IMPROVE QUALITY OF LIFE AND CONTROL OF ASTHMA WITH HIGH DOSE PULMICORT(r) AND OXIS(r)

New FACET data highlights additional benefits of two leading AstraZeneca compounds

Lund, Sweden, December 9 /PRNEWSWIRE/ - Using inhaled Oxis(r) (formoterol), a fast-acting and long-lasting bronchodilator, together with the inhaled corticosteroid Pulmicort(r) (budesonide), both delivered via Turbuhaler(r), provides a significant and sustained improvement in health-related quality of life (HRQoL), in addition to better clinical efficacy. These were the key findings from the FACET quality of life study, published in the current issue of the European Respiratory Journal1.

The FACET (Formoterol And Corticosteroid Establishing Therapy) study was a one-year long study of 852 patients with moderate to severe asthma, from nine countries who had persistent symptoms despite treatment with inhaled corticosteroids. The benefits in HRQoL from adding regular inhaled Oxis to a low and a high dose of the inhaled corticosteroid Pulmicort are in addition to the improvements seen in asthma exacerbation rates, symptoms and lung function, previously reported in the New England Journal of Medicine.2

"These new data are extremely important as they represent the first evidence to show long term health-related quality of life benefits in relation to modern asthma treatment," according to lead investigator Professor Elizabeth Juniper, McMaster University Medical Centre, Hamilton, Canada. "These are also the first data to show that improvements in health-related quality of life are sustained when asthma control remains stable," she adds.

"Previously, clinicians have wondered whether asthma interventions really produce a sustained improvement and have suggested that patients may go through a 'honeymoon' period: feeling better at the start of therapy and then relapsing. Now, through FACET, we have positive evidence to show that using formoterol and budesonide together not only significantly improves health-related quality of life, but also, if the improvement in clinical indices is also maintained, improvement in health-related quality of life is sustained," continues Professor Juniper.

The new FACET quality of life data were obtained by repeatedly assessing 470 patients from five countries (Belgium, Canada, Holland, Luxembourg and the UK), using the Asthma Quality of Life Questionnaire (AQLQ), a very sensitive indicator of how asthma limits people's lives.

The AQLQ scores settled after two-three months very much in the same steady state patterns as the conventional clinical indices. However, the greatest improvements in HRQoL were measured in the group of patients receiving a twice-daily dose of 400 micrograms Pulmicort plus 12 micrograms Oxis (the 'Bud800+F' group). When looking at the whole group, improvements in HRQoL matched improvements in clinical outcomes;

after randomisation, the best degree of asthma control, as measured by symptoms, lung function and fewer exacerbations, were achieved in the 'Bud800+F' group.

"When looking at the individual patient, some people with only small improvements in their clinical indices felt much better with treatment, while others with considerable clinical improvement did not feel much better. However, this does not negate the conclusions drawn from the patient population taken as a whole. The FACET data clearly demonstrates that treatment with formoterol and budesonide together produces a significant and sustained improvement in quality of life in asthma, which is excellent news for people with this condition," says Professor Juniper.

The study authors also analysed the FACET data in terms of the number of patients that would need to be treated with a twice-daily dose of 400 micrograms Pulmicort plus 12 micrograms Oxis for one patient to have a clinically meaningful improvement in their asthma quality of life. The figure derived was 12 patients, which compares favourably with the number of patients needed to be treated with cholesterol-lowering drugs to prevent a stroke, which is more than 200 - a form of clinical intervention that is recommended in many treatment guidelines worldwide.

Professor Juniper summarises the study findings by saying: "The AQLQ provides an excellent measure of the components of asthma that are most important to patients; it has been suggested that it should be included in all asthma studies. The long-term benefits that patients themselves experience, in terms of their physical, social, occupational and emotional functioning, cannot be inferred from conventional clinical measurements of asthma control and severity; they must be measured directly using validated quality of life questionnaires," she concludes.

Notes to Editors:

Inhaled corticosteroids are now widely recommended as first line therapy for the control of persistent asthma. The FACET study used the corticosteroid Pulmicort (budesonide) from AstraZeneca, which has a high local anti-inflammatory effect in the lungs, and added AstraZeneca's new fast-acting and long-lasting beta2-agonist Oxis (formoterol).

Both types of drug were administered via Turbuhaler, the dry powder inhaler system invented by Astra. Patients find Turbuhaler easy to use, and it has the advantage of more effective delivery of the inhaled drug to the lungs, when compared to corresponding pressurised metered dose inhalers, and is also free from potentially irritating propellants or lubricants.

FACET was a double blind, parallel group study involving 852 people in nine countries - Belgium, Canada, Holland, Israel, Italy, Luxembourg, Norway, Spain and the UK. Participants were randomly assigned to one of four twice daily treatment groups (total daily doses given): budesonide 200 micrograms plus placebo (BUD 200); budesonide 200 micrograms plus a dose of 24 micrograms formoterol (BUD 200+F); budesonide 800 micrograms plus placebo (BUD 800); or budesonide 800 micrograms plus formoterol 24

micrograms (BUD 800+F), following a run-in period of 4 weeks in which their asthma was stabilised using a high dose of 1600 micrograms per day of budesonide only. (see diagram) For the budesonide Turbuhaler, the nominal dose (the dose on the package labelling) is the same as the metered dose (the dose contained within and dispatched from the dosing unit in the inhaler); the delivered dose (the one leaving the inhaler when it is activated) is 75% of the metered dose. In contrast, for the formoterol Turbuhaler, the labelling, ie the nominal dose, is based on the delivered dose rather than the metered dose. For example, a formoterol Turbuhaler with a metered dose of 12 micrograms actually delivers 9 micrograms of active drug and 9 micrograms appears on the label.

The Asthma Quality of Life Questionnaire (AQLQ) has previously been shown to accurately detect changes in patients who respond to treatment, or who have natural fluctuations in their asthma ($p<0.001$), and to differentiate these patients from those who remain stable ($p<0.001$). 3

When using the AQLQ, patients answer questions about the five most important activities that have been limited by their asthma during the last two weeks. They were also asked about discomfort and distress caused by their asthma, coughing, worries about the availability of their medication, and feelings of frustration as result of their asthma.

AstraZeneca provides a range of products for the treatment of respiratory diseases:

* Bricanyl Turbuhaler(r) (terbutaline)
* Oxis Turbuhaler(r) (formoterol)
* Pulmicort Turbuhaler(r) (budesonide)
* Salbutamol Turbuhaler(r) (salbutamol)
* Rhinocort Turbuhaler(r) (budesonide for rhinitis and recurrent polyps in the nose)
* Accolate(r) (zafirlukast)
* Bambec(r) (bambuterol)

References

1. Juniper EF et al. Asthma quality of life during 1 year of treatment with budesonide with or without formoterol. *European Respiratory Journal* 1999; **14**: 1-6.

2. Pauwels RA *et al.* Effect of inhaled formoterol and budesonide on exacerbations of asthma. *NEJM*. 1997; **337** (20): 1405-1411.

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Patricia O'Connor
CPR Worldwide
Tel: +44 171 282 1200
Fax: +44 171 282 1282