Raloxifene Did Not Increase Lupus Activity

The drug was safe and well tolerated in postmenopausal women who were treated for 12 months.

BY DIANA MAHONEY

FROM THE ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY

LONDON– Raloxifene did not increase lupus activity or flares in a 1-year trial of postmenopausal women who had systemic lupus erythematosus without hypercoagulability risk factors, Dr. Chi Chiu Mok reported.

Raloxifene has been shown in previous studies to preserve bone mineral density (BMD) after menopause in women with systemic lupus erythematosus (SLE). However, mild to moderate disease flares occurred in some patients in these small studies. Lupus flares are rare in postmenopausal women, so this finding suggested a possible association between raloxifene (Evista) and disease activity, explained Dr. Mok of Tuen Mun Hospital in Hong Kong.

Dr. Mok and his colleagues analyzed subgroup data from a 12-month, randomized, controlled trial that assessed bone turnover and BMD in 62 postmenopausal women who had no risk factors for arterial or venous thromboembolism and were being treated with glucocorticoids. The women were randomized to receive either 60 mg/day of raloxifene (30) or placebo (32) in addition to 1,000 mg/day of calcium and 0.25 mcg/day of calcitriol, Dr. Mok explained.

"The primary study outcome was [BMD] of the hip and spine, and secondary outcomes were bone-turnover markers and new vertebral fractures at 12 months," he said.

'As previous studies have shown, raloxifene offers protection against bone mineral density loss in postmenopausal women with lupus receiving long-term glucocorticoids.'

In the overall study population, the mean duration of menopause was 7.2 years, the mean duration of treatment with prednisolone (mean daily dose of 6.8 mg) was 87 months, and the mean Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score at entry was 1.8, Dr. Mok said. The basic clinical characteristics were similar between the two groups, he noted.

After 12 months, "there was a significant gain in bone mineral density at the lumbar spine in the raloxifene patients but not in the placebo group. And there was a gain, though not significant, in the bone mineral density of the hip in the raloxifene-treated patients," Dr. Mok reported. Similarly, markers of bone resorption and formation decreased significantly in the treatment group, he said.

At 12 months, there was no significant difference in the mean area under the curve SLEDAI scores, which were 18.7 in the raloxifene group and 20.3 in the placebo group, or in the mean area under the curve patient global assessments, which were 2.2 for raloxifene patients and 2.3 for placebo patients, Dr. Mok said.

Regarding disease flares, "there were three episodes of mild to moderate flares in the raloxifene patients, compared with nine in the placebo group," he stated.

The researchers also assessed the effect of raloxifene on homocysteine and high-sensitivity C-reactive protein (hsCRP) levels and changes in atherosclerotic risk factors.

They observed a trend of decrease in homocysteine level in raloxifene patients only, no statistically significant changes in hsCRP levels in either group, significant increases in total and LDL cholesterol in the placebo-treated patients only, and no significant changes in systolic and diastolic blood pressure values in either group, Dr. Mok stated. "In the treatment group, [raloxifene] was well tolerated and there were no thromboembolic complications," he said.

"As previous studies have shown, raloxifene offers protection against bone mineral density loss in postmenopausal women with lupus receiving long-term glucocorticoids," Dr. Mok said in an interview. "These results show that it's safe and well tolerated in this population and does not increase lupus disease activity or disease flares."

Dr. Mok disclosed having no financial conflicts of interest. ■

VITALS

Major Finding: After 12 months, mean area under the curve SLEDAI scores were 18.7 for raloxifene-treated patients and 20.3 for placebo-treated patients, and mean area under the curve patient assessment scores were 2.2 in the treated group and 2.3 in the placebo group.

Data Source: A subgroup analysis of data from a 12-month randomized controlled trial looking at the effect of raloxifene and placebo on bone turnover, BMD, and disease activity in 62 postmenopausal women with SLE.

Disclosures: Dr. Mok reported having no financial conflicts of interest to disclose.

Cardiovascular Risk Factors Predict Damage, Death in SLE

BY SHARON WORCESTER

Researchers have identified a number of predictors of damage and/or death in patients with systemic lupus erythematosus.

Data from the inception cohort of 160 SLE patients show that predictors of new damage or death in this population include older age at diagnosis (odds ratio, 1.02), hypercholesterolemia (OR, 2.67), antiphospholipid syndrome (OR, 2.97), BILAG (British Isles Lupus Assessment Group)-2004 mucocutaneous grade A or B disease activity score (OR, 2.75), BILAG-2004 haematological grade A or B score (OR, 18.20), cumulative hydroxychloroquine (per gram) exposure (OR, 0.98), and cumulative mepacrine (per gram) exposure (OR, 1.96×10^{-10}), according to Dr. Chee-Seng Yee, a postdoctoral clinical research fellow at the University of Birmingham (England).

Factors found not to be associated with damage or death were other BILAG-2004 system scores, sex, ethnicity, hypertension, smoking status, prior damage, and cumulative exposure to immunosuppressives/biologic therapies, Dr. Yee said at the annual European Congress of Rheumatology in London.

The investigators included only SLE patients from the multicenter study, which began in 2004, who achieved the fourth American College of Rheumatology criteria for an SLE diagnosis within 12 months at the time of recruitment. Patients had a mean age of 35 years, and the median follow-up was 39 months with a total follow-up of 497 patient years.

Two of the 160 patients died, and 35 instances of damage occurred in 30 patients.

Damage was musculoskeletal in 31% of cases; ophthalmic in 23% of cases; neuropsychiatric in 17% of cases; renal, vascular, or diabetes mellitus in 6% of cases each; and pulmonary, cardiac, cutaneous, or a malignancy in 3% of cases each.

The incident rates of development of damage across the follow-up period were 73, 86, 82, 42, 24, and 112 cases per 1,000 patient-years for follow-up years 1-6, respectively, and about 70 cases per 1,000 patient-years overall.

'My results highlight the importance of managing cardiovascular risk factors and carefully monitoring patients with associated antiphospholipid syndrome.'

As demonstrated by these data, the development of damage starts in the first year and most commonly affects the musculoskeletal, ophthalmic, and neuropsychiatric systems. The rate at which damage occurs, however, is slower compared with that seen in previous studies, Dr. Yee said, noting that antimalarials appear to confer some protection against damage and death.

Findings from previous studies have shown that hydroxychloroquine provides such protection, so this was not a surprising finding. In the current study, though, there was only a 2% reduction in risk with hydroxychloroquine, Dr. Yee said.

"Mepacrine, however, was strongly protective in our study, and this was somewhat surprising," he added, noting that the finding should be interpreted with caution pending confirmation in future studies.

Dr. Yee said this study is the only one of which he is aware to report on the development of damage from a well-characterized inception cohort of SLE patients who were followed-up prospectively.

"My results highlight the importance of managing cardiovascular risk factors and carefully monitoring patients with associated antiphospholipid syndrome," he said, noting that there is a need for more interventional studies on SLE patient with associated antiphospholipid syndrome, as this group of patients is often excluded from clinical trials.

Dr. Yee disclosed that he has received grant and/or research support from Aspreva/Vifor Pharma, and has served as a consultant for Genentech, Parexel, and Teva. ■