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# Effect of Natriuretic Peptide–Guided Therapy on Hospitalization or Cardiovascular Mortality in High-Risk Patients With Heart Failure and Reduced

# Ejection Fraction

## A Randomized Clinical Trial

G. Michael Felker, MD, MHS<sup>1</sup>; Kevin J. Anstrom, PhD<sup>1</sup>; Kirkwood F. Adams, MD<sup>2</sup>; [et al](#)

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### Key Points

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**Question** Does a strategy of titrating therapy to a specific amino-terminal pro–B-type natriuretic peptide (NT-proBNP) target improve clinical outcomes in high-risk patients with heart failure and reduced ejection fraction?

**Findings** In this randomized clinical trial including 894 adults, a strategy of NT-proBNP–guided therapy compared with usual care did not significantly improve time to first hospitalization or cardiovascular mortality (hazard ratio, 0.98).

**Meaning** These findings do not support NT-proBNP–guided therapy for management of heart failure with reduced ejection fraction.

### Abstract

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**Importance** The natriuretic peptides are biochemical markers of heart failure (HF) severity and predictors of adverse outcomes. Smaller studies have evaluated adjusting HF therapy based on natriuretic peptide levels (“guided therapy”) with inconsistent results.

**Objective** To determine whether an amino-terminal pro–B-type natriuretic peptide (NT-proBNP)–guided treatment strategy improves clinical outcomes vs usual care in high-risk patients with HF and reduced ejection fraction (HFrEF).

**Design, Settings, and Participants** The Guiding Evidence Based Therapy Using Biomarker Intensified Treatment in Heart Failure (GUIDE-IT) study was a randomized multicenter clinical trial conducted between January 16, 2013, and September 20, 2016, at 45 clinical sites in the

United States and Canada. This study planned to randomize 1100 patients with HFrEF (ejection fraction  $\leq 40\%$ ), elevated natriuretic peptide levels within the prior 30 days, and a history of a prior HF event (HF hospitalization or equivalent) to either an NT-proBNP–guided strategy or usual care.

**Interventions** Patients were randomized to either an NT-proBNP–guided strategy or usual care. Patients randomized to the guided strategy ( $n = 446$ ) had HF therapy titrated with the goal of achieving a target NT-proBNP of less than 1000 pg/mL. Patients randomized to usual care ( $n = 448$ ) had HF care in accordance with published guidelines, with emphasis on titration of proven neurohormonal therapies for HF. Serial measurement of NT-proBNP testing was discouraged in the usual care group.

**Main Outcomes and Measures** The primary end point was the composite of time-to-first HF hospitalization or cardiovascular mortality. Prespecified secondary end points included all-cause mortality, total hospitalizations for HF, days alive and not hospitalized for cardiovascular reasons, the individual components on the primary end point, and adverse events.

**Results** The data and safety monitoring board recommended stopping the study for futility when 894 (median age, 63 years; 286 [32%] women) of the planned 1100 patients had been enrolled with follow-up for a median of 15 months. The primary end point occurred in 164 patients (37%) in the biomarker-guided group and 164 patients (37%) in the usual care group (adjusted hazard ratio [HR], 0.98; 95% CI, 0.79-1.22;  $P = .88$ ). Cardiovascular mortality was 12% ( $n = 53$ ) in the biomarker-guided group and 13% ( $n = 57$ ) in the usual care group (HR, 0.94; 95% CI; 0.65-1.37;  $P = .75$ ). None of the secondary end points nor the decreases in the NT-proBNP levels achieved differed significantly between groups.

**Conclusions and Relevance** In high-risk patients with HFrEF, a strategy of NT-proBNP–guided therapy was not more effective than a usual care strategy in improving outcomes.

**Trial Registration** [clinicaltrials.gov Identifier: NCT01685840](https://clinicaltrials.gov/Identifier/NCT01685840)

#### Editorial

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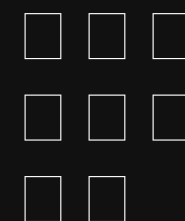
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