Belimumab Shows Efficacy in Second Lupus Trial

BY MITCHEL L. ZOLER

Significantly more lupus patients responded to belimumab than placebo in a randomized trial with more than 800 patients followed for a year, the second positive outcome from a pivotal trial of the investigational monoclonal antibody in lupus this year.

After successfully meeting the primary end point in two large, separate lupus-treatment trials, Human Genome Sciences and GlaxoSmithKline, the two companies jointly developing belimumab (Benlysta), plan to file a new drug application with the Food and Drug Administration during the first half of 2010, said H. Thomas Watkins, president of HGS, during a conference call for investors.

'The lupus community has waited decades for one positive phase III trial of an investigational drug developed for lupus. Now we have two.'

If approved, it would be the first drug to receive a labeled indication for lupus in more than 50 years. Belimumab acts by blunting B-cell activity.

Initial results for the more recent of the two pivotal trials, the Belimumab in Subjects with Systemic Lupus Erythematosus (BLISS)-76 study, were announced by HGS and GlaxoSmithKline in a press release, with a full report of the findings expected next summer. Initial results from the first pivotal trial, BLISS-52, were first released last July.

The primary outcome benefit from belimumab treatment was "solid," said Dr. Joan T. Merrill, a specialist in treating systemic lupus erythematosus (SLE) who was a co-investigator on BLISS-76.

"The lupus community has waited decades for one positive phase III trial of an investigational drug developed for lupus. Now we have two." Belimumab "may emerge as a significant new treatment for lupus," said Dr. Merrill, professor of medicine at the University of Oklahoma Health Sciences Center in Oklahoma City. Dr. Merrill has served as a consultant to and has received research funding from HGS and GlaxoSmithKline as well as from several other drug companies.

BLISS-76 randomized 819 patients at 136 sites in 19 countries in North America and Europe. Enrollment criteria were not released for this study, but the similarly designed BLISS-52 trial included SLE patients with a score of 6 or more on the Safety of Estrogens in Lupus Erythematosus National Assessment version of the SLE Disease Activity Index (SELENA SLEDAI). Patients also had to be seropositive for at least either antinuclear antibody at a level of 1:80 or greater or for anti–double stranded DNA at a level of 30 IU/mL or greater.

Patients were randomized to 1 mg/kg intravenous belimumab, 10 mg/kg intravenous belimumab, or placebo. Treatment occurred on days 0, 14, 28, and then every subsequent 28 days for 1 year. The study's primary end point was the percent of patients meeting the SLE Responder Index (SRI) after 52 weeks of treatment.

In BLISS-76 the SRI end point was reached by 43% of patients on the 10 mg/kg dosage, 41% of patients receiving 1 mg/kg, and 34% of patients on placebo. The difference in the outcome rate was statistically significant between the 10-mg/kg arm and placebo, but not between the 1-mg/kg arm and placebo. In BLISS-52, the rate of SRI responses at 52 weeks was 58% with the 10-mg/kg regimen compared with 44% in patients on placebo, also a statistically significant difference. The 10-mg/kg dosage is the one that HGS will pursue in its FDA filing, company officials said.

The safety profile of belimumab looked good in this study, as it had in BLISS-52, with no significant difference in the rates of malignancies, deaths, infections, serious infections, total adverse events, or serious adverse events among the treatment groups. ■

Anti-TNF Agents May Up Skin Cancer Risk

BY DENISE NAPOLI

PHILADELPHIA — Two studies showed an increased risk for nonmelanoma skin cancer in patients who take anti–tumor necrosis factor therapies, and should prompt physicians to evaluate the use of these drugs in patients who are at risk for skin cancer, according to the researchers.

Previous studies have been too small to show a definitive link between biologic therapy for rheumatoid arthritis (RA) and skin malignancy, although RA previously has been well established as a risk factor for skin cancer, according to Dr. Prahba Ranganathan.

She presented the results of her retrospective cohort study of RA patients in the Department of Veterans Affairs national database at the annual meeting of the American College of Rheumatology.

According to Dr. Ranganathan, among 16,829 patients with RA, 3,096 were treated with anti-TNFs at the VA between Oct. 1, 1998, and Sept. 30, 2006. The incidence of nonmelanoma skin cancer was 25.9 per 1,000 patient-years in this cohort, compared with 19.6 per 1,000 patient-years in the biologic-naive cohort, a 34% increased risk.

