Olmesartan May Help Prevent Microalbuminuria

BY DOUG BRUNK

SAN DIEGO — Olmesartan reduced the risk of microalbuminuria by 23% in normoalbuminuric patients with type 2 diabetes and at least one additional cardiovascular disease risk factor, results from a large European trial showed.

The angiotensin receptor blocker also yielded unprecedented blood pressure control for this population of patients.

Those are the first key findings from the Randomized Olmesartan and Diabetes Microalbuminuria Prevention (ROADMAP) study, which were unveiled during a press briefing at the annual meeting of the American Society of Nephrology.

"Despite all of our efforts, we still have problems effectively treating diabetic nephropathy," said the study's steering committee chair, Dr. Hermann G. Haller of the department of nephrology at Hannover (Germany) Medical School. "The problem for prevention is that we have to diagnose and treat it early. Microalbuminuria is the first sign of the pathogenesis of diabetic nephropathy. It is also an important marker of early development of cardiovascular disease and can indicate microvascular disease."

The primary end point of the study was the occurrence of microalbuminuria based on two or more positive morning spot urine measurements. Secondary end points were cardiovascular events, renal function, and microvascular morbidity.

With support from Daiichi Sankyo, which markets olmesartan, researchers in 19 countries enrolled 4,449 patients, aged 18-75 years, with well-controlled type 2 diabetes. All patients were normoalbuminuric (defined as a level of 25 mg/g or less for men and 35 mg/g or less for women) and had at lease one additional cardiovascular risk factor, such as high triglyceride levels or hypertension. None of the participants had received an ACE inhibitor or an angiotensin receptor blocker within 6 months of participation.

The patients were randomized to receive either 40 mg olmesartan per day or placebo (conventional antihypertensive treatment without blockade of the renin-angiotensin system). The urine albumin-creatinine ratio was determined every 6 months. Patients were followed for an average of 3.2 years.

At their discretion, study investigators could add calcium channel blockers, diuretics, or beta-blockers to the regimen to help patients achieve the target blood pressure goal of 130/80 mm Hg.

The patients' mean age was 58 years, mean duration of diabetes was 6 years, mean hemoglobin A_{1c} level was 7.6%, and mean body mass index was 31 kg/m^2. The mean baseline blood pressure was 141/84 mm Hg.

Dr. Haller reported that nearly 80% of patients in the olmesartan group reached the target BP of 130/80 mm Hg at 42 months, compared with about 75% of patients in the placebo group. "The percentage of patients reaching the blood pressure goal was very high," he said. "ROADMAP will need further analysis to find out what this high percentage of control actually means."

Over the study period, microalbuminuria occurred in about 8% of the patients in the olmesartan group and 10% of the patients in the placebo group, a statistically significant difference (hazard ratio 0.77). This translated into a risk reduction of 23% for the olmesartan group, compared with the placebo group.

After 1 year, the first incidence of microalbuminuria occurred in about 3% of patients in both groups. For the remainder of the study, fewer patients in the olmesartan group experienced microalbuminuria, compared with patients in the placebo group. "The divergence after 1 year indicates that the specific effects of olmesartan are not due to early hemodynamic changes that would have happened in the first couple of months," Dr. Haller said in an interview. "We think that olmesartan has a specific, perhaps structural effect on the kidney, either in the glomeruli or in the basal membrane, in the microcirculation."

Dr. Haller disclosed that he has received honoraria and is a paid consultant for several pharmaceutical companies, including Daiichi Sankyo. ■