Aliskiren Bests Ramipril for Diabetic Hypertension

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MADRID — Aliskiren, the novel renin-blocking drug, improved 24-hour blood pressure control and showed greater systolic pressure reductions, compared with ramipril, in diabetics with uncontrolled hypertension, according to data presented at the annual meeting of the European Society of Hypertension.

Aliskiren also can be safely combined with the ACE inhibitor in this population, the combination giving the greatest degree of pressure reduction.

Aliskiren works by blocking the renin-regulated conversion of circulating angiotensinogen to angiotensin-1. The new drug, also known by the brand name Rasilez, is the first of a new class of renin blockers. It is being considered for approval by regulatory authorities in Europe and the United States.

Dr. Yagiz Uresin, professor of clinical pharmacology at Istanbul (Turkey) University, presented a multicenter international study of 837 patients with diabetes and hypertension. At baseline, the patients had blood pressures of over 155 mm Hg systolic and 98 mm Hg diastolic.

After a washout period and a 2- to 4-week placebo run-in, the patients were randomized to aliskiren monotherapy, 150 mg/day; ramipril monotherapy, 5 mg/day; or a combination of 150 mg aliskiren plus 5 mg ramipril per day. After 4 weeks, the investigators doubled the doses in all study groups.

After 8 weeks, aliskiren gave mean pressure reductions of 14.7 mm Hg systolic and 11.3 mm Hg diastolic. This was significantly better than the 12.0- and 10.7-mm Hg reductions obtained with ramipril alone. In combination, the two drugs gave mean pressure reductions of 16.6 mm Hg systolic and 12.8 mm Hg diastolic.

Using a target pressure of 130/80 mm Hg, slightly over 8% of the patients in the monotherapy arms could be considered well controlled by the end of the study. Combination therapy bumped this up to 13%. The low number of patients who were able to reach target pressures reflects the difficulty of treating longstanding hypertension in diabetic patients.

A separate subgroup analysis drawn from the same international cohort showed that aliskiren alone and in combination with ramipril gave significantly better round-the-clock diastolic pressure control than did ramipril alone.

A total of 173 patients, 55 on ramipril alone, 57 on aliskiren alone, and 61 on the combination, underwent 24-hour ambulatory monitoring. Using the smoothness index, a scale that measures the consistency of pressure control over a 24-hour period, the investigators found that aliskiren alone and in combination with ramipril provides significantly greater consistency over the course of a day. Smoothness index scores correlate with reversal of left ventricular hypertrophy and carotid artery wall thickening.

The difference between renin-blockade and ACE inhibition was greatest in the early morning hours. At 21-24 hours post dose, the renin blocker alone and in combination with ramipril gave significantly better pressure control than did ramipril alone. Systolic pressures remained between 4 and 12 mm Hg below baseline in patients on aliskiren or aliskiren plus ramipril. In the ramipril group, systolic pressure rose to near baseline levels at the end of the 24-hour dosing cycle.

The impact of side effects was low in all treatment groups, said Dr. Uresin. About one-third of the patients in each monotherapy group had some untoward effects, the most common being headache, cough, nasopharyngitis, and diarrhea. These were mild and self-limiting in the vast majority. Just over 2% of the ramipril monotherapy group and just under 3% of the aliskiren group had serious side effects; the incidence was reduced to 1.4% for the combination.

The addition of aliskiren to ramipril can cut the incidence of coughing, which is the most common reason patients quit ACE inhibitor therapy. Dr. Uresin pointed out that incidence of cough was just under 5% in the ramipril-alone group, and just over 2% for aliskiren. The rate was 1.8% among those taking the combination. The difference was statistically significant.

"This was definitely not expected," said Dr. Uresin.

Though the mechanism underlying the cough attenuation is not clear, it may have to do with reduced bradykinin levels following renin blockade, he said. ■