



HYDRALAZINE/NITRATES FOR HEART FAILURE IN BLACK PATIENTS July 2005

Based upon the results of the recent African American Heart Failure Trial (A-HeFT),(1) the US Food and Drug Administration (FDA) has approved the drug BiDil for use in the treatment of heart failure in self-identified black patients.(2) BiDil is a fixed dose combination of two drugs, hydralazine and isosorbide dinitrate, that are individually available in generic form. In response to both the publication of the A-HeFT results and the FDA approval of BiDil, we have received questions about the potential impact of these developments on the current CMS/JCAHO quality measure for ACE-inhibitor therapy in heart failure.

A-HeFT was a randomized blinded placebo-controlled trial of 1,050 patients who were self-identified as black with left ventricular systolic dysfunction and advanced heart failure symptoms despite standard medical therapy. Patients were randomized to receive either BiDil or placebo. The primary study endpoint was a composite of mortality, hospital admission, or changes in health related quality of life. Of note, among the patients studied, approximately 69% were treated with an ACE-inhibitor, 17% with an angiotensin receptor blocker, and 74% with a beta-blocker. The investigators found significant improvements in the primary composite outcome and in the components of the primary outcome among patients treated with BiDil. This included a 43% relative reduction in the risk of death (ARR=4%, NNT=25). Largely on the basis of this study, the FDA approved the drug for use in self-identified black individuals, the group in whom the study was performed.

Several implications of this study deserve specific focus:

- 1) A-HeFT was performed in the context of contemporary medical therapy for heart failure, including nearly universal use of ACE-inhibitors or ARBs. Thus, BiDil was shown to be an important addition to ACE-inhibitor or ARB therapy in patients selected for the trial.
- 2) A-HeFT did not demonstrate (and was not constructed to demonstrate) that black patients fail to benefit from ACE-inhibitors or ARBs. Existing guidelines recommend the use of ACE-inhibitors in the absence of contraindications in all patients with LVSD regardless of race.
- 3) A prior study designed to compare the combination of hydralazine/nitrates with ACE-inhibitors demonstrated the superiority of ACE-inhibitors. (3) Although there has been some debate about the comparative efficacy of hydralazine/nitrates vs. ACE-inhibitors in black patients, the evidence does not adequately support the equivalence or superiority of hydralazine/nitrates over ACE-inhibitors in any patient population (barring those with contraindications to ACE-inhibitors).

Based upon the current evidence, including the A-HeFT results and the FDA decision resulting from the study, the current quality measures for ACE-inhibitors or ARB in patients with heart failure and LVSD will not change. All patients without contraindications should continue to receive ACE-inhibitors or ARB as first-line therapy, regardless of the patient's race. In some cases, hydralazine and isosorbide may be useful as additional treatment, but this does not affect the existing measure that assesses the use of ACE-inhibitors or ARB in eligible patients without treatment-specific contraindications.



REFERENCES

- 1) Taylor AL, Ziesche S, Yancy C, Carson P, D'Agostino R, Jr., Ferdinand K, Taylor M, Adams K, Sabolinski M, Worcel M, Cohn JN. Combination of isosorbide dinitrate and hydralazine in blacks with heart failure. *N Engl J Med* 2004;351(20):2049-57.
- 2) FDA Approves BiDil Heart Failure Drug for Black Patients. June 23, 2005. <http://www.fda.gov/bbs/topics/NEWS/2005/NEW01190.html>. Accessed July 22, 2005.
- 3) Cohn JN, Johnson G, Ziesche S, Cobb F, Francis G, Tristani F, Smith R, Dunkman WB, Loeb H, Wong M. A comparison of enalapril with hydralazine-isosorbide dinitrate in the treatment of chronic congestive heart failure. *N Engl J Med* 1991;325(5):303-10.