

Fluvastatin XL Least Likely to Cause Myalgias

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CHICAGO — Fluvastatin XL, either alone or in combination with ezetimibe, is an effective, well-tolerated, and safe option for lowering LDL cholesterol in patients who can't tolerate other statins because of muscle-related side effects, Dr. Evan A. Stein said at the annual scientific sessions of the American Heart Association.

Statin-associated mild to moderate muscle-related side effects such as myalgias, cramping, and weakness are far more common and debilitating in daily practice than suggested by high-profile, highly selective clinical trials.

And fluvastatin XL, in particular, is less likely than other statins to cause these problems, said Dr. Stein, director of the Metabolic and Atherosclerosis Research Center, Cincinnati.

He presented a randomized double-blind placebo-controlled clinical trial restricted to patients forced to discontinue



Roughly 85% of participants could be maintained on fluvastatin XL without having any muscle-related problems.

DR. STEIN

statins other than fluvastatin (Lescol) because of muscle-related side effects.

The results of that investigation showed that roughly 85% of participants could be maintained on fluvastatin XL at 80 mg/day or fluvastatin XL 80 mg plus ezetimibe (Zetia) at 10 mg/day without experiencing any muscle-related problems.

Moreover, the dropout rate owing to muscle-related side effects in those two arms of the 12-week study was less than 5%, even though everyone in the trial had already discontinued another statin for that very reason.

Dr. Stein stressed he was not talking about myopathy and rhabdomyolysis, serious but rare side effects of statin therapy. He focused instead on mild to moderate muscle pain, cramping, and weakness.

The big randomized trials suggest the prevalence of such problems is 2%-4%, but the experience of many clinicians has been that the true figure in everyday practice is much higher, he said.

In the trial conducted at 27 U.S. and European centers, 199 patients with a history of intolerance to statins other than fluvastatin due to muscle-related side effects were randomized to 12 weeks of ezetimibe plus placebo, fluvastatin XL plus placebo, or both drugs.

LDL cholesterol lowering with fluvastatin, with or without ezetimibe, was greater than with ezetimibe alone (see box on following page).

Muscle-related side effects in the two fluvastatin arms were slightly lower than with ezetimibe. And when such side ef-

fects occurred in patients on fluvastatin alone, they began in the first month, whereas with ezetimibe they started any time during the 3-month trial.

The combination therapy's synergistic effect upon C-reactive protein lowering is difficult to explain but has consistently been seen in other studies of ezetimibe plus various statins, Dr. Stein said at the meeting.

Mean baseline LDL cholesterol in the study cohort was 175 mg/dL. Eighty per-

cent of subjects were high risk by National Cholesterol Education Program (NCEP) criteria. Fluvastatin XL enabled many of them to reach their NCEP LDL cholesterol goal, which otherwise would not have been possible because of their muscle problems on other statins.

An estimated 1-2 million patients have discontinued statin therapy due to such muscle-related side effects, the physician said.

The impression among physicians that

prevalence of mild to moderate muscle-related side effects to statins is much higher in practice than in clinical trials was recently borne out in an observational study involving an unselected population of 7,924 French patients on high-dose statin therapy.

The study—the Prediction of Muscular Risk in Observational Conditions (PRIMO)—was the first ever to look at statin-related muscle side effects in clinical practice. The conclusion: Muscular symptoms

Advertorial

Helping Change the Cycle of Migraine

A RICHER UNDERSTANDING OF PATIENTS' MIGRAINE IMPAIRMENT



The renowned Diamond Headache Clinic recently hosted a meeting featuring the results of the landmark American Migraine Communication study (AMCS). The study revealed that, during office visits for migraines, patients heard mostly closed-ended or short-answer questions (91%), which prompted limited responses.¹ Such questions may tell you about frequency and severity but may fall short in clarifying the patient's total level of impairment due to migraine.

AMCS reveals prevention is often overlooked

Despite the fact that many patients met the American Migraine Prevalence and Prevention study criteria for prevention, discussions were initiated in only 50% of the office visits.¹

TOPAMAX Tablets and TOPAMAX Sprinkle Capsules are indicated for adults for the prophylaxis of migraine headache. The usefulness of TOPAMAX in the acute treatment of migraine headache has not been studied.

TOPAMAX is contraindicated in patients with a history of hypersensitivity to any component of this product.

IMPORTANT SAFETY INFORMATION

TOPAMAX has been associated with serious adverse events, including:

- Hyperchloremic, non-anion gap metabolic acidosis—lowering of bicarbonate levels in the blood. Measurement of baseline and periodic serum bicarbonate is recommended.
- Acute myopia and secondary angle-closure glaucoma—patients should be cautioned to seek medical attention if they experience

blurred vision or ocular pain.

- Oligohidrosis and hyperthermia—decreased sweating and increased body temperature, especially in hot weather. The majority of reports have been in children.
- Cognitive/psychiatric side effects including cognitive dysfunction, psychiatric/behavioral disturbances including suicidal thoughts or behavior, and somnolence and fatigue.

