**Refractory Hypertension Dips With Drug Combination**

**Chicago** — Nearly three-fourths of patients with uncontrolled hypertension on monotherapy achieved national blood pressure targets on a fixed-dose combination of amlodipine and valsartan that will soon be available, Dr. Joseph L. Izzo Jr. reported at the annual meeting of the American Society of Hypertension.

Two different formulations of Novartis’ single-tablet combination drug, which was approved in June and will be marketed as Exforge, were evaluated in a double-blind, multicenter study that randomized 443 patients to amlodipine 5 mg/valsartan 160 mg, 10 mg/valsartan 160 mg after 8 weeks, hydrochlorothiazide (HCTZ) could be added on, first at 12.5 mg, and then at 25 mg.

Among those with diabetes, 25 of the 61 patients (41%) on the low-dose combination and 27 of the 59 patients (46%) on the high-dose combination reached a BP of less than 130 mm Hg.

Switching patients to the combination therapy resulted in an average additional 20-mm Hg drop in systolic BP, compared with reductions seen with their previous medications. Dr. Izzo, professor of medicine, State University of New York at Buffalo, said at a press briefing. BP control rates were similar when stratified by prior medication, age, and ethnicity. There was little increased response after 8 weeks that could be attributed to the addition of HCTZ therapy.

Adverse events were similar between groups, although the incidence of edema was higher with the 10 mg/160-mg dose than with the lower dose (25% vs. 8%). Exforge was approved by the Food and Drug Administration last month. It is indicated for the treatment of hypertension in patients whose blood pressure has not been adequately controlled with a calcium channel blocker or an angiotensin II receptor blocker alone.

The majority of patients, including 145 (16%) of whom had type 2 diabetes, had been previously treated with a β-blocker, angiotensin receptor antagonist, ACE inhibitor, calcium channel blocker, or diuretic.

At admission, their mean age was 58 years, more than 90% were white, and their mean BP was 150/90 mm Hg, said Dr. Izzo, who has received research support and is a consultant for Novartis, 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 (JNC7)—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 8 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/m² in the losartan group and 38 kg/m² in the placebo group. For both groups, the average waist circumference was 45 inches, and the average BP was 152/99 mm Hg.

Entry criteria included use of two or fewer antihypertensive agents, and no diagnosis of diabetess mellitus.

In all, 105 patients in each group completed the study, which was sponsored by Merck & Co. Inc. 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 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 56% achieved diastolic BP control to less than 90 mm Hg. In comparison, control rates on placebo were 18% for systolic 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. Dr. Oparil has received research support from Merck.

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