

Results from a 1-year retrospective analysis have suggested that COPD patients treated with the anticholinergic, Spiriva[®], have a significantly slower decline in FEV₁ compared with placebo.

Spiriva[®] may slow decline in FEV₁, a measure of lung function in patients with chronic obstructive pulmonary disease

A 1-year retrospective study of patients with chronic obstructive pulmonary disease (COPD) who were treated with the anticholinergic, Spiriva[®], has demonstrated a significantly lower decline in forced expiratory volume in 1 second (FEV₁) compared with placebo, according to a publication by Anzueto, Tashkin, Menjoge and colleagues in a recent issue of *Pulmonary Pharmacology and Therapeutics* (18[2], 75–81 [2005]).

The study examined the rate of FEV₁ decline which is considered to be the most accurate predictor of disease progression and has been used in previous studies to assess the long-term impact of medications for the airway. However, never before has it been demonstrated that inhaled medications may reduce the loss of lung function in COPD patients.

Professor Anzueto, Department of Pulmonary/Critical Care, University of Texas Health Science Center (TX, USA) and principal author of the study commented, "These are interesting findings that support further investigation into the potential long-term benefits of Spiriva." He continued that, "The observations are particularly encouraging in advance of the

4-year UPLIFT [Understanding Potential Long-term Impacts on Function with Tiotropium] trial, currently in progress to prospectively evaluate Spiriva's ability to reduce lung function decline and disease progression in patients with COPD."

COPD is the fourth leading cause of death worldwide and is responsible for 2.75 million deaths annually

The study involved the analysis of two 1-year, randomized, placebo-controlled studies of inhaled tiotropium (18 µg once daily) in COPD patients with a mean age of 65 years and a smoking history of 60-pack-years. Results indicate that Spiriva may slow pre-dose FEV₁ decline and significantly improve pre-dose FEV₁ versus placebo. In addition, it was shown that the effect of the drug was independent of smoking status as in both smokers and ex-smokers, the rate of decline of pre-dose FEV₁ was lower with Spiriva than placebo.

According to a 2003 report by the World Health Organization (WHO), COPD is the fourth leading cause of death worldwide and is responsible for 2.75 million deaths annually. Further

studies are currently being carried out to confirm the results of the current study. The most significant of these, the UPLIFT trial, a 4-year, randomized, double-blind, placebo-controlled trial of 6000 COPD patients over 37 countries, aims to determine whether tiotropium reduces the rate of decline in lung function over time in COPD patients. Results are expected in 2008.

Spiriva is the first inhaled therapy for COPD to provide significant and sustained improvements in lung function through targeting cholinergic constriction, which helps to maintain the opening of narrowed airways over a 24 h period. The most commonly reported side effect associated with the use of Spiriva was dry mouth, which was generally mild.

Spiriva also demonstrated increased and more sustained improvements in FEV₁ compared with Atrovent[®], the current first-line inhaled aerosol therapy for the treatment of COPD. Treatment guidelines published by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) has suggested that long-acting bronchodilators such as tiotropium should be the preferred treatment option for COPD maintenance therapy.

Rimonabant shows positive results for weight loss and reduction of cardiovascular risk factors in overweight patients

Results of a trial carried out by researchers at the University Hospital Antwerp (Belgium) examining the effects of rimonabant use in combination with a hypocaloric diet over a period of 1 year have shown a significant decrease in body weight as well as an improvement in cardiovascular risk factors in overweight patients.

The drug, a selective CB1 endocannabinoid receptor antagonist, was administered to patients with a body mass index (BMI) greater than or equal to 30 kg/m² presenting with dyslipidemia, hypertension, or both, in conjunction with a hypocaloric diet. The study demonstrated that after 1 year, weight loss was greater in patients treated with 5 or 20 mg rimonabant compared with placebo. In addition, patients enrolled in the 20 mg group experienced greater improvements in waist circumference and cardiovascular risk factors including high-density lipoprotein (HDL) cholesterol, triglycerides, insulin resistance and prevalence of metabolic syndrome compared with placebo.

Reports of serious adverse events were no more frequent in patients receiving the drug when compared with placebo, and the most common side effects were depressed mood disorders.

