

Antimalarials Help Heart Health in Lupus Patients

BY TIMOTHY F. KIRN
Sacramento Bureau

SNOWMASS, COLO. — Antimalarials may not only treat active lupus, but also benefit the heart, W. Joseph McCune, M.D., said at a symposium sponsored by the American College of Rheumatology.

Lupus patients have an elevated risk of heart disease, and antimalarials have been shown to have a number of cardioprotective properties, said Dr. McCune, profes-

sor of internal medicine at the University of Michigan, Ann Arbor.

Such benefits may help offset the deleterious effects of prednisone, which has been shown to increase cholesterol levels. Each 10-mg titration in prednisone dosage is estimated to increase serum cholesterol by 7.5 mg/dL.

Several studies have shown that antimalarials are associated with lipid profile improvements in lupus patients. Each of those studies has treated patients some-

what differently and has shown slightly different results. "But the body of the studies clearly show that when a benefit is looked for, it is found mostly in lowering LDL cholesterol," Dr. McCune said.

In one study involving lupus patients not on corticosteroids, antimalarial therapy was associated with a 4% drop in total cholesterol at 3 months and a 1% drop at 6 months, compared with baseline levels. In patients on a corticosteroid, antimalarial therapy was associated with an 11% drop in total cholesterol at 3 months and a 9% drop at 6 months (J. Rheumatol. 1999;26:325-30).

Among diabetes patients, antimalarials have been shown to lower glucose levels in non-insulin-dependent patients. They also reduce insulin requirements in insulin-dependent patients. The dosages used have tended to be much higher than those typically used to treat lupus. However, even at the lower dosages used for

treating lupus, it's believed that there is some positive effect on glucose tolerance, Dr. McCune said.

Other drugs have been shown to have beneficial secondary effects in lupus patients, but the supporting evidence is generally less robust, he said.

Dehydroepiandrosterone, which can be steroid sparing when it is added to lupus treatment, may produce increases in bone density that could offset steroid-induced osteopenia. But this has not been shown in patients with lupus, and the evidence is not definitive.

Statins clearly have immunomodulatory effects and have been shown to help prevent transplant rejection and to improve rheumatoid arthritis symptoms. They obviously primarily lower cholesterol, and they may have positive effects on bone formation. But at present there are no trials of statins used in patients with lupus, Dr. McCune said. ■



'But the body of the studies clearly show that when a benefit is looked for, it is found mostly in lowering LDL cholesterol.'

DR. McCUNE

and a one-year study of once weekly FOSAMAX® (alendronate sodium) 70 mg the rates of discontinuation of therapy due to any clinical adverse experience were 2.7% for FOSAMAX 10 mg/day vs. 10.5% for placebo, and 6.4% for once weekly FOSAMAX 70 mg vs. 8.6% for placebo. The adverse experiences considered by the investigators as possibly, probably, or definitely drug related in ≥2% of patients treated with either FOSAMAX or placebo are presented in the following table.

	Osteoporosis Studies in Men Adverse Experiences Considered Possibly, Probably, or Definitely Drug Related by the Investigators and Reported in ≥2% of Patients			
	Two-year Study		One-year Study	
	FOSAMAX 10 mg/day % (n=146)	Placebo % (n=95)	Once Weekly FOSAMAX 70 mg % (n=109)	Placebo % (n=58)
Gastrointestinal				
acid regurgitation	4.1	3.2	0.0	0.0
flatulence	4.1	1.1	0.0	0.0
gastroesophageal reflux disease	0.7	3.2	2.8	0.0
dyspepsia	3.4	0.0	2.8	1.7
diarrhea	1.4	1.1	2.8	0.0
abdominal pain	2.1	1.1	0.9	3.4
nausea	2.1	0.0	0.0	0.0

Prevention of osteoporosis in postmenopausal women

The safety of FOSAMAX tablets 5 mg/day in postmenopausal women 40-60 years of age has been evaluated in three double-blind, placebo-controlled studies involving over 1,400 patients randomized to receive FOSAMAX for either two or three years. In these studies the overall safety profiles of FOSAMAX 5 mg/day and placebo were similar. Discontinuation of therapy due to any clinical adverse experience occurred in 7.5% of 642 patients treated with FOSAMAX 5 mg/day and 5.7% of 643 patients treated with placebo.

