Real-World Treatment of COPD Mirrors Clinical Trial Experience

Patients with chronic obstructive pulmonary disease (COPD) who were managed in primary care settings achieved improvements in physical functioning that were similar to those that were observed in clinical trials of combination therapy with tiotropium+salmeterol.

The findings extend the clinical trial results in a carefully controlled treatment environment to an unselected patient population in a real-life clinical setting, according to a report by Thomas Glaab, MD, and Heike Rau-Berger, Boehringer Ingelheim Pharma, Frankfurt, Germany.

To compare the clinical trial and clinical practice experience, 230 office-based pulmonologists in Germany enrolled 1280 patients with COPD who required treatment with a long-acting bronchodilator. Patients initiated treatment with tiotropium at a dose of 5 µg daily (two 2.5 µg puffs) and returned for a follow-up evaluation after 6 weeks.

At baseline and Week 6, physical function was assessed by the 10-item Physical Function (PF-10) Subdomain of the Short Form-36 health status questionnaire. Possible total scores on the assessment ranged from 0 to 100. The primary endpoint of the study was therapeutic success at Week 6, defined as a 10-point increase in the PF-10, validated as the minimally important difference for the PF-10.

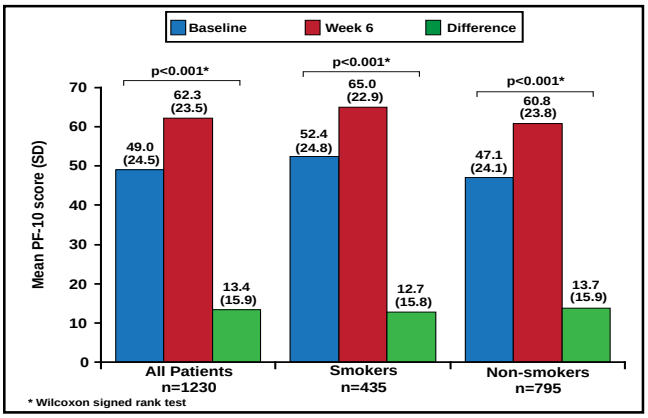
Principal secondary outcomes were absolute change in PF-10 score, change in Physician's Global Evaluation (PGE) from baseline to Week 6, and patient satisfaction with treatment, assessed by means of a 7-point scale with a range of "very satisfied" to "very dissatisfied." Investigators also analyzed the results according to patient smoking status.

Men accounted for about 60% of the total patient population, 35% of whom were current smokers and 48% former smokers. Current smokers averaged 39 pack-years, and ex-smokers had a cumulative exposure of 33 pack-years.

The study population had a mean PF-10 score of 49 at baseline. After 6 weeks of treatment, 61.5% of patients achieved therapeutic success. The rate did not differ between current/former smokers (61.4%) and nonsmokers (61.6%).

The absolute change in PF-10 scores averaged 13.4, representing a statistically significant improvement from baseline ($p<0.001$; Figure 1). The change in PF-10 averaged 12.7 among smokers ($p<0.001$) and 13.7 among nonsmokers ($p<0.001$; Figure 1). The mean absolute change did not differ significantly between smokers and nonsmokers.

Figure 1. Absolute Change in PF-10 Scores.



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PGE scores reflected a change in patients' general condition during the 6-week treatment period. The proportion of patients who were rated as poor (score of 1 or 2) declined from 16.2% to 3.0%, and the proportion that was rated as good increased from 23% to 54.6%.

With regard to patient satisfaction, 76.9% was satisfied or very satisfied with the inhalation device.

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Adverse events were reported by 4% of patients, and 0.5% of patients had serious adverse events. Adverse events led to discontinuation in 2.8% of patients. No patients died during the study.

Prostacyclin Analog Shows Chemoprevention Potential

Treatment with an oral prostacyclin analog improved endobronchial dysplasia in former smokers in a randomized pilot study of lung cancer chemoprevention, presented by Robert Keith, MD, Denver VA Medical Center and the University of Colorado, Denver, CO.

All measures of dysplasia (airway damage) improved in patients who were treated with iloprost, whereas the same parameters worsened in patients who were randomized to placebo. Consistent with results from previous studies, only former smokers benefited from treatment, suggesting that smoking cessation is a necessary component of chemoprevention.

Clinical and preclinical evidence has suggested that regulation of prostaglandin production (PGI_2 and PGE_2) plays a major role in the risk, evolution, and progression of lung cancer. For example, manipulation of prostacyclin synthase (PGI) has been shown to prevent tumor formation in mouse models of lung cancer (Keith et al. *Cancer Res* 2002; Keith et al. *Cancer Res* 2004).

To test the chemopreventive potential of iloprost, investigators enrolled 152 current and former smokers with a smoking history of at least 20 pack years, no history of cancer, and sputum cytologic atypia. Study participants were randomized to placebo or to oral iloprost (not available in the United States) at a starting dose of 50 µg BID, increasing to a maximum dose of 150 µg BID.

Participants underwent bronchoscopy at baseline and after 6 months of treatment. The primary endpoint was the change from baseline in total dysplasia score at 6 months, based on bronchial biopsy samples that were obtained from six prespecified sites. The dysplasia score was derived from the 8-point World Health Organization classification system for preneoplasia (ranging from normal=1 to invasive cancer=8). Investigators employed three separate histological measures: average histology over all biopsies, worst histology, and dysplasia index, determined by the percentage of biopsies with dysplasia score ≥4 (moderate dysplasia).

The study population comprised 81 current smokers and 71 former smokers. At the 6-month evaluation, all three histological parameters favored iloprost in former smokers. On average, the worst-histology score in the iloprost group decreased from 4.25 at baseline to 3.85 at 6 months, whereas worst histology increased from 3.91 to 4.14 in the placebo group (p=0.038). In addition, twice as many participants in the iloprost group had at least a 1-point improvement in worst histology (40% vs 20%; p=0.014).

Each of the three measures of the primary outcome declined in former smokers who were randomized to iloprost but increased among former smokers in the placebo group. Between-group differences for all three parameters achieved statistical significance (p=0.010 to p=0.002). In contrast, none of the outcome measures differed significantly between current smokers who were treated with iloprost or placebo.

Investigators have begun planning another chemoprevention trial that will be limited to former smokers and will have lung cancer incidence as the primary outcome.

Assessing Young Children's Ability to Use a Novel Propellant-Free Inhaler

With parental assistance and use of a spacer, young children can correctly use a novel propellant-free metered-dose inhaler to treat respiratory conditions, German investigators reported.

Only one of 99 children aged younger than 5 years did not use the Respimat® Soft Mist™ inhaler correctly. Technical failure occurred as a result of the child's refusal to cooperate rather than an inability to use the inhaler, Wolfgang Kamin, MD, Children's Hospital, Hamm, Germany, and colleagues reported.

The Respimat® Soft Mist™ is a handheld, multidose, propellant-free inhalation device that generates a slow-moving cloud that contains a high, fine-particle medication dose. Because spray generation is independent of inspiratory flow, the device might afford opportunities to treat young children with respiratory disorders.

To assess the ability of young children to use the novel inhalation device, investigators at two centers in Germany recruited 99 pediatric patients with a variety of respiratory disorders. The children were grouped by age (<1, 1 to <2, 2 to <3, 3 to <4, and 4 to <5 years) and their inhaler usage skills were evaluated by direct observation of the investigators.

Dr. Kamin reported that all but one child aged younger than 3 years were able to use the Respimat® Soft Mist™