Priority Paper Alerts

Efficacy of coenzyme Q10 in migraine prophylaxis: a randomized controlled trial.

Sandor PS, Di Clemente L, Coppola G *et al. Neurology* 64(4), 713–715 (2005).

This double-blind, randomized, placebo-controlled trial compared the effect of coenzyme Q10 (CoQ10) and placebo on migraine prophylaxis in 42 migraine patients and reported that CoQ10 was more effective than placebo for attack frequency, headache days and days with nausea in the third month of treatment. In addition, it was found that CoQ10 was efficacious and well tolerated, with a 50% responder rate for attack frequency of 14.4% for placebo and 47.6% for CoQ10.

Weight gain and new-onset diabetes associated with olanzapine and risperidone.

Farwell WR, Stump TE, Wang J, Tafesse E, L'Italien G, Tierney WM. *J. Gen. Intern. Med.* 19(12), 1200–1205 (2004).

This retrospective cohort study was carried out to examine whether there is any association between newer antipsychotic medications, weight gain and the development of diabetes. The trial assessed 3115 patients prescribed a single antipsychotic drug over a period of at least 1 year and the results examined for independent predictors of significant weight gain and new onset of diabetes mellitus in the first year of antipsychotic drug treatment. Results demonstrated that 25% of patients taking older phenothiazines had weight gain compared with 40% taking olanzapine and 37% taking risperidone. No association was found between significant weight gain and the development of diabetes. Results of the trial indicate that the use of olanzapine and risperidone was associated with weight gain in the first year, but only olanzapine was associated with the development of diabetes mellitus.

Blood-pressure control for renoprotection in patients with nondiabetic chronic renal disease (REIN-2): multicenter, randomized controlled trial.

Ruggenenti P, Perna A, Loriga G *et al. Lancet* 365(9463), 913–914 (2005).

This multicenter, randomized controlled trial of patients with nondiabetic proteinuric nephropathies receiving background treatment with ramipril sought to investigate the effect of intensified versus conventional blood-pressure control on progression to end-stage renal disease. Results showed that, in these patients, no additional benefit can be seen from further blood-pressure reduction using felodipine.

Pfizer suspend sales of painkilling drug, Bextra®

The US Food and Drug Administration (FDA) have announced that their request to Pfizer to suspend sales of its painkilling drug Bextra® have been adhered to, following suspicions of an associated link with cardiovascular complications. The FDA has also requested that the US government add its strictest warning to Celebrex®, also produced by Pfizer, and that other, milder painkillers such as aspirin and ibuprofen, should carry cautions highlighting the possible risks of associated cardiovascular and gastrointestinal complications.

The drug had previously been passed by a panel of doctors who concluded that the benefits of the drug were enough to justify its sale; however, it did carry a high warning highlighting a link between use of the drug and the development of a skin reaction known as Stevens–Johnson.

It was later decided by the FDA that this side effect, when combined with the associated cardiovascular risks, was enough to warrant the withdrawal of the drug, which generated US\$1.29 billion in sales for Pfizer in 2004. Despite the high revenue already obtained from the drug, Pfizer is positive that the move will have very little effect on company shares.

“It’s never good when a company has to pull a drug, but Bextra won’t have that much effect on profit”, commented Hanne Leth Hillman, who helps to manage stock in Copenhagen, and holds Pfizer shares. “I would have been a lot more worried if they pulled a drug like Lipitor.”

Pfizer have meanwhile said in a statement that it is opposed to the FDA’s decision and it will be holding talks in an attempt to return the drug to the market.

Biogen Idec psoriasis study reaches primary end point

Results of a Phase III study examining the efficacy and safety of Biogen Idec and Fumapharm AGs oral fumarate, for the treatment of moderate-to-severe psoriasis have been announced, with reports that the trial has now met the primary end point. Patients involved in the study who were administered with the drug, BG-12, are reported to have demonstrated a statistically significant clinical improvement after 16 weeks of treatment compared with patients receiving placebo, as measured by median psoriasis severity scores.

The results of the study were met with enthusiasm by Burt Adelman, Executive Vice President of Biogen

Idec, who commented on the company’s future plans for the drug “These data will be used to support a filing for market authorization in Germany this year.” He continued, “We will work with our partner, Fumapharm, to determine the next steps for the BG-12 program. Additional Phase III studies would need to be conducted for applications in the US and the rest of Europe.”

