Belimumab Shows Effectiveness in Phase III Trial

BY ROBERT FINN

The monoclonal antibody belimumab appears to be effective for the treatment of systemic lupus erythematosus, according to the results of a randomized, placebo-controlled trial involving 865 patients.

Human Genome Sciences and Glaxo SmithKline, which codeveloped the biologic, announced the results during a conference call for security analysts. The results have not yet undergone peer review. The trial, BLISS-52, was conducted at 90 clinical sites in 13 countries, primarily in Asia, South America, and Eastern Europe. A second phase III trial, BLISS-76, is in its final stages with 826 patients at 133 clinical sites in 19 countries, primarily in North America and Europe. Patients in BLISS-52 were followed for 52 weeks, while patients in BLISS-76 will be followed for 76 weeks.

H. Thomas Watkins, president and chief executive officer of Human Genome Sciences, said that results from BLISS-76 will be announced in November. If the results are positive, the companies will submit marketing applications in the United States, Europe, and other regions during the first half of 2010, he said.

The two trials have similar designs. Patients were randomized to receive either standard of care plus placebo or standard of care plus 1 mg/kg or 10 mg/kg of belimumab. The drug (or placebo) was delivered intravenously on days 0, 14, 28, and every 28 days thereafter.

The primary end point of BLISS-52 was "patient response," defined as an improvement in SELENA-SLEDAI instrument scores of 4 or more at week 52 with no clinically significant flare in the BILAG index or worsening of the Physician's Global Assessment score. SELENA SLEDAI refers to the Safety of Estrogen in Lupus Erythematosus National Assessment trial version of the Systemic Lupus Erythematosus Disease Activity Index. BILAG is an index developed by the British Isles Lupus Assessment Group.

Dr. Joan T. Merrill, head of clinical pharmacology at the Oklahoma Medical Research Foundation, Oklahoma City, said in an interview: "The use of these two instruments in the trial design was very clever. The two major weaknesses of the SLEDAI have been overcome in this trial. It is not as sensitive to change as the BILAG, so if you do see a 4-point drop you are impressed. However, the 4-point drop in the overall score could happen while there is significant worsening in some organs, and this was addressed using the BILAG and the Physician's Global Assessment to eliminate such patients from the responder group."

At week 52, 44% of the patients taking placebo met the primary efficacy end point, compared with 52% of the patients taking 1 mg/kg belimumab, and 58% of the patients taking 10 mg/kg belimumab. Both doses of belimumab proved superior to placebo with a high degree of statistical significance.

'By showing an effect on both the efficacy end point and the steroid taper, the treatment impact is more robust than it might seem just looking at the primary outcome.'

There were also significant improvements in several secondary end points. For example, investigators observed improvement in Physician's Global Assessment scores in 4-8 weeks. A significantly higher proportion of patients in both belimumab groups were able to reduce their average prednisone dose by at least 25% from baseline to 7.5 mg/day or less during the final 12 weeks of the study. Health-related quality of life at week 52, as measured by the SF-36 Physical Component Summary score, was significantly better in both belimumab treatment groups.

"This is an outstanding result," according to Dr. Merrill, who is also the medical director of the Lupus Foundation of America. "By showing an effect on both the efficacy end point and the steroid taper, the treatment impact is more robust than it might seem just looking at the primary outcome."

Rates of adverse events, serious adverse events, infections, and fatalities were similar in the belimumab and placebo groups. The most common adverse events were headache, arthralgia, upper respiratory tract infection, urinary tract infection, and influenza.

Dr. Merrill is a consultant for Genentech Inc., Bristol-Myers Squibb Co., MedImmune Inc., and other companies that develop products for lupus. She was not an investigator in the study being discussed but is involved in the ongoing phase III trial that includes sites in the United States and Western Europe. The companies plan to market belimumab under the trade name Benlysta. ■

Wait Time for New Pediatric Derm Patients Is 6-8 Weeks

BY KERRI WACHTER

PHILADELPHIA — A quarter of pediatric dermatologists report that new patients have to wait more than 12 weeks to get an appointment, and the average overall wait time for pediatric dermatologists is 6-8 weeks, according to a recent survey of 243 pediatricians, general dermatologists, and pediatric dermatologists.

In comparison, the reported median wait time for a new-patient visit is less than 2 weeks to see a pediatrician and less than 5 weeks for a general/adult dermatologist, Dr. Kristen Cam reported in a poster presented at the annual meeting of the Society for Pediatric Dermatology.

"A significant shortage of pediatric dermatologists is perceived by pediatricians, dermatologists, and pediatric dermatologists," wrote Dr. Cam, a dermatology resident at the Children's Hospital of Philadelphia, and her colleagues.

They conducted the survey to assess anecdotal evidence that patients experience long wait times to see a pediatric dermatologist.

The researchers asked approximately 800 physicians from the American Academy of Pediatrics, the American Academy of Dermatology, and the Society for Pediatric Dermatology to complete a 45-question online survey. In all, 243 completed the survey. Of these, 19% identified themselves as pediatricians, 28% as general or adult dermatologists, and 53% as pediatric dermatologists.

More than 90% of the survey respondents perceived a shortage of available pediatric dermatology services. Almost half of the pediatric dermatologists reported that their practices are actively recruiting additional pediatric dermatologists. A quarter of them reported actively recruiting for more than a year, the investigators reported.

Almost two-thirds of pediatric dermatologists practiced in urban areas. More pediatric dermatologists practiced in academic and hybrid academic/private practice settings than in private practice.

Slightly more than half of the pediatric dermatologists had completed a categorical pediatrics residency and almost half had completed fellowship training.

Median salary ranges were comparable for pediatric dermatologists and general/adult dermatologists—$200,000 to $250,000—despite additional subspecialty training.

In comparison, the median salary range for pediatricians was $100,000 to $150,000.

"Salary was perceived to be the strongest factor deterring physicians from entering pediatric dermatology," Dr. Cam and her associates wrote. ■