Roflumilast Cut Exacerbation Rate in COPD

BY BRUCE JANCIN

SAN DIEGO — Roflumilast improved lung function and prevented exacerbations in patients with COPD 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 that roflumilast is an important potential advance in the treatment of a subset of patients with chronic obstructive pulmonary disease, Dr. Andrew McIvor said 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—one of two co-primary study end points—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.

The other primary end point was improvement in lung function as reflected in mean change from baseline in forced expiratory volume in 1 second (FEV_1) prior to administration of a bronchodilator.

Again, roflumilast showed a highly significant advantage, with a 33-mL increase in FEV_1 as compared to a 25-mL decrease with placebo over the course of 12 months.

The change over time in postbronchodilator FEV_1—a secondary end point—consisted of a 44-mL increase with roflumilast as compared to a 17 mL decrease with placebo, also a significant difference.

The other prespecified secondary end point was time to death from any cause, which was similar in the two study arms at 201 days for roflumilast and 215 days for placebo. All-cause mortality was 3% per year in each group.

Adverse events were mostly 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 the subjects in each treatment group withdrew from the study during the course of the year.

COPD is a highly prevalent disease with a broad spectrum of manifestations. In addition to the sort of patients who were enrolled in M2-125, the other subset of COPD patients in which roflumilast has shown compelling efficacy in large clinical trials is those with moderate to severe COPD who are on long-acting bronchodilators, according to Dr. McIvor.

The M2-125 study was sponsored by Nycomed, formerly Altana Pharma. Dr. McIvor is a consultant to the company. ■

Vocal Cord Dysfunction Apes Asthma

BY DOUG BRUNK

SAN DIEGO — About one-third of patients referred to an asthma specialty clinic who were believed to have difficult to control asthma actually had vocal cord dysfunction, results from a single-center study showed.

"If patients have been on many different medicines—they've been on oral or inhaled steroids and they're not responding—it's worth checking to see if they actually have asthma or not," study coauthor Catherine Vitari, R.N., said in an interview during a poster session at an international conference of the American Thoracic Society.

In a study led by her associate, Dr. Sally E. Wenzel, a pulmonologist and the director of the Asthma Institute at the University of Pittsburgh Medical Center,

Of 119 patients, 33% didn't have asthma. 'We didn't expect to see this. That's a pretty high percentage of people referred for asthma who didn't actually have asthma.'

the researchers reviewed the charts of 152 new patients evaluated at the institute between December 2006 and September 2008 in an effort to verify the diagnosis of severe asthma.

Of the 152 patients, 119 (78%) had a presenting diagnosis of asthma while 33 had another diagnosis such as dyspnea, cough, and emphysema.

Ms. Vitari, a clinical research nurse at the Asthma Institute, reported that 40 of the 119 patients who presented with an asthma diagnosis underwent methacholine challenges with laryngoscopy because their history and physical suggested asthma may not be the primary diagnosis. Of these 40 patients, 39 had a negative test, which precluded the diagnosis of asthma in 33% of the 119 patients. "We didn't expect to see this," she commented. "That's a pretty high percentage of people referred for asthma who didn't actually have asthma."

Dr. Wenzel performs a laryngoscopy at the time of the methacholine challenge "to see if the vocal cords are closing or spasming, indicating vocal cord dysfunction, or if it's truly asthma," Ms. Vitari explained. "If you send the patient to ENT instead to do a laryngoscopy and they don't see anything, it could be that the vocal cord dysfunction isn't acting up at that time since the spasms can be episodic and/or related to triggering events or stimuli."

She acknowledged certain limitations of the study, including its single-center design and the fact that only one physician did the assessments. The researchers had no conflicts to disclose. ■