Nesiritide in Acute Decompensated Heart Failure

TO THE EDITOR: In an editorial accompanying an article by O'Connor et al. on the effect of nesiritide in patients with acute decompensated heart failure (July 7 issue), Topol describes the meandering path of nesiritide from approval by the Food and Drug Administration (FDA) on the basis of limited data through an ultimately disappointing pivotal trial. This discussion of the unfortunate legacy of nesiritide criticizes the manufacturer as the “chief culprit” here but mentions too quickly the role that physicians played in potentially “creating a monster” at great expense to patients and payers.

Although the FDA may base approvals on murky surrogate end points, the clinical community could have taken a more skeptical stance and demanded more rigorous evidence. Only clinicians had the power to critically evaluate the available evidence and withhold prescriptions in the absence of better data. This judiciousness surely would have encouraged the manufacturer to conduct the necessary research more quickly.

Physicians (particularly when they are assessing new and expensive interventions) must take more seriously their responsibility as the arbiter of prescribing. FDA approval is not a substitute for our own judgment. It is easy to blame optimistic marketing or inadequate regulation for a “lost decade.” But ultimately, physicians must demand better science in support of new drugs and devices.

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Dr. Kramer reports serving as a consultant to the FDA Circulatory Systems Advisory Panel. No other potential conflict of interest relevant to this letter was reported.


THE AUTHORS REPLY: We agree with Kramer that clinicians should demand evidence before the exuberant use of a therapy. However, we also believe that individuals are unlikely to exert influence unless they do so collectively under a professional banner. Likewise, regulatory policies can provide incentives for producing new therapies and can encourage proper evaluation of the risk–benefit balance of treatments.

The FDA guidance for approval of nesiritide was met by the Vasodilation in the Management of Acute Congestive Heart Failure (VMAC) study. Unfortunately, incentives to conduct pragmatic outcome trials were lacking, despite the clear need for such studies. Before 2001, the last drug approved for heart failure was milrinone, and the most commonly used therapies (e.g., diuretics, nitroglycerin, inotropes, and ultrafiltration) currently have sparse data to support rational decision making about their optimal use.

We believe that Kramer is mistaken to consider improvement in dyspnea as a surrogate end point for clinical outcomes. An improvement in dyspnea is indeed an important patient-reported outcome, but the overall safety of a therapy must still be rigorously evaluated in adequately powered, pragmatic outcome trials.

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Since publication of their article, the authors report no further potential conflict of interest.