BiDil's impact

To the editor:

We were greatly disturbed to read your editorial in the August issue (*Nat. Biotechnol.* **23**, 903, 2005) which made disparaging comments about BiDil, a new heart failure medication for blacks that has been shown clearly to be safe and effective. Despite misleading claims in your editorial, research shows African Americans do bear a disproportionate burden of heart failure. Therefore, it is important to remember three crucial facts.

One, the need is real. Heart failure is often a death sentence, carrying with it a 50% chance of death within five years, a high likelihood of repetitive hospitalizations and a quality of life that can rival that of the most severely affected cancer patient. Describing heart failure as a "major public health problem in blacks," the recently updated American College of Cardiology and American Heart Association guidelines clearly establish that heart failure is more common in African Americans, affecting approximately 3% of all black adults—reflecting a 50% higher incidence of the disease than that of the general population[1]. According to 2001 data from the US Centers for Disease Control and Prevention (CDC), African Americans aged 45 to 64 are 2.5 times more likely to die from the heart failure than their white counterparts[2]. These numbers stand alone in representing a growing disparate epidemic that modern medicine must continue to address, as it has most recently with the US Food and Drug Administration's (FDA) approval of BiDil (isosorbide dinitrate/hydralazine).

Two, the science supporting BiDil is solid. Medical advances are the result of the building blocks laid down beforehand, and indeed discovery by serendipity is more the rule than the exception. Vasodilator–Heart Failure Trials I and II (V-HeFT I and II), which set the basis for the African-American Heart Failure Trial (A-HeFT), were well conceived and met the standards of their time. More importantly, they provided the 'signal' that, within the bounds of traditional inquiry, medical science needed to follow. The resulting A-HeFT represented the confirmatory study and its outcomes have met the highest standards of leading medical publications. This was not "scientifically dubious" work and to assert such is inappropriate.

And three, the clinical benefits seen with BiDil in A-HeFT are incontrovertible. BiDil, when added to current therapies, saves lives, reduces the risk of first hospitalization and significantly increases patients' improvement in symptoms—data so compelling the trial's safety board halted the study early.

The fact that race is an imperfect marker is a given; opposing arguments are empty because they offer no alternative. The use of race as the only basis of medical treatment is clearly insufficient; but the self-identification of 'African American' in this instance serves as an indicator that BiDil *may* be beneficial for certain patients, as demonstrated in A-HeFT. On the basis of the available clinical data and our increasing understanding of genomics and other factors, it is clear BiDil provides great benefit for many, but not all, African Americans, although its potential is not limited solely to African Americans. Clearly more research is needed. In the meantime, physicians should continue best practices by approaching all patients comprehensively, taking all factors into account, not just race, and treating them with the best available agents.

Finally, we could not disagree more with the assertion that the FDA's approval of BiDil represents a "regressive step in medicine." We were there. The FDA functioned at a very high order in this case and subjected these data to intense scrutiny. Based on the weight of evidence—not politics—patients with heart failure (in this case African Americans) now have available a remarkably effective drug to treat a life-altering and life-threatening disease. If we have plausible reason to believe that a medication for such a deadly disease can benefit a certain subpopulation at this magnitude of benefit, how can we legitimately refuse that population this lifesaving treatment?

We are pleased that these discussions have highlighted the issues of heart disease in at-risk groups and are enthused that a new therapy has the potential to favorably influence the lives of thousands of patients. That to us is no "regressive step in medicine" but rather an exciting advancement that may pave the way for future personalized treatments for people of all backgrounds.

Gary Puckrein[1] & Clyde W. Yancy[2]

[1]National Minority Health Month Foundation, 1200 New Hampshire Avenue, NW Suite 575, Washington, DC 20036, USA and [2]A-HeFT investigator, the University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390, USA.
e-mail: GPuckrein@americanvisions.com

1. Hunt, S.A. *et al. ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult. 5.2 Ethnic Considerations* (American College of Cardiology, Bethesda, MD, 2005). http://www.acc.org/clinical/guidelines/failure//index.pdf
2. US Department of Health and Human Services; US Centers for Disease Control and Prevention; US National Center for Health Statistics; Office of Analysis, Epidemiology, and Health Promotion; Compressed Mortality File compiled from CMF 1999–2001, series 20, No. 2G 2004 on CDC WONDER online database. http://wonder.cdc.gov/mortICD10J.html

Nature Biotechnology responds:

In citing their three 'crucial' facts, Puckrein and Yang sidestep the main point of our editorial: BiDil is a poor example of targeted medicine. As far as we know, skin pigmentation has not yet been genetically linked to (less still shown to be an underlying cause of) heart disease, and yet the FDA has accepted it as a means for deciding who should receive a promising heart disease therapy and who should not.

There are many diseases for which there are race-differentials in both disease incidence and mortality. The key issue is not simply that such disparities exist. Rather it is how or whether they can be linked to an underlying genetic or biochemical difference.

In the case of BiDil, we never said that the trials themselves were "scientifically dubious."