A-HeFT Drug Combo Reverses LV Remodeling

BY DAMIAN McNAMARA
Miami Bureau

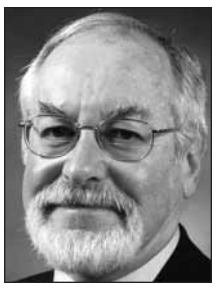
BOCA RATON, FLA. — Fixed-dose isosorbide dinitrate and hydralazine significantly reduces left ventricular volume and increases ejection fraction in African American patients with moderate to severe heart failure, according to a subanalysis of the African American Heart Failure Trial.

Decreases in brain natriuretic peptide corresponded with the 6-month improvements in cardiac remodeling.

In the African American Heart Failure Trial (A-HeFT), the drug combination (BiDil, Nitromed Inc.) was associated with a 43% increase in survival for African Americans with moderate to severe heart failure (N. Engl. J. Med. 2004;351:2049-57). The magnitude of this finding surprised some because the A-HeFT patients were already aggressively treated for heart failure: 87% were already taking β-blockers, 78% were on ACE inhibitors, 39% were on aldosterone inhibitors, and 28% were taking angiotensin receptor blockers.

Regarding A-HeFT mortality, "the survival benefit versus placebo became obvious at 6 months or 7 months, and then the curves spread out remarkably after that," Jay N. Cohn, M.D., said during a late-breaking clinical trial session at the annual meeting of the Heart Failure Society of America. He and his associates performed a subanalysis of the A-HeFT data to determine whether improvements in left ventricular structure and function could explain the improvement in survival. They compared echocardiographic findings and blood levels of brain natriuretic peptide (BNP) taken at baseline and after 6 months of treatment. One cardiologist evaluated all the digitized echocardiograms in blinded fashion.

Of the 1,050 self-identified African Americans enrolled in A-HeFT, 666 had ejection fraction values recorded at baseline and 6 months. Of this group, 329 were treated with combination therapy and 337 with placebo. In addition, there were 678 participants with left ventricular internal diameter in diastole (LVIDd) values taken at baseline and at 6 months. Of this group, 337 were treated with the combination and 341 with placebo.



The striking difference in BNP levels at 6 months supports the cardiac remodeling improvements.

DR. COHN

At 6 months, there was a significant increase in ejection fraction in the combination group versus placebo, said Dr. Cohn, professor of medicine and director, Rasmussen Center for Cardiovascular Disease Prevention, University of Minnesota in Minneapolis. There also was a highly significant difference in LVIDd in the treatment group versus placebo group.

A meeting attendee asked about possible variation with the measurements in the study. "I'm more comfortable with the consistency of the LVIDd measurements, compared with the ejection fraction measurements, which can be interpreted differently," Dr. Cohn responded.

The mean baseline BNP level was 300 pg/mL. By 6 months, the treatment group had a greater mean decrease, 28 pg/mL, compared with the placebo group, 11 pg/mL. Dr. Cohn called this a "striking difference between groups" that supports the cardiac remodeling improvements.

Another attendee asked how well the BNP values tracked with changes to left ventricular volume. Dr. Cohn said, "We don't know that yet, the tracking between the two is not always perfect. BNP is not always perfect. BNP is a continuum, but the lower the better."

When asked if remodeling was dose dependent, Dr. Cohn replied, "We haven't looked at that yet." He and his associates plan to perform subgroup analyses. "I would be surprised if the benefit on remodeling is confined to the African American population," he said.

"The combination of isosorbide dinitrate and hydralazine induces regression of left ventricular remodeling in patients already treated with neurohormonal inhibitors," Dr. Cohn said. "These data provide further support for the growing database that favorable effects on outcomes in heart failure can be attributed to favorable effects on left ventricular structural remodeling." ■