

Data from largest GOLD Stage II patient population treated with tiotropium highlight the benefits of earlier treatment of COPD

New UPLIFT[®] analysis shows tiotropium significantly improves lung function and quality of life in COPD patients with early stage disease

28 August 2009 – A new analysis of the landmark UPLIFT[®] trial, published today in the *Lancet*, shows that tiotropium (SPIRIVA[®] Handihaler[®] 18 µg) administered to Chronic Obstructive Pulmonary Disease (COPD) patients with moderate disease severity (GOLD – Global Initiative for Chronic Obstructive Lung Disease – Stage II) produced significant and sustained improvements in lung function for up to 4 years.¹ This pre-specified subgroup analysis involved 2,739 patients - the largest group of early stage COPD patients treated with a long-acting anticholinergic in a randomised, placebo-controlled study.

The new UPLIFT[®] analysis shows that in patients with GOLD Stage II COPD, tiotropium may slow the progression of COPD as measured by the rate of decline in lung function. Tiotropium reduced the rate of decline in postbronchodilator FEV₁^{*} over 4 years compared with control[†] (43 mL per year vs. 49 mL per year; p=0.024). The rate of decline in prebronchodilator FEV₁^{*} was similar between the groups.

Improvements in pre- and postbronchodilator FEV₁ were maintained vs. control throughout the trial (101-119 mL and 52-82 mL respectively; p<0.0001). GOLD Stage II patients taking tiotropium had an 18% lower risk for exacerbations and 20% fewer exacerbations (p<0.0001) compared with control. Health-related quality of life, as measured by the St. George's Respiratory Questionnaire (SGRQ), was better in patients treated with tiotropium than in control patients throughout the study (p≤0.006). There was also a trend for reduced mortality with tiotropium compared with control.¹

* FEV₁ = Forced expiratory volume in one second. Postbronchodilator FEV₁ was measured after giving the study drugs - tiotropium or placebo - and additional administration of short acting bronchodilators. Prebronchodilator FEV₁ was measured before administration of study drugs.

† All patients from both the tiotropium group and the control group were allowed to continue with their normally prescribed respiratory medication, including dose adjustment throughout the trial, except inhaled anticholinergics.

“These results are very important for clinical practice because this is the first large, long-term study to show that treatment with a long-acting anticholinergic has substantial benefits in patient in the early stages of COPD. UPLIFT has shown that a significant decline in lung function occurs early in the disease, and it is known that exacerbations accelerate disease progression. Therefore this new analysis confirms that we should treat COPD in the early stages with a medication such as tiotropium that can improve lung function and quality of life, and reduce exacerbations,” said Professor Marc Decramer, UPLIFT lead investigator, Professor of Medicine and Chief of the Respiratory Division at the Katholieke Universiteit Leuven, Belgium.

The social and economic burden of COPD increases steadily, with patients becoming less independent as the disease gets worse.² GOLD Stage II is typically when patients may start to realise their lung function is abnormal and experience breathlessness on exertion. As COPD progresses, lung function continues to decline and physical activity becomes severely limited, disrupting the patients’ and their caregivers’ ability to lead a full life, interfering with everyday tasks and participation in family routines.² This can lead to people feeling afraid, anxious, frustrated, isolated and depressed.^{2,3} It is therefore important to ensure that patients are diagnosed and treated as early as possible, including smoking cessation.

“The results from the UPLIFT analysis in GOLD Stage II patients are extremely heartening. They clearly demonstrate that if patients seek treatment from their primary care physicians earlier they may be able to impact the clinical course of their disease and improve their quality of life,” said Dr. Anders Østrem, Specialist in Family Medicine, Norway and Director, International Primary Care Respiratory Group.

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Notes to Editors

About COPD

COPD is a progressive yet treatable disease that restricts patients' lives over time and is a major cause of death and disability throughout the world. Symptoms include cough, sputum (mucus or phlegm) production, and breathlessness on exertion. Worsening of these symptoms often occurs and can restrict a patient's ability to perform normal daily activities.² The latest World Health Organization (WHO) figures estimate that 210 million people are currently living with COPD and more than 3 million people died from the disease in 2005⁴ - more than breast cancer and diabetes combined.⁵ Dyspnoea (breathlessness), the main symptom of COPD, is characteristically persistent and progressive and has a serious impact on patients' quality of life.² At its most severe, it even limits a patient from performing simple tasks such as washing and dressing.