The incidence of melanoma also was increased by about 50%, with about 3.7 cases per 1,000 patient-years seen in the anti-TNF-treated group, vs. 2.6 cases per 1,000 patient-years in the biologic-naive cohort. Both results were significant.

A second study presented at the press conference confirmed these findings. Dr. Kimme Hyrich of the University of Manchester (England) looked at RA patients from the British Society for Rheumatology's biologics register, a prospective cohort study begun in 2001 to monitor the long-term safety of anti-TNFs.

Dr. Hyrich found that among 11,598 RA patients who were treated with anti-TNFs and had no prior nonmelanoma skin cancer, the incidence of a malignancy was 3.5 per 1,000 patient-years. In contrast, among 8,975 similar patients who were treated with nonbiologic therapies, the incidence of new nonmelanoma skin cancers was 2.4.

That was a 70% increased risk for the anti-TNF–treated patients, although the data were not significant, Dr. Hyrich reported.

Dr. Hyrich pointed out that patients treated with anti-TNF drugs typically have more contact with their physicians, which could have introduced a surveillance bias.

Dr. Ranganathan cautioned that even in patients with multiple skin cancer risks anti-TNFs are still a good choice for patients who've failed other treatments. "People with risk factors should be watched more closely and maybe have periodic skin exams," she said.

Dr. Ranganathan, Dr. Hyrich, and their respective research teams did not report having any financial conflicts relative to their studies. ■

Oral Ivermectin Proves Superior to Insecticide for Treating Head Lice

BY BRUCE JANCIN

BERLIN — Oral ivermectin proved superior to conventional therapy with malathion lotion for the treatment of difficult to eradicate head lice infestations in a large multinational randomized trial.

The number needed to treat—that is, the number of patients who needed to be treated with two doses of oral ivermectin 1 week apart instead of two applications of topical malathion in order for one additional patient to become louse-free—was 9.8, Dr. Olivier Chosidow reported at the annual congress of the European Academy of Dermatology and Venereology.

"Our randomized trial suggests strongly that ivermectin could be valuable, at least in patients who've previously failed standard therapy because their head lice aren't sensitive enough to local insecticides," said Dr. Chosidow of the University of Paris.

He reported on 812 patients with head lice infestation in 376 randomized households. All participants were at least 2 years old and weighed at least 15 kg. At enrollment, all had live head lice detected by combing which had not been eradicated by topical insecticide therapy 2-6 weeks earlier. The households were randomized to double-blind/double-placebo supervised treatment with two single doses of oral ivermectin (Stromectol, Mectizan) at 400 mcg/kg or 0.5% malathion lotion, both administered on days 1 and 8.

The primary study end point was the absence of head lice upon inspection by combing on day 15. The success rate was 95% in the ivermectin group, compared with 85% in the malathion group. The secondary end points were the absence of head lice on days 2, 8, 22, and 29. The ivermectin group fared significantly better at each time point.

Generally mild treatment-related adverse events were noted in 7.5% of the ivermectin group and 10.9% who received malathion. There were no serious adverse events. It is well-established that ivermectin does not cross the human blood/brain barrier, according to Dr. Chosidow. Families appreciated the convenience of oral therapy.

'Ivermectin could be valuable, at least in patients who've previously failed standard therapy.'

DR. CHOSIDOW

Oral ivermectin is not approved by the Food and Drug Administration for the treatment of pediculosis. However, the Centers for Disease Control and Prevention guidelines recommend it for the treatment of scabies as an alternative to first-line topical 5% permethrin.

Dr. Erwin Tschachler, EADV secretary-general elect, singled out Dr. Chosidow's study as one of the infectious disease highlights of the congress.

"This is the first time an oral therapy for this parasitic infestation has been successful," commented Dr. Tschacler, head of the research division for biology and pathobiology of the skin at the University of Vienna Medical School.

Although head lice are associated with low socioeconomic status, no socioeconomic stratum is immune to infestation, and outbreaks are a growing problem in many European countries, he added.

Dr. Chosidow received a research grant from Johnson & Johnson, which sponsored the ivermectin study. ■