Nebulized Levalbuterol in Elderly Patients with Asthma


In an exploratory analysis of data collected on the management of elderly Medicaid patients with clinical asthma, treatment with nebulized levalbuterol (Xopenex®, Sepracor, Inc.) resulted in a substantial cost savings when compared with the standard use of racemic albuterol sulfate (AccuNeb®, Dey; Ventolin®, GlaxoSmithKline).

From 2001 through 2002, the Medstat Market Scan Medicaid Database was used to identify Medicaid patients with a first prescription for levalbuterol or racemic albuterol. Health care utilization costs, such as doctors’ and emergency department visits, and associated costs were compared across six month pre-index and six-month post-index periods for 913 patients taking nebulized levalbuterol and for 22,566 patients treated with racemic albuterol.

According to this analysis, more than twice as many patients treated with racemic albuterol needed emergency department care during the post-index period than in the pre-index period, compared with the patients receiving levalbuterol. The fewer emergency department visits in the levalbuterol group accounted for a median cost savings of $1,145 per patient. Overall, considering all aspects of the differences in cost by treatment, the levalbuterol patients spent less money than the patients receiving racemic albuterol.

Add-on Omalizumab in Asthma Exacerbations

Speaker: Sally E. Wenzel, MD, Professor and Co-Director, Clinical Research Unit, Medicine, National Jewish Medical and Research Center, and Professor of Medicine, Division of Pulmonary Sciences and Critical Care Medicine, University of Colorado Health Science Center, Denver, Colorado.

Add-on therapy with omalizumab (Xolair®, Genentech, Novartis), the first humanized therapeutic monoclonal antibody for the treatment of asthma that was approved to target the antibody immunoglobulin E (IgE), significantly reduced the exacerbation rate annually by 37% in patients needing oral corticosteroids. This decrease was similar to the 37% reduction in exacerbations in the patients who did not require oral corticosteroids; however, the reduction reported in the patients needing oral corticosteroids was greater in absolute terms because of the higher exacerbation rates seen in these patients, indicative of their more severe disease.
**Budesonide/Formoterol in Asthma**  
**Speaker:** Anthony D. P'Urzo, MD, MSc, Family Physician and Director, Primary Care Asthma Clinic, and Lecturer, Department of Family and Community Medicine, University of Toronto, Toronto, Ontario, Canada.

The combination of AstraZeneca’s budesonide (Pulmicort®) and formoterol (Oxis® [BUD/FORM]) (Symbicort®, Single Inhaler Therapy™, AstraZeneca, Canada), administered for both maintenance and relief in patients with asthma, reduced the exacerbation burden, compared with salmeterol plus fluticasone propionate (SAL/FLU) (Advair® Diskus, GlaxoSmithKline) in a real-life setting.

Because the burden of asthma is most apparent during an exacerbation, researchers assessed the number of exacerbations, unscheduled visits leading to a treatment change, oral steroid days, and emergency visits or hospital days to compare BUD/FORM for maintenance or as needed (p.r.n.) or SAL/FLU twice daily plus salbutamol (i.e., albuterol), as needed, over a 12-month period. This randomized, open-label study included 2,143 adolescents and adults with asthma, with a 73% predicted mean forced expiratory volume/second (FEV1) and mean inhaled corticosteroids 884 mcg/day.

Patients were given a starting dose of BUD/FORM 160/45 mcg two inhalations twice daily and as needed or SAL/FLU 50/250 mcg twice a day plus salbutamol as needed. From the fourth week, maintenance treatment was titrated for both groups in accordance with the instructions of the attending physicians.

A total of 1,076 patients were randomly enrolled in the SAL/FLU group, and 921 patients completed the study; 1,067 patients were randomly assigned to receive BUD/FORM, and 945 patients completed the study.

Patients receiving BUD/FORM experienced fewer exacerbations (0.25 events per patient) than the SAL/FLU patients (0.31 events per patient). The BUD/FORM patients made 117 unscheduled visits that led to a treatment change, and the SAL/FLU patients made 154 unscheduled visits that led to a treatment change, for a 24% reduction favoring BUD/FORM usage. The BUD/FORM patients took oral steroids for 1,980 days, and the SAL/FLU patients took them for 2,978 days, resulting in a 34% reduction in usage favoring BUD/FORM.

