

Irbesartan Protects Against Overt Nephropathy

BY MARY ANN MOON
Contributing Writer

Irbesartan decreases biomarkers of inflammatory activity in patients who have type 2 diabetes with microalbuminuria, reported Dr. Frederik Persson, of the Steno Diabetes Center in Gentofte, Denmark, and his associates.

Further study is needed to determine whether this anti-inflammatory effect translates into fewer cardiovascular events

in this high-risk population, the investigators noted.

The Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria (IRMA-2) study showed that daily irbesartan inhibited the angiotensin II type 1 receptor and protected against the development of overt nephropathy over the course of 2 years. It also hindered the progression of some cardiovascular outcomes, including heart failure. However, the mechanism of the drug's action was unclear.

The pathogenesis of nephropathy in diabetes is thought to involve endothelial dysfunction, low-grade inflammation, growth factors such as transforming growth factor (TGF)- β , and advanced glycation end product (AGE) peptides. Any or all of these may have been affected by irbesartan's influence on the renin-angiotensin-aldosterone system in IRMA-2.

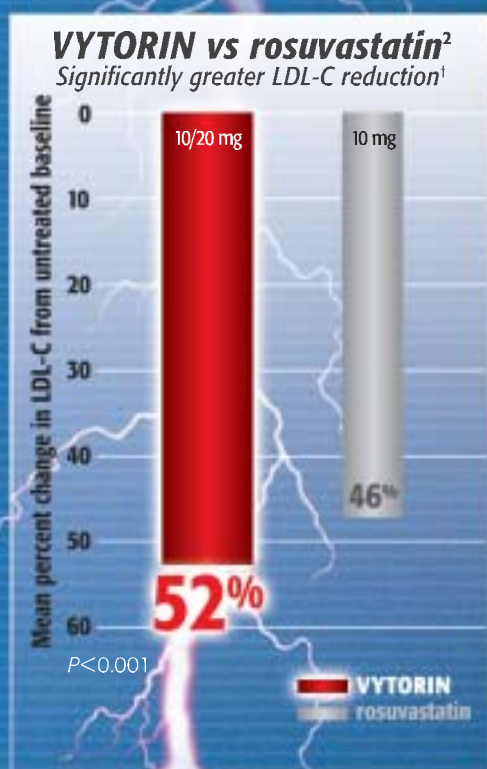
Dr. Persson and his associates conducted a post hoc analysis in a subset of 269 of the IRMA-2 subjects to examine the drug's

effect on a broad range of these biomarkers, all of which are associated with the progression of both nephropathy and cardiovascular disease.

Compared with placebo, irbesartan significantly decreased levels of the inflammatory biomarkers high-sensitivity C-reactive protein and fibrinogen. The drug also attenuated the time-related increase in another marker of inflammatory activity, interleukin-6, they said (Diabetes 2006;55:3550-5).

enough, in 2 separate head-to-head studies

VYTORIN provide that atorvastatin 50%^{1,2,3} at a usual starting dose mean LDL-C reduction



- VYTORIN 10/40 mg lowered LDL-C more than rosuvastatin 20 mg (55% vs 52%, $P=0.001$).²
- VYTORIN 10/80 mg lowered LDL-C more than rosuvastatin 40 mg (61% vs 57%, $P<0.001$).²

[†] Data from a multicenter, randomized, double-blind, active-controlled, 6-arm, parallel-group study designed to evaluate the efficacy and safety of VYTORIN vs rosuvastatin over a 6-week period. Patients with hypercholesterolemia ($N=2,959$) were randomized to 1 of 6 treatment groups: VYTORIN 10/20, 10/40, or 10/80 mg or rosuvastatin 10, 20, or 40 mg. Mean baseline LDL-C level for both VYTORIN 10/20 mg and rosuvastatin 10 mg was 172 mg/dL.²

SELECTED CAUTIONARY INFORMATION (cont)

The concomitant use of VYTORIN and fibrates (especially gemfibrozil) should be avoided. Although not recommended, the dose of VYTORIN should not exceed 10/10 mg if used with gemfibrozil. The benefit of further alterations in lipid levels by the combined use of VYTORIN with niacin should be carefully weighed against the potential risks of myopathy. The dose of VYTORIN should not exceed 10/10 mg daily in patients receiving cyclosporine or danazol, and 10/20 mg daily in patients receiving amiodarone or verapamil.

Liver: It is recommended that liver function tests be performed before the initiation of treatment and thereafter when clinically indicated. Additional tests are recommended prior to and 3 months after titration to the 10/80-mg dose, and semiannually for the first year thereafter.

VYTORIN is not recommended in patients with moderate or severe hepatic insufficiency.

In clinical trials, the most commonly reported side effects, regardless of cause, included headache (6.8%), upper respiratory tract infection (3.9%), myalgia (3.5%), influenza (2.6%), and extremity pain (2.3%).

Please read the brief summary of Prescribing Information on the adjacent page.

References: 1. Ballantyne CM, Abate N, Yuan Z, King TR, Palmisano J. Dose-comparison study of the combination of ezetimibe and simvastatin (Vytorin) versus atorvastatin in patients with hypercholesterolemia: the Vytorin Versus Atorvastatin (VIVA) Study. *Am Heart J*. 2005;149:464-473. 2. Catapano AL, Davidson MH, Ballantyne CM, et al. Lipid-altering efficacy of the ezetimibe/simvastatin single tablet versus rosuvastatin in hypercholesterolemic patients. *Curr Med Res Opin*. 2006;22:2041-2053. 3. IMS HEALTH, NPA PlusSM, NRx, July 2006.

POWER MADE PRACTICAL

VYTORIN
(ezetimibe/simvastatin)
tablets