Door Opened to Biomarker-Guided HF Therapy

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CHICAGO – Using N-terminal prohormone brain natriuretic peptide levels to guide therapy in patients with systolic heart failure proved superior to standard -of-care management in terms of cardiovascular event rates, quality of life, and echocardiographic parameters in the randomized prospective PROTECT trial.

"If duplicated in larger cohorts, treatment guided by NT-proBNP may represent a new paradigm for heart failure care," Dr. James L. Januzzi Jr. said at the meeting.

PROTECT (the ProBNP Outpatient Tailored Chronic Heart Failure Therapy study) was a single-center unblinded trial of 151 patients with systolic heart failure and a mean left ventricular ejection fraction of 27%. They were randomized to standard guideline-driven management on the basis of heart failure signs and symptoms or to the same approach with the added goal of reducing NT-proBNP levels to 1,000 pg/mL or less, a threshold previously shown to predict risk in heart failure patients.

Participants were scheduled for quarterly clinic visits, with extra ones as needed to achieve therapeutic goals, said Dr. Januzzi, director of the cardiac intensive care unit at Massachusetts General Hospital, Boston.

The study was halted early for ethical reasons after 10 months. At that point, a total of 100 cardiovascular events – worsening heart failure, heart failure hospitalization, acute coronary syndrome, ventricular arrhythmias, cerebral ischemia, or cardiovascular death – had occurred in the standard-treatment group, compared with 58 events in patients on NT-proBNP–guided therapy

The NT-proBNP–guided arm had a lower likelihood of worsening heart failure or heart failure hospitalization.

DR. JANUZZI

The major difference between the two study arms was the sharply lower likelihood of worsening heart failure or heart failure hospitalization in the NT-proBNP–guided arm.

Importantly, the reduction in cardiovascular events was similar in patients over age 75 and in those who were younger, Dr. Januzzi said.

The secondary outcome of quality of life, assessed using the Minnesota Living with Heart Failure Questionnaire, also showed significantly greater improvement in the guided-treatment arm. In all, 61% of subjects in the NT-proBNP–guided arm achieved at least a 10-point improvement over baseline, considered clinically meaningful, compared with 39% on standard management.

The guided-treatment group also did significantly better in terms of secondary echocardiographic end points, with larger improvements in left ventricular ejection fraction and in ventricular remodeling as reflected by changes in LV end-systolic and end-diastolic volume index, the cardiologist continued.

NT-proBNP–guided therapy proved safe and was well tolerated, with no significant increase in adverse events.

Patients in the guided-treatment arm had a median of six clinic visits, compared with five with standard management. The median baseline NT-proBNP level in the guided-therapy arm was 2,344 pg/mL. It fell to 1,125 pg/mL, with 44% of subjects in the guided-therapy arm attaining an NT-proBNP of 1,000 pg/mL or less.

Session cochair Dr. Gregg C. Fonarow said in an interview that he views PROTECT as a successful proof-of-concept study. But before biomarker-guided treatment of heart failure becomes part of guideline-recommended, routine outpatient care, it will be necessary to see if the Massachusetts General Hospital experience can be extended to other settings, including primary care practices, where many patients with heart failure receive their treatment. This will require a large multicenter trial with a diverse group of clinicians; randomization by site; and hard clinical end points, including mortality.

A proposal for such a study has been presented to the National Heart, Lung, and Blood Institute for funding consideration.

"It's a large and expensive trial, but the impact is potentially profound," said Dr. Fonarow, professor of medicine and director of the Ahmanson-UCLA Cardiomyopathy Center, Los Angeles. "Given the costs of heart failure and the tremendous number of outpatient visits for this disease, if we truly had a well-validated guide using biomarkers, that would be a phenomenal advance."

The PROTECT trial was sponsored in part by Roche Diagnostics. Dr. Januzzi declared he serves as a consultant to and speaker for the company. ■