About UPLIFT[®]

UPLIFT[®] (Understanding Potential Long-term Impacts on Function with Tiotropium) was a four-year, multicentre (470 sites), multinational (37 countries), randomised, double-blind, placebo-controlled, parallel-group trial which commenced in December 2002. The study included 5993 male and female COPD patients. Patients were randomised 1:1 to receive either 18 µg tiotropium or placebo once daily. In both arms, patients were allowed to take all other respiratory medications usually prescribed for the treatment of COPD, except for inhaled anticholinergics. Results of the UPLIFT[®] trial demonstrated that tiotropium produced sustained improvements in lung function for up to 4 years (p<0.001), although it did not alter the rate of decline in lung function.⁶

About tiotropium (SPIRIVA[®])

Tiotropium, a long-acting inhaled anticholinergic medication, is the first inhaled treatment to provide significant and sustained improvements in lung function with once-daily dosing. Tiotropium positively impacts the clinical course of COPD, helping to change the way patients live with their disease.^{7,8} It is the most prescribed medication for the treatment of COPD in the world.

Tiotropium works through targeting a dominant reversible mechanism of COPD – cholinergic bronchoconstriction. Tiotropium helps COPD patients breathe easier by opening narrowed airways and helping to keep them open for 24 hours.

Tiotropium has demonstrated significant and sustained bronchodilation (opening of the airways)⁹ and reduction in hyperinflation (air trapping).^{10,11} In placebo-controlled studies, patients treated with tiotropium had less activity-induced breathlessness and improved exercise endurance.⁷ They required fewer doses of rescue medications, had fewer exacerbations and COPD-related hospitalizations.⁹ In clinical trials, the most common adverse reaction reported with tiotropium was dry mouth, which was usually mild and often resolved spontaneously during treatment.⁹ Long-acting bronchodilators, including tiotropium, are a preferred maintenance therapy for COPD from stage II onwards according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) treatment guidelines.²

About Boehringer Ingelheim

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References

- ¹ Decramer M, Celli B, Kesten S, et al. Effect of tiotropium on outcomes in patients with moderate chronic obstructive pulmonary disease (UPLIFT): a prespecified subgroup analysis of a randomized controlled trial. *Lancet* Published Online August 28, 2009 DOI:10.1016/S0140-6736(09)61298-8.
- ² Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease. NHLBI/WHO workshop report. Bethesda, National Heart, Lung and Blood Institute, April 2001; Update of the Management Sections, GOLD website (<http://www.goldcopd.com>). Updated: 2008.
- ³ Maurer J, Rebbapragada B, Borsen S et al. Anxiety and Depression in COPD. *Chest* 2008;134:43S-56S
- ⁴ World Health Organisation. *Global Alliance Against Chronic Respiratory Diseases*. <http://www.who.int/mediacentre/factsheets/fs315/en/index.html>. (Accessed 17 July 2009).
- ⁵ World Health Organization. *World Health Report 2004*. Statistical Annex. Annex table 2 and 3: 120-131.
- ⁶ Tashkin DP, Celli B, Senn S, et al. A 4-year trial of tiotropium in chronic obstructive pulmonary disease. *N Engl J Med* 2008; **359**:1543-54.
- ⁷ Casaburi R, Kukafka D, Cooper CB et al. Improvement in exercise tolerance with the combination of tiotropium and pulmonary rehabilitation in patients with COPD. *Chest* 2005; **127**:809-817.
- ⁸ Vincken W, van Noord JA, Greefhorst APM et al. Improved health outcomes in patients with COPD during 1 year's treatment with tiotropium. *Eur Respir J* 2002; **19**:209-216.
- ⁹ Casaburi R, Mahler DA, Jones PW et al. A long-term evaluation of once-daily inhaled tiotropium in chronic obstructive pulmonary disease. *Eur Respir J* 2002; **1**:217-224.
- ¹⁰ Celli B, ZuWallack R, Wang S et al. Improvement in resting inspiratory capacity and hyperinflation with tiotropium in COPD patients with increased static lung volumes. *Chest* 2003; **124**:1743-1748.
- ¹¹ O'Donnell DE, Fluge T, Gerken F et al. Effects of tiotropium on lung hyperinflation, dyspnoea and exercise tolerance in COPD. *Eur Respir J*. 2004 **23**(6):832-48.