Hypertension Mitigated by Two-Drug Combination

BY PATRICE WENDLING
Chicago Bureau

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 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 BP 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.

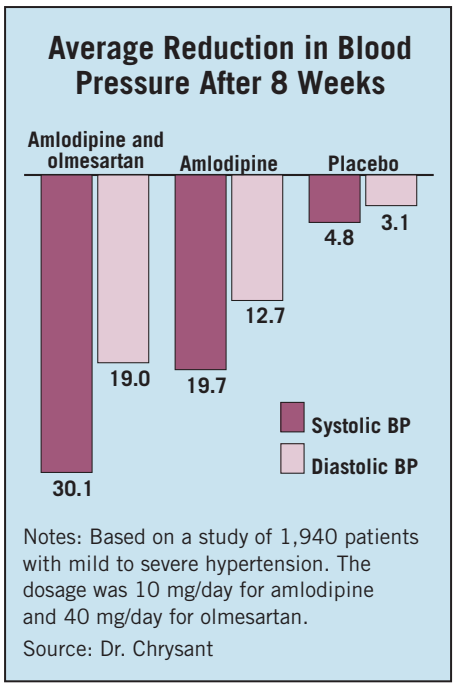
After 8 weeks, all combinations of amlodipine and olmesartan reduced blood pressure significantly more than either medication alone or placebo, said Dr. Chrysant, a cardiologist at the Oklahoma Cardiovascular and Hypertension Center, University of Oklahoma, Oklahoma City. Pressure reductions were dose 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. In contrast, 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 the groups, occurring in 511 of 970 (53%) combination therapy patients and 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, said Dr. Chrysant. He suggests this could be an added benefit of the combination regimen, because many hypertensive patients stop taking their medication because of swollen feet. ■



Monitor Blood Pressure Well In Patients Taking NSAIDs

BY FRAN LOWRY
Orlando Bureau

ORLANDO — Chronic use of nonsteroidal anti-inflammatory agents promotes sodium-retention weight gain and can cause blood pressure to rise by an average of 5 mm Hg, Dr. Matthew R. Weir said at a meeting sponsored by the National Kidney Foundation.

Calcium channel blockers have been shown to help alleviate any blood pressure–related change with NSAIDs.

DR. WEIR

The increase is "not insignificant" when one considers how widely used these drugs are, said Dr. Weir, professor of medicine at the University of Maryland, Baltimore.

Most clinicians are familiar with the renal syndromes caused by NSAIDs and tend to be concerned about acute kidney disease or dysfunction. However, these effects tend to be reversible.

The effects of NSAIDs on blood pressure may pose a more serious issue, Dr. Weir said. "One has to view NSAIDs as antinatriuretic compounds. This is a concern because, depending on how much salt you eat, the actual dose of the NSAID you are taking, and your preexisting levels of blood pressure, you can get very different effects on overall changes in blood pressure over time."

The age-related changes in renal blood supply that occur over time may be an important issue in older patients, who are more likely to be using NSAIDs for conditions such as arthritis.

To avoid adverse cardiovascular effects, always use the lowest possible dose of anti-inflammatory drug, regardless of class. Consider using shorter-acting agents, which may allow the kidney to restore its sodium and water balance, he advised.

Advise patients who are taking NSAIDs to try to avoid dietary sodium, Dr. Weir said.

Blood pressure must be monitored carefully in persons taking NSAIDs, and blood pressure medications adjusted accordingly.

Calcium channel blockers in particular appear to retain their lowering effect on blood pressure despite chronic NSAID use.

"We are not sure why, but calcium channel blockers may have natriuretic properties that are independent of so-called prostaglandin-dependent mechanisms within the kidney," he said.

"We studied this years ago and found that calcium channel blockers helped alleviate any blood pressure–associated change with nonsteroidal anti-inflammatory drugs," Dr. Weir said.

Don't overlook over-the-counter NSAIDs, he added. "Take a careful history on the use of over-the-counter nonsteroidal anti-inflammatory drugs. They don't often appear on medication lists." ■

Obese Hypertensives Show Encouraging Response to Losartan

BY PATRICE WENDLING
Chicago Bureau

CHICAGO — The angiotensin II blocker losartan, alone or in combination with the diuretic hydrochlorothiazide, appears efficacious in the treatment of obesity-associated hypertension, new data suggest.

Current guidelines—based on the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)—do not specify particular treatments for obesity-related hypertension or for the related metabolic syndrome.

The prominent role of angiotensin II in obesity-induced hypertension, however, suggests the possibility that angiotensin receptor blockade may be useful in its treatment, Dr. Suzanne Oparil said at the annual meeting of the American Society of Hypertension (ASH).

She presented preliminary data from a double-blind trial in which 261 patients from 51 sites were randomized to either placebo or losartan 50 mg/day for 4 weeks, titrated to 100 mg/day. Hydrochlorothiazide 12.5 mg/day was added in the active treatment group at week 8 and titrated to 25 mg/day at week 12.

At admission, the average body mass index was 37 kg/m^2 in the losartan group and 38 kg/m^2 in the placebo group. For both groups, average waist circumference was 45 inches, and average BP was 152/99 mm Hg. Entry criteria included use of two or fewer antihypertensive agents, and no diagnosis of diabetes mellitus.

In all, 105 patients in each group completed the study, which was sponsored by Merck & Co. Inc., which has provided research support to Dr. Oparil.

Losartan 50 mg reduced the average sitting systolic BP to 140 mm Hg at week 4 and maintained it there through week 8. Adding hydrochlorothiazide to the 100-mg losartan dosage caused significant further reductions to about 133 mm Hg at week 16.

Similarly, losartan 50 mg decreased the average sitting diastolic BP to 90 mm Hg at week 4 through week 8. Add-on hydrochlorothiazide decreased the diastolic BP reading to about 85 mm Hg at week 18.

At week 16, 75% of patients on losartan achieved systolic BP control to less than 140 mm Hg, and 77% achieved diastolic BP control to less than 90 mm Hg.

In comparison, control rates for patients on placebo were 18% for systolic BP and 38% for diastolic.

All changes in the losartan group were significantly greater than those in the placebo group for all time points, said Dr. Oparil, president of the ASH and director of the vascular biology and hypertension program at the University of Alabama, Birmingham.

The losartan-based treatment regimen had a similar safety and tolerability profile as placebo, she said. ■