Tiotropium Backed for COPD Exacerbation

BY ELIZABETH MECHCATIE

SILVER SPRING, MD. — A Food and Drug Administration advisory panel voted 11-1 that evidence from two studies provided enough evidence to support approval of a claim that treatment with the inhaled, dry-powder formulation of tiotropium reduces exacerbations in patients with chronic obstructive pulmonary disease.

At the meeting, 11 of the 12 members of the FDA's Pulmonary-Allergy Drugs Advisory Committee also voted that data from one of those studies, the Understanding Potential Long-Term Impacts on Function with Tiotropium (UPLIFT) trial, "adequately addressed" the potential safety signals of an increased risk of stroke and adverse cardiovascular outcomes associated with this product that have been recently identified in pooled data and meta-analyses of tiotropium studies.

The dry-powder formulation of tiotropium is marketed as the Spiriva HandiHaler by Boehringer Ingelheim and Pfizer. It was approved in the United States in January 2004 for the long-term maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. It is administered once daily; each inhalation contains a dose of 18 mcg of tiotropium, an anticholinergic.

The companies proposed that Spiriva be approved for reductions in COPD exacerbations based on the UPLIFT trial and the Veterans Affairs (VA) Exacerbations Trial. In the 6-month VA study, there were approximately 1,800 patients with COPD, most of whom were men and whose mean age was 68 years. The

Roflumilast Shows Promise For COPD

SAN DIEGO — Roflumilast improved lung function and prevented exacerbations in patients with chronic obstructive pulmonary disease with chronic bronchitis and severe airflow obstruction in a large 12-month randomized trial.

Results of the 1,568-patient, double-blind, placebo-controlled study known as the M2-125 trial indicate roflumilast is an important potential new advance in the treatment of a subset of patients with COPD, Dr. Andrew McIvor declared at the annual meeting of the American College of Chest Physicians.

Roflumilast (Daxas) is an investigational selective phosphodiesterase 4 inhibitor, a drug class that represents a novel approach to the treatment of COPD. Taken orally once daily, roflumilast targets the inflammation that's a hallmark of the disease, explained Dr. McIvor of St. Joseph's Healthcare Hamilton, Ont.

Participants in the eight-nation M2-125 trial had to have at least one documented moderate or severe COPD exacerbation during the year prior to enrollment. They were randomized to roflumilast 500 mcg once daily or placebo for 1 year, on top of background long-acting $beta_2$-agonist or short-acting anticholinergic therapy at stable doses, along with short-acting $beta_2$-agonists as needed. Long-acting anticholinergics and inhaled corticosteroids were not permitted.

The rate of moderate to severe COPD exacerbations requiring systemic steroids and/or treatment in a hospital was 1.21 cases per patient per year in the roflumilast group and 1.49 in controls, for a highly significant 18.5% relative risk reduction. Roflumilast showed a highly significant advantage, with a 33-mL increase in forced expiratory volume in 1 second (FEV_1) as compared to a 25-mL decrease with placebo over 12 months.

All-cause mortality was 3% per year in each group. Adverse events were mild in nature. The two that were more frequent in the roflumilast arm were diarrhea and weight loss, affecting 9% and 8% of patients, respectively. Nearly one-third of subjects in each treatment group withdrew from the study. The study was sponsored by Nycomed, formerly Altana Pharma, where Dr. McIvor is a consultant.

—Bruce Jancin