The most commonly reported adverse events from the study were flushing and diarrhea, with one patient being hospitalized for pneumonia and another for kidney stones. Results from the trial are expected to be presented at a forthcoming medical meeting.

Noven and Shire report positive preliminary results from ADHD treatment studies

Positive preliminary results from clinical trials of Shire Pharmaceuticals Group's methylphenidate transdermal system (MTS), which is under development with Noven Pharmaceuticals Inc. for the treatment of children with attention deficit hyperactivity disorder (ADHD), have been announced recently.

The results are from two studies, a Phase II and III, which examined the use of the MTS in children between the ages of 6 and 12 years who had been previously diagnosed with ADHD, and showed that the MTS was well tolerated in each group. Additional results from the trial are expected to be released by Shire in May 2005 as part of a R&D update.

Chief Executive Officer of Shire Matthew Emmens commented "These results demonstrate that MTS has the potential to provide significant benefits for children with ADHD, especially those that have difficulty taking oral medications and those that find a once-a-day patch more appropriate for their lifestyle. As the ADHD market develops, new choices of treatment are emerging, including specialized delivery systems (such as MTS) to meet the needs of different patients. Shire aims to have a range of medicines in its ADHD portfolio, with Adderall XR[®] being the most prescribed treatment for ADHD in the USA. If approved, this product will be a strong addition and we

Recently released preliminary results by Shire and Noven Pharmaceuticals of a methylphenidate transdermal system for the treatment of children with attention deficit hyperactivity disorder have shown promise in Phase II and III studies.

look forward to advancing its development further."

This statement was further strengthened by Robert Strauss, President, Chief Executive Officer and Chairman of Noven Inc., who commented "Today's news is an important step forward in the development of our methylphenidate patch. The next step is preparation of an amendment to the pending New Drug Application, and we expect to be working

closely with our partner Shire to achieve that goal."

Further comment was added by Robert Findling of Case Western Reserve University (OH, USA) and *Therapy* Editorial Board member who reported that "Methylphenidate has been shown to be an effective treatment, used orally, for children with ADHD for decades. Upon approval, MTS holds the promise of being a welcome additional treatment option for children with ADHD."

Rheumatoid arthritis indicated as an independent risk factor for heart failure

Findings from studies carried out by researchers at the Mayo Clinic (AZ, USA) investigating the possibility of a link between rheumatoid arthritis (RA) and the risk of congestive heart failure (CHF) have indicated RA as a risk factor, independent of established risk factors for heart attack and a history of atherosclerosis. The report, which was published in the February 2005 issue of *Arthritis & Rheumatism* has revealed that in a study of over 1100 subjects with RA over the age of 46 years, the chances of developing CHF are doubled.

Researchers from the Mayo Clinic examined the medical records of 575 patients with RA and 583 without, paying particular attention to a family history of hypertension, high cholesterol, diabetes and atherosclerotic heart disease, as well as collecting data on cigarette smoking status, body-mass index and other established risk factors for heart disease.

During a follow-up period of 15 years, 165 patients with RA and 115 without were diagnosed with CHF and, following adjustments for certain risk factors and other factors, it was concluded that RA patients were at twice the risk for CHF when compared with controls.

Paulo Nicola, researcher with the study group, commented on the importance of the findings by noting that "Physicians who care for patients with RA should be aware of the increased risk of CHF in these patients." "This increased risk may be present at the earliest stages of the disease and may occur in the absence of overt cardiovascular risk factors or heart disease. Further research should address characteristics that predict CHF incidence, severity and survival in these patients, as well as determine the role of RA therapy" she continued.

Proteins involved in the spread of cancer identified

A team of researchers at Tufts University have successfully identified several key proteins on the surface of cancer cells that play a key role in aiding the spread of these cells.

Furthermore, it was found that by destroying these proteins, the ability of the cells to invade healthy cells was greatly reduced. The discovery of these proteins could result in a potential new target for the development of anticancer drugs.

The results of the study were reported at the Experimental Biology meeting that took place recently in San Diego (CA, USA).