Combination Tops Monotherapy for Hypertension

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CHICAGO — Combining the calcium channel blocker amlodipine with the angiotensin receptor blocker olmesartan provides greater reductions in blood pressure than does either agent used as monotherapy, Dr. Steven G. Chrysant said at the annual meeting of the American Society of Hypertension.

Daiichi Sankyo Inc. filed a new drug application in November 2006 for a fixed-dose combination of the two antihypertensives.

Known as Azor, this investigational agent is currently under regulatory and trade name review in the United States.

Lead investigator Dr. Chrysant reported data from a phase III double-blind, placebo-controlled factorial study in which 1,940 patients with mild to severe hypertension were randomized to either monotherapy or co-administration of amlodipine 5-10 mg/day and olmesartan 10-20-40 mg/day for 8 weeks.

Hypertension was defined as seated diastolic BP between 95 mm Hg and 120 mm Hg.

At admission, the average age of patients was 54 years, and their mean blood pressure was 164/102 mm Hg; 13.5% of patients had diabetes, and 34% were hypertensive treatment–naive, said Dr. Chrysant, who reported that he has received grant and research support from the study sponsor, Daiichi Sankyo Pharma Development.

After 8 weeks, all of the combinations of amlodipine and olmesartan resulted in significantly greater blood pressure reductions than either medication alone or placebo, said Dr. Chrysant, a cardiologist at the Oklahoma Cardiovascular and Hypertension Center, University of Oklahoma, Oklahoma City. Blood pressure reductions were dose related.

Amlodipine 10 mg/day plus olmesartan 40 mg/day produced the best results, reducing systolic BP an average of 30.1 mm Hg and diastolic BP an average of 19.0 mm Hg.

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DR. CHRYSANT

In contrast, the average reductions were 19.7/12.7 mm Hg for amlodipine 10 mg alone and 4.8/3.1 mm Hg for placebo.

"Only the high-dose combination dropped the pressure below 140 over 90 [mm Hg]," Dr. Chrysant said at a press briefing.

Adverse events were comparable between groups, occurring in 511 of 970 (53%) combination therapy patients and in 91 of 162 placebo-treated patients (56%). There was one stroke in the olmesartan monotherapy group that was possibly drug related, he said.

Reports of headache, fatigue, and dizziness were highest in the placebo group. The highest incidence of edema (25%) was reported in the amlodipine monotherapy group.

But adding on 40 mg of olmesartan halved this incidence rate, Dr. Chrysant said. He suggests this could be an added benefit of the combination regimen, because many hypertensive patients stop taking their medication because of swollen feet. ■