospective analysis was developed using repeated measures regression models with restricted cubic splines. The timescale used was the number of days before HFH or end of follow-up and relied on prespecified trial visits to minimize confounding between patient health and timing of ascertainment of NP concentrations. This allowed us to estimate the average trajectory of NP concentrations that would have been observed if patients had been continuously monitored. NP data were log-transformed and summarized with geometric means ($\pm 95\%$ confidence interval).

Patients had a mean \pm SD age of 60 \pm 10 years, body mass index of 30 \pm 6 kg/m², and estimated glomerular filtration rate of 76 \pm 24 mL \cdot min⁻¹ \cdot 1.73 m⁻². Of the 5450 included patients, 151 (3%) subsequently experienced HFH during a median follow-up of 26 months. The NP concentrations of patients who did not experience HFH declined continuously during

