"This observation indicates that a ceiling effect on exercise duration may occur on leg deconditioning that can impact the potential improvements observed through improved lung mechanics," Dr. Magnussen noted.

Comorbidity Burden in Clinical Trials Versus Clinical Practice

Epidemiological studies have documented a high prevalence of comorbid conditions among patients who have chronic obstructive pulmonary disease (COPD), including hypertension, ischemic heart disease, hypercholesterolemia, diabetes, and anxiety and depression (Barr RG et al. *Am J Med* 2009; Carrasco-Garrido P et al. *BMC Pulm Med* 2009; Finkelstein J et al. *Int J COPD* 2009). The epidemiological data underscore the need to know whether clinical trial results have come from studies that adequately represent the comorbidities of COPD patients.

To examine comorbidities in clinical trials of tiotropium, Marc Miravitlles, MD, Ciber de Enfermedades Respiratorias, Barcelona, Spain, and colleagues analyzed data from 26 placebo-controlled clinical trials that were at least 4 weeks in duration. Baseline evaluation included documentation of patients' concomitant diseases and relevant medical history of the previous 5 years.

The analysis comprised 17,014 patients with COPD whose mean age was 64.6 years. The data showed that 76% of the patients were men, 84.4% was Caucasian, and baseline mean forced expiratory volume in one second (FEV_1) was 41% of predicted.

Information on baseline comorbid conditions was available for 15,375 patients. Overall, 90.4% of the patients had concomitant diseases at baseline.

The most frequently cited categories of comorbid conditions were vascular disorders (44.0%), musculoskeletal and connective tissue disorders (35.2%), gastrointestinal disorders (32.6%), metabolism and nutrition disorders (28.8%), dyslipidemia (16.7%), diabetes (9.8%), and anxiety or depression (13.7%).

Because COPD and cardiovascular conditions frequently occur together, the investigators analyzed the data for specific references to individual disorders within the broader category of cardiovascular disease. They found that 38.7% of patients had hypertension, 15.6% had conditions that were suggestive of ischemic heart disease, and 16.7% had hypercholesterolemia or hyperlipidemia.

With the exception of lipid and cholesterol abnormalities, the comorbidities of patients in the tiotropium clinical trials had prevalences that were similar to those of previous epidemiological studies, investigators concluded. Epidemiological data have generally shown higher rates of hypercholesterolemia or hyperlipidemia among patients with COPD.

Effects of COPD Therapies on Lung Function Parameters

A year of treatment with tiotropium significantly improved blood gas parameters in hypoxemic patients with severe chronic obstructive pulmonary disease (COPD), as compared with inhaled corticosteroids plus a long-acting beta-agonist (LABA), reported Maria-Christina L. Machado, MD, Federal University, Sao Paulo, Brazil.

Partial arterial oxygen pressure (PaO_2) increased significantly ($p<0.001$) from baseline and partial carbon dioxide pressure ($PaCO_2$) decreased significantly ($p<0.01$) during treatment with tiotropium versus the standard therapy. Additionally, forced expiratory volume in one second (FEV_1) increased significantly ($p<0.001$) with the bronchodilator compared with inhaled steroids plus LABA.

"These results confirm that tiotropium usage has a significant impact on lung function variables, including arterial blood gas levels in hypoxemic stable outpatients with COPD under long-term oxygen therapy," said Dr. Machado.

Despite the proven benefits of tiotropium on lung function in COPD patients, the agent's impact on spirometric and arterial blood gas parameters remained uncertain in hypoxemic and severe COPD, according to Dr. Machado. In an effort to resolve the uncertainty, she and her colleagues evaluated outcomes in 67 consecutive patients with severe COPD and a requirement for long-term oxygen therapy. Each patient successively completed 12 months of treatment with each of two therapies: Treatment 1: inhaled steroids plus LABA; Treatment 2: inhaled corticosteroids + LABA and tiotropium. The primary objective was to compare the relative effects of the two therapeutic strategies on three parameters of lung function: PaO_2, $PaCO_2$, and FEV_1.

Analysis of baseline characteristics showed that the patients had a mean PaO_2 of 49.9 mm Hg, mean $PaCO_2$ of 47.9 mm Hg, and mean FEV_1 of 34% of predicted. After 12 months of treatment with inhaled corticosteroids and