Aliskiren's Benefits May Go Beyond BP Control

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BARCELONA — The investigational antihypertensive agent aliskiren, alone or with add-on hydrochlorothiazide, effectively maintained 24-hour blood pressure control in a large, 1-year, phase III clinical trial, Dr. Domenic Sica reported at a joint meeting of the European Society of Cardiology and the World Heart Federation.

Moreover, the drug's strong tissue penetration and long half-life meant that rebound hypertension upon discontinuation was a nonissue. When a subset of participants in the 1,625-patient trial were switched double-blind to placebo for a month following 11 months on aliskiren, their blood pressure (BP) increased only gradually and stayed significantly lower than at baseline, added Dr. Sica, professor of medicine and pharmacology and chairman of clinical pharmacology and hypertension at the Medical College of Virginia, Richmond.

Aliskiren (Rasilez) is a novel once-daily oral agent, first in a new class known as direct renin inhibitors. The drug is now under review by the Food and Drug Administration. Novartis, its developer, anticipates marketing approval by next spring as monotherapy and in fixed-dose combination with hydrochlorothiazide (HCTZ), the physician said in an interview.

The company plans to file for European marketing approval by the end of 2006.

Participants had mild to moderate hypertension and were initially randomized to 150 or 300 mg of aliskiren once daily. The 53% whose blood pressure wasn't adequately controlled on 300 mg/day received add-on HCTZ at 12.5 or 25 mg/day as required.

After 1 year, 86% of subjects were classified as responders, meaning their sitting diastolic BP was below 90 mm Hg and/or at least 10 mm Hg lower than baseline. Pa-

Aliskiren Augured As First-Line Tx

In a combined analysis of in more than 7,000 patients enrolled in seven randomized, controlled trials of aliskiren, perhaps the most notable finding was the new drug's safety, Dr. Matthew R. Weir said at the meeting.

During 6-8 weeks of daily treatment, patients had adverse effect profiles similar to those of the placebo arms, with fewer than 1% having a serious adverse effect or withdrawing from treatment because of adverse effects.

The trial results also showed that treatment with aliskiren led to incremental reductions in diastolic BP in patients who were already treated with an ACE inhibitor (ramipril), a calcium-channel blocker (amlodipine), or a thiazide diuretic. Aliskiren failed to produce additional BP lowering when it was added to an angiotensin-receptor blocker (valsartan), said Dr. Weir, professor of medicine and chief of nephrology at the University of Maryland in Baltimore.

Aliskiren dosages in the studies ranged from 75 to 600 mg/day. Patients enrolled in the seven studies had BPs at baseline of about 100 mm Hg diastolic and 151-157 mm Hg systolic. After 6-8 weeks of treatment with aliskiren, diastolic pressure fell by an average of 7-8 mm Hg, and systolic pressure fell by 10-11 mm Hg. The effect of aliskiren on BP reduction was dose-dependent, with a plateau reached once the dosage was 300-600 mg/day. The age and gender of patients appeared to have no effect on the degree of BP reduction.

All studies included in the analysis were sponsored by Novartis, from which Dr. Weir has received honoraria.

The drug, once available, will be a good choice for both initial therapy and in combination with other antihypertensives, Dr. Weir said. Aliskiren would be an attractive first-line agent given its good safety profile and low rate of interactions with other drugs. "The major question is whether inhibiting the renin-angiotensin system [with aliskiren] gives us an opportunity to better protect blood vessels and target organs," he said.

—Mitchel L. Zoler