Most common adverse events associated with TOPAMAX 100 mg vs placebo were: paresthesia, 51% vs 6%; anorexia, * 15% vs 6%; fatigue, 15% vs 11%; nausea, 13% vs 8%; diarrhea, 11% vs 4%; weight decrease, 9% vs 1%; taste alteration, 8% vs 1%.

The possibility of decreased contraceptive efficacy and increased breakthrough bleeding should be considered in patients taking combination oral contraceptive products with TOPAMAX.

occurred in 10.5% of patients, and the negative impact upon quality of life was far greater than generally appreciated. Thirty-eight percent of patients with muscle-related side effects reported that muscular pain prevented even moderate exertion during everyday activities, Dr. Stein said.

The PRIMO investigation, sponsored by Novartis Pharmaceuticals, showed that the rate of muscle symptoms was 10.9% with pravastatin at 40 mg/day, 14.9% with atorvastatin at 40-80 mg/day, and 18.2% with simvastatin at 40-80 mg/day. In contrast, fluvastatin XL at 80 mg/day was associated with a 5.1% rate

(Cardiovasc. Drugs Ther. 2005;19:403-14).

Audience members at the meeting argued that Dr. Stein's trial should have featured an arm involving rechallenge to a previously offending statin.

Dr. Stein rejected that as impractical. Most patients found their muscle symptoms sufficiently unpleasant that they would balk at reexposure. And many had experienced continued muscle problems despite switching to two or three different statins, further complicating rechallenge, he said.

Dr. Stein is a consultant to Novartis, which funded the trial. ■

Results of Fluvastatin With and Without Ezetimibe at 12 Weeks

	Ezetimibe	Fluvastatin	Fluvastatin + Ezetimibe
Patients having muscle-related side effects	24.2%	17.4%	14.1%
Patients dropping out of study because of muscle-related side effects	7.6%	4.3%	3.1%
Patients reaching LDL-cholesterol level <100 mg/dL	1.5%	33.3%	67.2%
Patients reaching NCEP LDL-cholesterol goal	10.6%	43.5%	73.4%
Reduction in:			
Level of LDL cholesterol (mean)	15.6%	32.8%	46.1%
Level of C-reactive protein (median)	0%	7.9%	18.6%

Note: Based on a study of 199 patients who had discontinued other statins because of muscle-related side effects.

Source: Dr. Stein

ELSEVIER GLOBAL MEDICAL NEWS

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COULD LEAD TO BETTER INFORMED TREATMENT DECISIONS.¹

Improving Communication Is Important to a Broader Assessment

Open-ended questions can help you gain a richer understanding of your patients' impairment during and *in between* their attacks.

The study showed that most patients gave brief yet informative responses to questions and prompts like these:¹

- "How do migraines make you feel—even when you aren't having one?"
- "Describe the total impact migraines have on your work, family, or social life."

A Subtle Communication Shift Can Help Make a Difference

You may find asking open-ended questions leads to a broader assessment of migraine impairment, and the disruption, disability, and frustration that can come with it. In fact, your patients' level of impairment may require a different treatment option.

Finding out if your patients are feeling trapped in a cycle of suffering, treating and worrying may open up an opportunity to discuss the need for preventive therapy. TOPAMAX can help stop migraines before they start—so your patients can get fewer of them.^{2,3} TOPAMAX offers proven efficacy and is the #1 prescribed brand for migraine prevention in the U.S.⁴

When evaluating migraine, consider using open-ended questions to assess the total degree of migraine impairment. Then talk about the possibility of preventive therapy with TOPAMAX.

The Migraine Discussion Continues

Look for the next installment of *Helping Change the Cycle of Migraine*, in which we'll continue to explore important topics regarding the migraine patient and strategies to help enhance patient care.



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Patients should be instructed to maintain an adequate fluid intake in order to minimize the risk of renal stone formation.

*Anorexia is defined as loss of appetite.

Please see brief summary of full Prescribing Information on following page.



Important

Avoid confusion with Toprol-XL® (metoprolol succinate) by spelling out TOPAMAX® (topiramate) on your prescription. Toprol XL is a registered trademark of the AstraZeneca group of companies.

References: 1. Hahn SR, Nelson M, Lipton RB. Provider-patient migraine discussions: Results of American Migraine Communication study (AMCS). Poster presented at: 58th American Academy of Neurology Annual Meeting, April 1-8, 2006; San Diego, California. 2. Silberstein SD, Neto W, Schmitt J, Jacobs D, for the MIGR-001 Study Group. Topiramate in migraine prevention: results of a large controlled trial. *Arch Neurol.* 2004; 61:490-495. 3. Brandes JL, Saper JR, Diamond M, et al, for the MIGR-002 Study Group. Topiramate for migraine prevention: a randomized controlled trial. *JAMA.* 2004; 291:965-973. 4. IMS Data. July 2006.