Patients taking BUD/FORM made 38 emergency visits and spent 59 days in the hospital, and the SAL/FLU patients made 45 emergency visits and spent 94 days in the hospital, thereby resulting in a reduction of 16% for emergency visits and a 37% decrease in hospital length of stay with BUD/FORM.

**Tiotropium Bromide in Chronic Obstructive Pulmonary Disease**  
**Speaker:** Andre-Bernard Tonnell, MD, Pulmonologist and Professor of Medicine, Service de Pneumo-Immuno-Allergologie, Centre Hospitalier, Universite de Lille, Lille, France.

Long-term maintenance with tiotropium bromide inhalation powder (Spiriva®, HandiHaler®, Boehringer Ingelheim/Pfizer) provided significant improvements in health-related quality-of-life (HRQOL) measures in patients with chronic obstructive pulmonary disease (COPD).

A randomized, double-blind, placebo-controlled study was designed to assess the effects of tiotropium, a once-daily anticholinergic agent with prolonged M1 receptor antagonism, on HRQOL in patients with COPD. A total of 554 COPD patients were enrolled in the study and were randomly assigned to take tiotropium or placebo once daily for nine months.

The primary endpoint was the response rate, as determined by the percentage of patients showing more than four points of improvement at the end of the study. The Saint George’s Respiratory Questionnaire was used to measure the endpoint. This tool consisted of three components (social, physical, and psychological). Responses were rated on a scale of 0 to 100, with 100 being the worst possible state.

HRQOL was also evaluated by the newer, simplified eight-item Visual Simplified Respiratory Questionnaire and by parameters of lung function, including forced expiratory volume in one second (FEV1), forced vital capacity (FVC), inspiratory capacity (IC), slow vital capacity (SVC), and forced inspiratory volume in one second (FIV1), measured throughout the treatment period.

At nine months of follow-up, the primary endpoints of a four-point increase in the Saint George Questionnaire were reached by 59.1% of patients taking tiotropium and by 48.2% of patients taking placebo. Patients who were using tiotropium also had higher mean Visual Questionnaire scores.

Patients receiving tiotropium experienced significant improvements in lung function compared to placebo-treated patients, as shown in all measures of lung function assessed. This effect was comparable in all of the tiotropium patients whether or not they received inhaled corticosteroids and irrespective of their disease severity or reversibility status at entry into the study.

**Inhaled Iloprost in Class IV Pulmonary Hypertension**  
**Speaker:** Horst Olschewski, MD, Professor and Chair, Division of Pulmonary Medicine, Medical University Clinic, Medical University, Graz, Austria.

In a subset analysis of patients with New York Heart Association (NYHA) class IV pulmonary hypertension (PH), treatment with iloprost (Ventavis®, CoTherix, Inc.), a prostacyclin that offers a noninvasive inhaled dosing approach, resulted in a significant improvement in the clinically relevant measures of efficacy.

Initially, a large, placebo-controlled, randomized phase 3 trial enrolled 203 adult patients with NYHA class III and IV PH. These patients were randomly assigned to treatment with inhaled iloprost 2.5 or 5 mcg, given six to nine times a day, or placebo, for 12 weeks. Each primary clinical endpoint—a composite of an improvement in NYHA functional class, an increase in the distance walked in six minutes of at least 10%, and no clinical deterioration or death—was achieved in the treated patients versus those taking placebo.

The subgroup analysis included 83 patients with NYHA class IV PH, prospectively categorized by idiopathic pulmonary arterial hypertension (PAH), associated PAH, and chronic thromboembolic PH (CTPH) who participated in the phase 3 clinical trial. Thirty-eight of those individuals had primary PH...
These responses were maintained throughout follow-up. During a median follow-up period of 8.4 months (range, 4–18 months), the patients achieved significant improvements in gas exchange, dyspnea scores, and the six-minute walking test. Variables were measured at the start of IFN therapy and after 12 months of therapy in the treated patients and at baseline and 12 months later in the control group. Changes consisting of either a decline or an improvement at 12 months were determined as a percentage from baseline measures.

Sixty-two patients were identified; 29 received IFN, and 33 did not. Those receiving IFN tended to be older and had higher spirometry scores and longer distances in the six-minute walking test. In the untreated patients, variables declined significantly from baseline values: FVC decreased by 18.3%; FEV₁, by 19.3%; DLCO, by 7.6%; and distance walked, by 38.1%. In contrast, after 12 months of therapy, patients in the IFN group showed stable spirometry values: FVC improved by 3.5%, FEV₁ improved by 2%, and DLCO improved significantly, by 19.2%. Walking distances also increased significantly—by 37.3%.