In a one-year, double-blind, multicenter study, the overall safety and tolerability profiles of once weekly FOSAMAX 35 mg and FOSAMAX 5 mg daily were similar.

The adverse experiences from these studies considered by the investigators as possibly, probably, or definitely drug related in 1% of patients treated with either once weekly FOSAMAX 35 mg, FOSAMAX 5 mg/day or placebo are presented in the following table.

	Osteoporosis Prevention Studies in Postmenopausal Women Adverse Experiences Considered Possibly, Probably, or Definitely Drug Related by the Investigators and Reported in ≥1% of Patients			
	Two/Three-Year Studies		One-Year Study	
	FOSAMAX 5 mg/day % (n=642)	Placebo % (n=648)	Once Weekly FOSAMAX 5 mg/day % (n=361)	Once Weekly FOSAMAX 35 mg % (n=362)
Gastrointestinal				
dyspepsia	1.9	1.4	2.2	1.7
abdominal pain	1.7	3.4	4.2	2.2
acid regurgitation	1.4	2.5	4.2	4.7
nausea	1.4	1.4	2.5	1.4
diarrhea	1.1	1.7	1.1	0.6
constipation	0.9	0.5	1.7	0.3
abdominal distention	0.2	0.3	1.4	1.1
Musculoskeletal				
musculoskeletal (bone, muscle or joint) pain	0.8	0.9	1.9	2.2

Concomitant use with estrogen/hormone replacement therapy

In two studies (of one and two years' duration) of postmenopausal osteoporotic women (total: n=853), the safety and tolerability profile of combined treatment with FOSAMAX 10 mg once daily and estrogen + progestin (n=354) was consistent with those of the individual treatments.

Treatment of glucocorticoid-induced osteoporosis

In two, one-year, placebo-controlled, double-blind, multicenter studies in patients receiving glucocorticoid treatment, the overall safety and tolerability profiles of FOSAMAX 5 and 10 mg/day were generally similar to that of placebo. The adverse experiences considered by the investigators as possibly, probably, or definitely drug related in 1% of patients treated with either FOSAMAX 10 mg/day (n=157), FOSAMAX 5 mg/day (n=161), or placebo (n=159), respectively, were: *Gastrointestinal*: abdominal pain (3.2%; 1.9%; 0.0%), acid regurgitation (2.5%; 1.9%; 1.3%), constipation (1.3%; 0.6%; 0.0%), melena (1.3%; 0.0%; 0.0%), nausea (0.6%; 1.2%; 0.6%), diarrhea (0.0%; 0.0%; 1.3%); *Nervous System/Psychiatric*: headache (0.6%; 0.0%; 1.3%).

The overall safety and tolerability profile in the glucocorticoid-induced osteoporosis population that continued therapy for the second year of the studies (FOSAMAX: n=147) was consistent with that observed in the first year.

Paget's disease of bone

In clinical studies (osteoporosis and Paget's disease), adverse experiences reported in 175 patients taking FOSAMAX 40 mg/day for 3-12 months were similar to those in postmenopausal women treated with FOSAMAX 10 mg/day. However, there was an apparent increased incidence of upper gastrointestinal adverse experiences in patients taking FOSAMAX 40 mg/day (17.7% FOSAMAX vs. 10.2% placebo). One case of esophagitis and two cases of gastritis resulted in discontinuation of treatment.

Additionally, musculoskeletal (bone, muscle or joint) pain, which has been described in patients with Paget's disease treated with other bisphosphonates, was considered by the investigators as possibly, probably, or definitely drug related in approximately 6% of patients treated with FOSAMAX 40 mg/day versus approximately 1% of patients treated with placebo, but rarely resulted in discontinuation of therapy. Discontinuation of therapy due to any clinical adverse experience occurred in 6.4% of patients with Paget's disease treated with FOSAMAX 40 mg/day and 2.4% of patients treated with placebo.

