Aliskiren May Be Safe, Effective in Heart Failure

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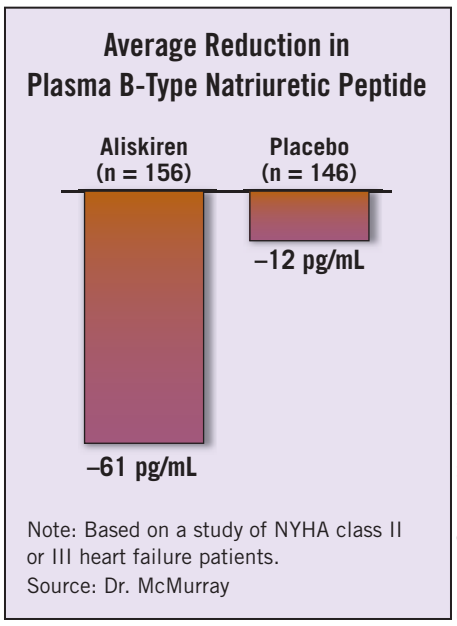
VIENNA — Treatment with the direct renin inhibitor aliskiren was safe and effective for improving surrogate measures of heart failure when used on top of an optimal regimen in a phase II study with about 300 patients with moderately severe disease.

"The results were encouraging enough to make the case for a large, phase III trial" with morbidity and mortality end points, Dr. John McMurray said at the annual meeting of the European Society of Cardiology.

This is the first report from a study with a sizable number of patients with heart failure who received aliskiren. Aliskiren (Tekturna), the first direct renin inhibitor, was approved by the Food and Drug Administration last March for treating hypertension. The drug has also raised interest as a treatment for heart failure because of the key role of the renin angiotensin aldosterone system in the disease, and because ACE inhibitors and angiotensin receptor blockers (ARBs) have become mainstays of heart failure treatment.



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What's unclear is whether a future phase III study should test aliskiren as an add-on treatment to an ACE inhibitor or ARB, or if aliskiren should be used as an alternative to these drugs, said Dr. McMurray, professor of medical cardiology at the University of Glasgow, Scotland. If the new drug is tested only as an add-on, "patients may get two drugs when all they need is one. An ACE inhibitor may not be needed with aliskiren," he said in an interview.

The ALOFT (Aliskiren Observation of Heart Failure Treatment) study enrolled 302 patients with New York Heart Association class II-IV heart failure who were already on optimal treatment with an ACE inhibitor or ARB as well as with a β-blocker. About a third of the patients were also on treatment with an aldosterone antagonist, either spironolactone or eplerenone.

All patients had either current or prior hypertension, and their level of plasma B-type natriuretic peptide (BNP) had to be greater than 100 pg/mL. The average left ventricular ejection fraction of the group was 31%, and their average age was 67 years. About 60% of patients had class II heart failure and the rest had class III. Patients were randomized to either 150 mg oral aliskiren once daily (156 patients) or placebo (146 patients), and were treated for 3 months.

Compared with patients in the placebo group, treatment with aliskiren led to significant drops in plasma renin activity, plasma BNP levels, and urinary aldosterone levels. Echocardiography measurements also showed significant reductions in the prevalence of mitral regurgitation and in left-ventricular filling pressure, compared with control patients, Dr. McMurray said. Treatment with aliskiren was well tolerated, with no significant increase in the rates of renal dysfunction, hypotension, or hyperkalemia.

The reduction in plasma BNP was probably the best indicator in the study of aliskiren's potential clinical efficacy. To get a better estimate of what this effect on BNP predicts for clinical end points, Dr. McMurray compared the cut in BNP seen with aliskiren treatment in this study (an average drop of 61 pg/mL, compared with an average reduction of 12 pg/mL in the placebo group) to average reductions of 15-39 pg/mL in three large, prior trials of heart failure treatment.

"We saw at least as much BNP lowering with aliskiren as [with any of the other treatments in the three prior trials], which were already shown to reduce morbidity and mortality," said Dr. McMurray, who is a consultant to Novartis, which makes aliskiren and which sponsored the ALOFT study. ■