# Combination Therapy With Perindopril Plus Amlodipine Promising in Hypertension

Written by Emma Hitt Nichols, PhD

Combination therapy of hypertension with perindopril and amlodipine resulted in a larger decrease in blood pressure (BP) compared with monotherapy with either agent or placebo. Stéphane Laurent, MD, PhD, Hospital Européen Georges Pompidou, Paris, France, presented data from a clinical trial evaluating fixed-dose combination of perindopril and amlodipine in patients with hypertension.

Many patients have uncontrolled hypertension even when taking combination therapy of current antihypertensive agents. Current treatment guidelines recommend the use of fixed combinations of antihypertensive therapies early in the disease course. The purpose of this trial was to evaluate a new generation of antihypertensive combination therapy with optimized doses for the first-line use in patients newly diagnosed with hypertension.

The primary end points included superiority of perindopril (3.5 mg) plus amlodipine (2.5 mg) compared with placebo and monotherapy and noninferiority of perindopril (3.5 mg) plus amlodipine (2.5 mg) compared with perindopril (5 mg) and amlodipine (5 mg). The secondary end points included the response rate and safety profile of combination therapy.

In the double-blind study, 1497 patients with hypertension were randomly assigned to receive perindopril monotherapy of 3.5 or 5 mg, amlodipine monotherapy of 2.5 or 5 mg, perindopril (3.5 mg) plus amlodipine (2.5 mg), or placebo for about 8 weeks. All patients received placebo during the 2- to 3-week run-in period. At baseline, the mean age was 51.7 years; 46.7% of patients were men; mean body mass index was 26.8 kg/m$^2$; mean weight was 77.7 kg; and mean abdominal waist circumference was 90.8 cm. In addition, 26.4% of patients were smokers; 26% consumed alcohol; 6.4% had hypercholesteremia; 5.9% had dyslipidemia; and 15% had metabolic syndrome.

The study met all the primary end points ($p<0.001$). Change in supine systolic BP from baseline was greatest in the perindopril + amlodipine arm (–22.0 mm Hg) and the amlodipine (5 mg) monotherapy arm (–21.8 mm Hg). The placebo (–14.2 mm Hg), perindopril (3.5 mg) monotherapy (–16.3 mm Hg), amlodipine (2.5 mg) monotherapy (–16.0 mm Hg), and perindopril (5 mg) monotherapy (–18.2 mm Hg) arms also showed a decrease in systolic BP from baseline. There was a similar trend for diastolic BP. In the combination therapy arm, 43.5% of patients experienced normalization, compared with 37.9%, 33.3%, and 26.6% in the amlodipine (5 mg), perindopril (5 mg), and placebo arms ($p<0.001$), respectively.

A greater rate of lower limb edema was noted in patients who received amlodipine (5 mg) monotherapy compared with perindopril monotherapy or combination therapy. In contrast, cough and orthostatic hypotension occurred more frequently in the perindopril monotherapy arm compared with the amlodipine monotherapy and combination therapy arms.

Dr. Laurent stated that data from this trial indicate that perindopril (3.5 mg) + amlodipine (2.5 mg) combination therapy provides a better benefit-risk ratio compared with monotherapy, as the combination resulted in a greater reduction in BP with a similar safety profile. Therefore, he suggested that combination therapy of hypertension with perindopril (3.5 mg) plus amlodipine (2.5 mg) may be suitable as first-line therapy.

# Dietary Nitrate Improves BP

Written by Toni Rizzo

Mammals are unable to metabolize nitrate, but symbiotic bacteria on the dorsal tongue surface reduce dietary nitrate to nitrite, which is then converted to the potent vasodilator nitric oxide [Duncan C et al. *Nat Med* 1995]. Vikas Kapil, MD, PhD, William Harvey Research Institute, Queen Mary University, London, United Kingdom, presented results of The Chronic Effects of Beetroot Juice in Hypertensive Subjects study, which assessed whether a once-daily ingestion of dietary nitrate would exert a sustained effect on blood pressure (BP) in hypertensive patients [NCT01405898].

A total of 68 patients with stage 1 hypertension were enrolled in this randomized, double-blind, placebo-controlled trial. The patients were stratified according to whether they were treatment naive or previously treated (not to target) for hypertension. Following a 2-week run-in period, the patients were randomized to a dietary supplement consisting of 250 mL/day of beetroot juice containing dietary nitrate (n=34) or to placebo consisting of nitrate-free beetroot juice (n=34) for 4 weeks.

The primary endpoint was change in clinic, ambulatory, and home BP. The secondary endpoints were pulse-wave velocity (PWV), endothelial function assessed by measurement of flow-mediated dilatation, and plasma nitrite and nitrate concentrations. Clinic BP was measured 3 times every 15 minutes for 1 hour. The second and third readings at each time point were averaged overall. Ambulatory BP was measured once