Statin Copays Adversely Affect Outcomes

BY BRUCE JANCIN
Denver Bureau

ATLANTA — Higher prescription statin copayments have unintended negative consequences, Teresa B. Gibson, Ph.D., said at the annual meeting of the American College of Cardiology.

Her study of the health records of more than 93,000 statin users in employer-sponsored health plans demonstrated that higher copays were associated with significantly lower medication adherence, which in turn was linked to more emergency department visits and cardiovascular hospitalizations.

Health plan managers and policy makers use copays as a means of controlling prescription drug costs. It's a strategy designed to reduce consumption of prescription drugs and steer patients to preferred, less expensive medications. The use of copays is likely to continue to rise. But in patients with chronic medical conditions—such as known cardiovascular disease, or hyperlipidemia predisposing to heart disease—it's a strategy with troublesome side effects, according to Dr. Gibson of Thomson Medstat, a health care research services company in Ann Arbor, Mich.

Only 58% of the 93,296 patients had a filled statin prescription on at least 80% of days. Higher copays were associated with a 37% reduction in adherence.

"In this large cohort of continuing users of statins, we saw increasing drug copayments are a financial barrier to statin adherence. Reduced cost-sharing might be an effective intervention for these patients," she observed.

The average statin copay during the study period of 2000-2003 was $12 per month. Overall adherence to statin therapy during the first 18 months was 58%, meaning only 58% of the 93,296 patients had a filled statin prescription on at least 80% of days during follow-up. Higher copays were associated with a 37% reduction in adherence.

Total expenditures measured during the second 18 months of the study period did not differ significantly between statin-adherent and nonadherent patients. Adherent patients had lower medical expenditures, but this was counterbalanced by higher prescription drug expenditures and more physician office visits than for nonadherent patients.

On the other hand, nonadherent patients had more adverse outcomes during the second 18 months as evidenced by significantly more emergency department visits, total hospitalizations, and cardiovascular hospitalizations. Dr. Gibson's study was funded by Pfizer. ■

Vytorin Lowers C-Reactive Protein

BY BRUCE JANCIN
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ATLANTA — The ezetimibe/simvastatin combination pill Vytorin has a markedly greater anti-inflammatory effect, as reflected in C-reactive protein–lowering, than either agent alone, Dr. Christie M. Ballantyne said at the annual meeting of the American College of Cardiology.

It's already established that Vytorin produces greater low density lipoprotein (LDL) reductions than does statin monotherapy.

In an effort to learn more about the combination agent's effect on C-reactive protein (CRP)—an emerging risk factor for cardiovascular disease—Dr. Ballantyne and coinvestigators conducted a post hoc pooled analysis of three multicenter, randomized, double-blind, placebo-controlled clinical trials.

The pooled analysis included 3,083 patients with baseline LDL of 145-250 mg/dL who were randomized to 12 weeks of placebo, ezetimibe at 10 mg/day, various doses of Vytorin comprised of ezetimibe 10 mg plus simvastatin 10-80 mg, or simvastatin monotherapy at 10-80 mg/day.

Ezetimibe alone wasn't significantly more effective than placebo at lowering CRP levels. In combination with the various doses of simvastatin, however, it re-

duced CRP by a mean of 31%, compared with 14.3% in the pooled simvastatin monotherapy group, reported Dr. Ballantyne, professor of medicine at Baylor College of Medicine, and director of the Center for Cardiovascular Disease Prevention at Methodist DeBakey Heart Center, Houston.

Simvastatin monotherapy lowered LDL by a mean of 38%, while Vytorin dropped it by 52.5%, he added.

The CRP cutpoint associated with reduced cardiovascular event rates in previous studies has been 2 mg/dL. In the pooled analysis, 47.7% of Vytorin-treated patients achieved both an LDL of less than 100 mg/dL and a CRP below 2 mg/dL, as did a collective 22.2% of patients on simvastatin monotherapy. The more stringent target of an LDL below 70 mg/dL plus a CRP of less than 2 mg/dL was met by 21.6% of the Vytorin group and 3.2% of patients on simvastatin alone.

That said, Dr. Ballantyne was quick to add that the clinical significance of reducing CRP in patients at increased cardiovascular risk has yet to be established and is the subject of ongoing randomized prospective investigations.

The clinical significance of reducing CRP has yet to be established.

DR. BALLANTYNE

Audience members inquired as to the mechanism underlying the apparent synergy between ezetimibe and simvastatin in robustly lowering CRP, an especially striking effect given ezetimibe's trivial impact as monotherapy.

"That's a good question. I wish I had the answer," Dr. Ballantyne replied. Hypotheses abound.

One such hypothesis is that there is an as-yet unidentified key interaction between the inhibition of cholesterol absorption by ezetimibe and the statin's 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibition.

It's noteworthy that no enhancement of CRP-lowering was seen in a study in which ezetimibe was combined with fenofibrate rather than a statin, he added.

Dr. Ballantyne is a consultant to Merck/Schering-Plough, which markets Vytorin. ■