PRESS RELEASE

Landmark UPLIFT study reaffirms the safety of Spiriva (tiotropium) in patients with Chronic Obstructive Pulmonary Disease

Prof. dr. Marc Decramer, head of pneumology of the University Hospitals Leuven, is lead investigator of the international UPLIFT study investigating treatment of COPD patients with tiotropium.Today he elaborates on the results.

Placebo-controlled, randomized, double-blind clinical trials provide the most comprehensive and strongest evidence of a drug's safety profile. The long-term exposure of thousands of patients with COPD to tiotropium in the UPLIFT study, which has closely and rigorously evaluated both efficacy and safety, provides a reaffirmation of the tiotropium safety profile and strong evidence that tiotropium does not increase the risk of all-cause or cardiovascular mortality.

UPLIFT (Understanding Potential Long-term impacts on Function with Tiotropium) is a four-year landmark multinational, multi-center, randomized, double-blind clinical COPD study trial involving 5,993 patients from 37 countries across the globe. This ambitious study investigated the benefits of Spiriva versus placebo over four years in a real-life treatment approach, allowing for use of all respiratory medications throughout the trial, other than inhaled anticholinergics.

The data from UPLIFT indicate that tiotropium does not increase the risk of death, cardiovascular death, myocardial infarction and stroke. Furthermore, examination of all serious cardiac and all serious lower respiratory tract adverse events indicates that tiotropium is associated with a decreased risk of experiencing a serious adverse event in these organ classes.

In UPLIFT, there were 2,986 tiotropium treated patients and 3006 placebo treated patients, who contributed to 9,468 and 8,746 patient years exposure respectively. Safety was monitored closely through a standardized adverse reporting process. An independent data and safety monitoring committee reviewed data throughout the trial and an independent committee adjudicated primary cause of death.

There was no evidence of an increased risk of death during the study. During treatment, fatal events occurred in 381 patients (12.8%) in the tiotropium-treated group and 411 (13.7%) in the placebo group (a 16% risk reduction in the tiotropium group, hazard ratio 0.84; 95% CI, 0.73 to 0.97). An intent to treat analysis was performed by including vital status information (i.e. alive, dead, and the cause of death) on patients who prematurely discontinued the study (i.e. no longer taking study drug). During the protocol defined treatment period (until day 1440), the hazard ratio was 0.87; 95% CI 0.72, 0.99). The corresponding hazard ratio up until the 30 day follow-up period (day 1470) was 0.89 (0.79, 1.02.

A specific analysis was conducted for cardiovascular death. There was no evidence for an increased risk of cardiovascular death during treatment (risk ratio 0.73, 95% CI 0.56, 0.95). As myocardial infarction and stroke have been discussed, we have specifically examined the risk for these events. Myocardial infarction developed in 67 patients in the tiotropium group and 85 in the placebo group (relative risk, 0.73; 95% CI 0.53, 1.00), and stroke developed in 82 in the tiotropium group and 80 in the placebo group (relative risk, 0.95; 95% CI 0.70, 1.29).

For further support of the safety of tiotropium, we have examined serious adverse events under the organ classes of cardiac and lower respiratory disorders. For total serious cardiac adverse events, the relative risk for tiotropium compared to placebo was 0.84 (95% CI 0.73, 0.98). For total serious lower respiratory tract adverse events relative risk for tiotropium verses placebo was 0.84 (95% CI, 0.77, 0.92).

Full safety and efficacy data on the UPLIFT study will be presented at the upcoming Annual Meeting of the European Respiratory Society in Berlin on October 5, 2008.

Note to the Editor: The UPLIFT study was sponsored by Boehringer Ingelheim and Pfizer

---

For more information

prof. dr. Marc Decramer, head of pneumologie (University Hospitals Leuven)
Mobile: 0032 475 57 06 87

UZ Leuven | Herestraat 49 | B - 3000 Leuven | www.uzleuven.be

University Hospitals Leuven