

Four studies published in *The Lancet* show roflumilast (Daxas™), a new oral approach to COPD, improves lung function and reduces exacerbations

- Once-a-day tablet roflumilast (Daxas™) is a treatment under development targeting inflammation, the underlying cause of chronic obstructive pulmonary disease (COPD)

Nycomed recently announced that results of four phase III trials have been published in the prestigious peer-reviewed medical journal, *The Lancet*, showing that roflumilast, a phosphodiesterase 4 (PDE4) inhibitor, improved lung function and reduced exacerbations in patients with moderate to severe COPD.

Oakville, Ontario, September 3, 2009 - COPD is an under-diagnosed progressive lung disease that may lead to death. In Canada, approximately 500,000 people over the age of 35 have been diagnosed with COPD, and it is estimated that an almost equal number of middle-aged Canadians may also have COPD, but are not aware of it.ⁱ In fact, by 2020, it is estimated that COPD will be the third leading cause of death worldwide.ⁱⁱ

Roflumilast, a once-a-day oral tablet, would be the first in a new class of treatment for COPD. The safety and efficacy are still under investigation and market authorization has not yet been obtained from Health Canada. The phase III placebo-controlled trials of roflumilast evaluated the treatment in two 12-month and two six-month studies, involving 4,500 patients in ten countries, including 367 patients in Canada. Details of the results of the four studies were just published in *The Lancet* this week.

“Roflumilast improves lung function on top of bronchodilation and over and above concurrent COPD treatments by acting on the underlying inflammation,” says Dr. Andrew McIvor, Professor of Medicine, McMaster University, Firestone Institute for Respiratory Health, St. Joseph's Healthcare. “Considering, the nature of the disease and its affect on people's lives, this presents a very exciting new option for those of us treating patients.”

About the studies

The two 12-month studies published in *The Lancet* demonstrated that roflumilast produced a statistically significant and clinically relevant reduction in exacerbations (lung attacks that need treatment with systemic steroids or lead to hospitalization), even for patients who were also taking long-acting bronchodilators. The studies showed a reduction in moderate to severe exacerbations by 17 percent per patient per year (rate of 1.14 events per year with roflumilast vs. 1.37 per year with placebo, $p < 0.001$). The reduction in exacerbations was irrespective of concomitant treatment with long-acting beta-2 agonists, a standard bronchodilator therapy.

When added to standard bronchodilator therapies in the two six-month studies, a clear trend for the reduction of exacerbations was observed with roflumilast, over and above what was achieved with these therapies alone. There was also a statistically significant difference with roflumilast in other prespecified endpoints, including median time to first exacerbation (moderate to severe in the salmeterol study, and mild, moderate and severe in the tiotropium study) and in the proportion of patients in both studies experiencing a mild, moderate, or severe exacerbation.

Lung function, as measured by FEV1 (how much volume can be exhaled in one second), was the primary or co-primary endpoint in all four studies. Across the studies, roflumilast demonstrated a statistically significant improvement in pre-bronchodilator FEV1, in the range of 48 to 80 mL (p<0.001).

Nausea, diarrhea and weight loss were the most common adverse events recorded in patients in the four trials, but they were generally mild to moderate in intensity and generally occurred in the first weeks of treatment.

About Roflumilast (Daxas™)

Roflumilast is an orally administered phosphodiesterase 4 (PDE4) enzyme inhibitor targeting cells and mediators in the body believed to be important in the COPD disease process. The safety and efficacy are still under investigation and market authorization has not yet been obtained by Health Canada. Current treatment for COPD patients includes the use of inhaled bronchodilators and inhaled corticosteroids.

About Nycomed Canada Inc.

Nycomed Canada Inc. is a Canadian company belonging to the Nycomed Group, a privately owned, global pharmaceutical company. Ranked by sales, the Nycomed Group is among the 30 largest pharmaceutical companies in the world. Nycomed Canada Inc. is based in Oakville, Ontario with more than 200 employees across the country. Through its innovative products and dedicated people, Nycomed Canada Inc. is committed to improving the health of Canadians by providing brand name, science-based medicines that matter. For more information, please visit www.nycomed.ca.

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ⁱ Ernst PP, Bourbeau J, Rainville B, Benayoun S, Suissa S. Underestimation of COPD as a cause of death. Eur Respir J 2000; 16 (Suppl. 31) :13s.

ⁱⁱ Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020; Global Burden of Disease Study. Lancet 1997; 349; 1498-504.