# BiDil Beneficial in HF With Low Blood Pressure

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ATLANTA — Heart failure patients placed on fixed-dose isosorbide dinitrate–hydralazine derive similar morbidity and mortality benefits regardless of baseline blood pressure, Dr. Inder S. Anand said at the annual meeting of the American College of Cardiology.

This may be because the drug combination possesses the remarkable property of exerting differential effects on blood pressure depending on a patient's baseline blood pressure, according to a new secondary analysis of the African American Heart Failure Trial (A-HeFT).

These A-HeFT data show isosorbide dinitrate–hydralazine (BiDil) lowered blood pressure only in patients with normal or elevated baseline systolic blood pressure. In patients in the lowest quartile of baseline systolic blood pressure—those with a value of 112 mm Hg or less— BiDil actually increased systolic pressure by a mean of 6.4 mm Hg, explained Dr. Anand, professor of medicine at the University of Minnesota and director of the heart failure program at the Veterans Affairs Medical Center, Minneapolis.

The new A-HeFT findings are extremely reassuring, he said. Despite the strongly positive primary results of A-HeFT and subsequent Food and Drug Administration approval of BiDil for use in African Americans with moderate to severe heart failure, many physicians have been leery of using the combination. That's because hydralazine has long been recognized to be a potent vasodilator.

There has been concern that the drug would drive blood pressure dangerously low in heart failure patients who have low baseline pressures. This worry stems from the observation that low blood pressure in heart failure patients is a significant predictor of increased morbidity and mortality—unlike in the general population, where lower is better.

A-HeFT, sponsored by NitroMed Inc., involved 1,050 African American heart failure patients randomized in a double-blind fashion to BiDil titrated to a target dose of 120 mg/day of isosorbide dinitrate plus 225 mg/day of hydralazine or to placebo, along with state-of-the-art medical management. Overall, BiDil conferred a highly significant 43% reduction in mortality risk during 10 months of follow-up, compared with the 10.2% incidence in the placebo arm, and a 37% decrease in the risk of the combined end point of mortality or first hospitalization for heart failure (N. Engl. J. Med. 2004;351:2049-57).

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The new secondary analysis showed that the magnitude of the reductions in mortality and hospitalization was actually slightly greater, albeit not significantly so, in patients whose baseline systolic blood pressure was below the median of 126 mm Hg than in those above the median, according to Dr. Anand.

"These data then would suggest that the combination is well tolerated by heart failure patients with low systolic blood pressure and [that] patients derive similar benefits regardless of baseline blood pressure. Since patients with low blood pressure are at the highest risk of bad outcomes, judicious use of the combination therapy in such patients is likely to lead to substantial benefit," the physician said.

Session cochair Dr. Peter E. Carson, of the Veterans Affairs Medical Center in Washington, commented, "The thing that physicians are particularly concerned about when I talk to them about this therapy is the low blood pressure—what will happen if the blood pressure is lowered? You clearly showed that it didn't affect them. That's obviously a very important finding."

In response to an audience question, Dr. Anand said hydralazine tolerability and titration were virtually identical in patients in all quartiles of baseline blood pressure.

"I was surprised, really, looking at that data. I thought patients with higher blood pressure would get more vasodilation and therefore more headache, but no," Dr. Anand said. ■