

# Combo as Initial Therapy in Diabetic Hypertension

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NEW YORK — Combination antihypertensive therapy must be used more aggressively as the first-line treatment for patients, especially those with diabetes, Dr. Joel M. Neutel said at the annual meeting of the American Society of Hypertension.

“We know that we need combination therapy to get patients to their goal blood pressure, but in practice [physicians in the

United States] are very reluctant to titrate multiple drugs,” said Dr. Neutel, medical director of clinical pharmacology at the Orange County Research Center in Tustin, Calif. “We need to be much more aggressive with combination therapy, and use even three or four drugs to get patients to their goal. All the evidence shows that there is no increase in adverse effects with more aggressive treatment.”

The added value of a two-drug combination compared with monotherapy was

documented by the results from two separate studies reported by Dr. Neutel at the meeting. One study examined adding the calcium channel blocker amlodipine to treatment with either quinapril or losartan. The second study looked at the effect of adding the angiotensin II receptor blocker (ARB) irbesartan to the diuretic hydrochlorothiazide (HCTZ).

Dr. Neutel acknowledged that the results from many prior studies had already proved the added efficacy and safety of combina-

tion therapy, but he stressed the importance of adding to this evidence base.

“We need to provide physicians with a lot of data to make them comfortable with the fact that we can have better blood pressure control with complementary combinations of drugs.” He noted that only about half of U.S. patients with diagnosed hypertension are on medical treatment, and within that fraction only about one-third have their blood pressure controlled to their goal level. Among patients with diabetes, fewer than 20% are at their goal pressure, which was set at less than 130/80 mm Hg in the National Heart, Lung, and Blood Institute’s Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).

“With more reports, we hope that physicians will be more willing to use combination therapy and use it as first-line therapy,” he said.

The first study enrolled diabetic patients with a systolic pressure of 140-170 mm Hg and a diastolic pressure of 90-110 mm Hg who were not on any treatment. Patients with a pressure of more than 135/80 mm Hg who were uncontrolled on either monotherapy or combination therapy were also included.

Patients were initially treated with either 20 mg/day of the ACE inhibitor quinapril or 50 mg/day of the ARB losartan. After 4 weeks, the daily dosages were titrated to 40 mg quinapril or 100 mg losartan. After another 4 weeks, patients were randomized to treatment with either 5 mg/day of amlodipine or placebo. After 6 weeks, the amlodipine dosage was increased to 10 mg/day.

The primary end point was the percentage of patients whose blood pressure was below 130/80 mm Hg after 6 weeks of treatment on the final, titrated regimen. This goal was met by 27.5% of the 211 patients in the combination-therapy group, and by 12.5% of the 200 patients treated with just one drug, a statistically significant difference. The combination regimens were as safe as monotherapy, with no excess incidence of adverse effects, Dr. Neutel reported.

The second study randomized nondiabetic patients to either combination therapy with 150 mg/day irbesartan plus 12.5 mg/day HCTZ, or to monotherapy with the ARB irbesartan alone at a dosage of 150 mg/day. After 1 week, the dosage received by all patients was doubled, to 300 mg irbesartan plus 25 mg HCTZ or to 300 mg of irbesartan alone. The primary end point was the percentage of patients with a diastolic pressure of less than 90 mm Hg after 5 weeks of treatment.

This goal was reached by 47% of the 423 patients in the combination arm, and by 33% of the 206 patients in the monotherapy group, a statistically significant difference. The study’s secondary end point was the percentage of patients with a pressure of less than 140/90 mm Hg, which was reached by 35% of patients on combination therapy and by 19% of those on monotherapy.

The adverse-effect profile and severity was similar in the two treatment groups, Dr. Neutel said. ■

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## INCREASED ACTIVITY OF THE ENDOCANNABINOID SYSTEM (ECS) IS ASSOCIATED WITH INCREASED WAIST CIRCUMFERENCE<sup>1,2</sup>

## INCREASED WAIST CIRCUMFERENCE, A MARKER FOR IAA, IS AN ESTABLISHED CARDIOMETABOLIC RISK FACTOR<sup>3</sup>

- Significantly increases the risk of myocardial infarction, death from cardiovascular disease, and all-cause mortality<sup>4</sup>
- Has been found to be an independent predictor of type 2 diabetes<sup>5</sup>

## ADIPOSE TISSUE IS A HIGHLY ACTIVE ENDOCRINE ORGAN<sup>6</sup>

- Fat cells (adipocytes) produce adiponectin<sup>6</sup>
  - In type 2 diabetes and obesity, adiponectin levels are reduced<sup>6</sup>

## TARGETING THE ECS MAY PLAY A POTENTIAL ROLE IN THE CONTROL OF MAJOR CARDIOMETABOLIC RISK FACTORS SUCH AS IAA\*

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### References

1. DiMarzo V, Matias I. Endocannabinoid control of food intake and energy balance. *Nat Neurosci*. 2005;8:585-589.
2. Cota D, Marsicano G, Tschöp M, et al. The endogenous cannabinoid system affects energy balance via central orexigenic drive and peripheral lipogenesis. *J Clin Invest*. 2003;112:423-431.
3. National Heart, Lung, and Blood Institute. National Cholesterol Education Program. *ATP III Guidelines At-A-Glance: Quick Desk Reference*. Bethesda, Md: National Institutes of Health; May 2001.
4. Dagenais GR, Yi Q, Mann JFE, et al. Prognostic impact of body weight and abdominal obesity in women and men with cardiovascular disease. *Am Heart J*. 2005;149:54-60.
5. Carey VJ, Walters EE, Colditz GA, et al. Body fat distribution and risk of non-insulin-dependent diabetes mellitus in women: the Nurses’ Health Study. *Am J Epidemiol*. 1997;145:614-619.
6. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. *J Clin Endocrinol Metab*. 2004;89:2548-2556.