Belimumab Use Leads to Steroid Sparing in SLE

BY NANCY WALSH
New York Bureau

PARIS — Treatment of patients with systemic lupus erythematosus with the monoclonal antibody belimumab permitted reductions in corticosteroids through 3 years of observation, according to a post hoc analysis of a large phase II study.

Treatment options for systemic lupus erythematosus (SLE) are limited, and most of the available options are associated with significant and even debilitating adverse effects.

Corticosteroids, for example, are associated with weight gain, risk of infection, psychosis, and hypertension and so generally are reserved for use during times of disease activity. An agent that could be steroid sparing remains a critical unmet need in the SLE treatment regimen, according to Dr. Daniel J. Wallace of Cedars-Sinai Medical Center, University of California, Los Angeles.

Belimumab targets and inhibits soluble B-lymphocyte stimulator (BLyS), a protein that is overexpressed in SLE. In the original trial, patients were randomized to receive belimumab in doses of 1 mg/kg, 4 mg/kg, or 10 mg/kg monthly or placebo plus standard-of-care background therapy for 52 weeks.

Perhaps belimumab use will let patients lower their doses of immunosuppressants.

DR. WALLACE

The use of steroids and tapering of steroids were standardized in the trial according to clinical need, Dr. Wallace explained at the annual European Congress of Rheumatology.

The primary end point was a reduction in disease activity as measured by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) as modified for the Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA) at 24 weeks.

Although the primary end point of the double-blind trial was not met, subsequent analyses of seropositive patients (72% of the original cohort) found that the drug reduced SLE activity and flare rate in patients with antinuclear antibody titers of 1:80 or higher and/or anti–double stranded DNA antibody levels of 30 IU/mL or greater.

Following the completion of the double-blind trial, patients were allowed to enroll in an open-label extension trial in which they received 10 mg/kg of belimumab monthly. A total of 296 participants chose to continue in the study and 233 remained enrolled at the time of Dr. Wallace's EULAR presentation.

At baseline, the majority of patients were women whose mean age was 42 years. Mean disease duration was 8.8 years, and most patients had a SELENA-SLEDAI score of 8 or higher, indicating moderate disease. A total of 69% were on daily prednisone, with a mean dose of 11 mg/day, and 36% were on doses higher than 7.5 mg/day. At the end of the randomized phase, reductions in average prednisone dose to 7.5 mg/day or lower were seen in 34%, 28%, 31%, and 44% of patients in the placebo, 1-mg/kg, 4-mg/kg, and 10-mg/kg groups, while increases from low-dose prednisone to doses of 7.5 mg/day or higher were needed in 17%, 11%, 10%, and 4%, respectively.

At the end of year 3, when patients from all groups were on the highest dose of active treatment, prednisone dose reductions were seen in 56%, 45%, 61%, and 62% of patients originally in the placebo, 1-mg/kg, 4-mg/kg, and 10-mg/kg groups, and predisone dose increases were seen in 8%, 5%, 12%, and 7%, respectively.

Among patients taking 7.5 mg prednisone per day plus immunosuppressants at baseline, more than 30% of belimumab treated patients were able to decrease the prednisone dose and stop the concomitant immunosuppressants by the end of year 3.

"Based on these initial analyses, belimumab has shown potential steroid-sparing activity in the treatment of SLE and may have an additional role as an immunosuppressant-reducing agent," Dr. Wallace wrote.

Dr. Wallace has declared no conflicts of interest. ■