Palivizumab for Prophylaxis of Respiratory Syncytial Virus Disease

Speaker: Alan H. Cohen, MD, Senior Director of Medical Affairs, MedImmune, Inc., Gaithersburg, Maryland.

Palivizumab (Synagis®, MedImmune), a humanized monoclonal antibody marketed for the prevention of respiratory syncytial virus (RSV) disease in high-risk children, appeared to be safe and effective in children younger than two years of age with cystic fibrosis (CF).

Because little information is available on the effects of RSV prophylaxis in young children with CF, a study was designed to evaluate the safety of the drug and the short-term outcomes and severity of RSV in the U.S. A total of 186 children were enrolled in a randomized, double-blind, placebo-controlled study that was conducted over three RSV seasons, beginning in November 1998. The children were randomly assigned to receive either palivizumab 15 mg/kg intramuscularly or placebo, administered monthly over one RSV season for five months. They were observed for 150 days to determine safety endpoints and for 360 days to determine additional clinical outcomes.

Overall, 97% of patients in each study group completed the study; 96% of the children in each group received all five monthly doses. The monthly administration of palivizumab had an acceptable safety profile, and the drug was well tolerated. The overall incidence of adverse drug events (ADEs) and serious ADEs was similar in the children who received active prophylaxis and in those who received placebo. No serious ADEs related to palivizumab were reported, and no children died during the study.

Clinically, patients receiving palivizumab had fewer positive RSV antigen results, including during outpatient testing,
with only 13% of those receiving the active drug versus 23% of those receiving placebo. No clinically meaningful differences were seen between the groups for multiple outcomes at follow-up.

Rimonabant in Maintenance of Smoking Cessation

Speaker: Raymond Nicura, PhD, Professor and Director of Research, The Center for Behavioral and Preventive Medicine, Brown Medical School and Butler Hospital, Providence, Rhode Island.

Patients who successfully stopped smoking cigarettes while taking rimonabant (Acomplia®, Sanofi-Aventis) experienced a decreased incidence of weight gain, a recognized barrier to successful abstinence from smoking. In a large-scale clinical trial, continued long-term therapy with rimonabant proved to be an effective, well-tolerated aid for maintaining smoking cessation and reducing post-cessation weight gain.

Initially, 5,055 cigarette smokers (those who smoked 10 or more cigarettes daily) who were motivated to quit smoking were enrolled in a multi-country, multicenter, double-blind, five-arm, placebo-controlled, two-year clinical trial. The patients were randomly assigned to take either rimonabant 5 or 10 mg each day.

At the 10th week, 1,661 successful quitters were randomly reassigned to receive either (1) rimonabant 5 mg/day (for those already receiving 5 mg in the initial clinical trial) or placebo, or (2) rimonabant 5 or 20 mg/day or placebo (for those already receiving 20 mg a day in the initial clinical trial).

Active treatment was continued for 42 weeks, followed by a 50-week off-drug period. The primary endpoint was the efficacy of rimonabant in enabling patients to abstain from cigarette smoking. Secondary endpoints included body weight, tobacco craving, quality of life, safety, and tolerability.

For the patients taking rimonabant 5 mg daily, no effect on maintenance was observed. The patients who were re-randomized to take placebo had relapse rates similar to those of patients receiving maintenance therapy with rimonabant 5 mg/day.

In contrast, at 52 weeks, a significant proportion of patients receiving rimonabant 5 mg or 20 mg daily during the maintenance period, who had initially received rimonabant 20 mg daily, continued to abstain from tobacco use; 41.8% of patients receiving 5 mg/day and 41.5% of those receiving 20 mg/day were able to maintain abstinence, compared with 32.1% of the placebo patients.

Rimonabant 20 mg/day significantly reduced post-cessation weight gain in those who achieved abstinence; however, weight gain after quitting cigarettes was similar for patients taking placebo and for those taking rimonabant 5 mg/day.

Fasting high-density lipoprotein-cholesterol concentrations were significantly increased with rimonabant 20 mg/day (by 9%) compared with placebo (by 0.8%).

Fasting triglyceride levels were significantly reduced with rimonabant 20 mg/day (by −0.18 mmol/L), compared with placebo (by 0.09 mmol/L).