Laboratory Test Findings

In double-blind, multicenter, controlled studies, asymptomatic, mild, and transient decreases in serum calcium and phosphate were observed in approximately 18% and 10%, respectively, of patients taking FOSAMAX versus approximately 12% and 3% of those taking placebo. However, the incidences of decreases in serum calcium to <8.0 mg/dL (2.0 mM) and serum phosphate to <2.0 mg/dL (0.65 mM) were similar in both treatment groups.

Post-Marketing Experience

The following adverse reactions have been reported in post-marketing use:

Body as a Whole: hypersensitivity reactions including urticaria and rarely angioedema. Transient symptoms of myalgia, malaise and rarely, fever have been reported with FOSAMAX, typically in association with initiation of treatment. Rarely, symptomatic hypocalcemia has occurred, generally in association with predisposing conditions.

Gastrointestinal: esophagitis, esophageal erosions, esophageal ulcers, rarely esophageal stricture or perforation, and oropharyngeal ulceration. Gastric or duodenal ulcers, some severe and with complications have also been reported (see WARNINGS, PRECAUTIONS, Information for Patients, and DOSAGE AND ADMINISTRATION).

Skin: rash (occasionally with photosensitivity), pruritus, rarely severe skin reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

Special Senses: rarely uveitis, rarely scleritis.

For more detailed information, please read the complete Prescribing Information.

FOSAMAX is a registered trademark of Merck & Co., Inc.



© 2004 Merck & Co., Inc., Whitehouse Station, NJ 08889, USA All rights reserved.

20406286(1)(025)-FOS

Lupus Patients Appear to Have Increased Skin Cancer Risk

BY MITCHEL L. ZOLER
Philadelphia Bureau

NEW ORLEANS — Patients with systemic lupus erythematosus have a 50% increased risk of also having skin cancer compared with people who don't have lupus, according to findings from a study involving nearly 500,000 people.

This is the first evidence to link systemic lupus erythematosus (SLE) with skin cancer, although a few prior reports documented an increased risk of breast cancer among female SLE patients, Ritu Khurana, M.D., said at the southern regional meeting of the American Federation for Medical Research.

The new study was done in patients seen at 10 collaborating Veterans Affairs medical centers, and involved a population that was 92% male.

Additional analysis of the same population also showed that patients with progressive, systemic sclerosis had an elevated risk of also having skin cancer or lung cancer.

Several prior reports have linked systemic sclerosis to lung cancer, breast cancer, lymphoproliferative disease, and to cancer in general, said Dr. Khurana, a rheumatologist at Louisiana State University in Shreveport.

The investigators reviewed case records for 484,226 people seen at the 10 VA medical centers during 1998-2004. Their average age was 61 years.

This group included 615 patients diagnosed with SLE, more than 76,000 diagnosed with cancer, and almost 19,000 patients specifically diagnosed with skin

cancer (basal cell carcinoma, squamous cell carcinoma, or melanoma).

In a multivariate analysis in which the investigators controlled for smoking history, age, race, and gender, SLE patients were 53% more likely to have skin cancer and 73% more likely to have cancer of any type compared with the other VA patients studied.

The study group also included 203 patients with systemic sclerosis. In the multivariate analysis, patients with scleroderma were 2.35-fold more likely to have lung cancer than the rest of the study population, 82% more likely to have skin cancer, and 61% more likely to have any cancer.

By comparison, patients who smoked had a 2.13-fold elevated risk for developing lung cancer compared with nonsmokers, Dr. Khurana said.

The increased prevalence of cancers in patients with either SLE or systemic sclerosis may be related to the impaired immunosurveillance in these patients, an increase in both systemic and cutaneous inflammation, and an increased susceptibility to viral infections, she said.

Patients with SLE or systemic sclerosis may also have a higher rate of genetic damage, such as chromosomal breaks or deletions.

The elevated risk for skin cancer in patients with SLE or systemic sclerosis means that they should be especially vigilant about sun avoidance and receive regular skin examinations, said Seth M. Berney, M.D., chief of rheumatology at Louisiana State University in Shreveport and a collaborator on these studies. ■