Angiotensin II Type 1 Receptor Blockers and Congestive Heart Failure

To the Editor:

We read with great interest the review on angiotensin II type 1 receptor blockers by Michel Burnier.1 He quotes previous investigations, including the results of the Losartan Heart Failure Survival Study (ELITE II)2 and states that “...losartan was not superior to captopril in reducing morbidity and mortality.” and concludes that “...one should be careful before concluding that the class of angiotensin receptor antagonists is less effective than ACE inhibitors in the treatment of congestive heart failure...” On the basis of the results of ELITE II and the preliminary results of the Valsartan Heart Failure Trial (Val-HeFT),3 we do not agree with this interpretation. Data from several large-scale clinical trials strongly support a benefit of treatment with β-blockers in patients with advanced stages of congestive heart failure.4

In ELITE II,2 in the subset of patients taking β-blockers at baseline (22% of the population), total mortality reduction differed significantly between the losartan and captopril groups in favor of the angiotensin-converting enzyme (ACE) inhibitor captopril. In Val-HeFT,3 ≈35% of the patients were taking β-blockers at baseline. Among these patients, the point estimate actually trended toward a negative effect with valsartan.

On the basis of the currently available data, one should conclude that, particularly in patients taking β-blockers (which are recommended for all patients with stable NYHA class II and III heart failure due to left ventricular systolic dysfunction without contraindication5), the class of angiotensin receptor antagonists is probably less effective than are ACE inhibitors in the treatment of congestive heart failure.

We agree with Burnier that angiotensin II receptor blockers may be considered in heart failure patients developing an ACE inhibitor–induced cough. Additional studies are ongoing, and their results will have to be taken into account to evaluate the definite place of angiotensin II receptor antagonists in heart failure.

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Response

Dr Auer and colleagues suggest that on the basis of the results of the Losartan Heart Failure Survival Study (ELITE II) and the Valsartan Heart Failure Trial (Val-HeFT), one should conclude that the class of angiotensin receptor antagonists is less effective than are angiotensin-converting enzyme (ACE) inhibitors in the treatment of congestive heart failure in patients taking β-blockers. I do not think that the results of these 2 studies allow such a conclusion.

In the ELITE II study, the number of patients included in the β-blocker subgroup analysis was small.1 Thus, as stated by Pitt and colleagues,1 “the interaction should be interpreted with caution.” Furthermore, the dose of losartan used in this study was low (50 mg) and certainly insufficient to block the renin-angiotensin system for 24 hours.2 Therefore, one cannot exclude the possibility that a higher dose of losartan would be as effective as an ACE inhibitor, even in patients receiving β-blockers.

With regard to the Val-HeFT study,3 several points should be taken into account. First, the results have not yet been published. It is difficult, therefore, to discuss the data in much detail. Second, the goal of Val-HeFT was not to compare the efficacy of an ACE inhibitor with that of an angiotensin II receptor antagonist but rather to evaluate the potential benefits of valsartan administered in addition to an ACE inhibitor. Third, to my knowledge, the randomization was not stratified on the basis of the concurrent use of β-blockers. Thus, there may be potential bias related to the reasons for administering β-blockers. Taken together, the results of Val-HeFT do not provide any solid information regarding the comparative efficacy of ACE inhibitors and angiotensin II receptor antagonists in patients with congestive heart failure who are being treated with β-blockers. It is important to mention, however, that in ACE-intolerant patients, valsartan was remarkably effective, which clearly indicates that heart failure patients can benefit from angiotensin II receptor blockade. With regard to the potential interaction between the use of β-blockers and the effects of angiotensin II receptor antagonists, specific studies should be designed to answer the question. In the meantime, I would not recommend the avoidance of angiotensin II receptor blockers in heart failure patients who are being treated with β-blockers.

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