AstraZeneca

SD-037-0699

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Oxis®

ACTIVE INGREDIENT: formoterol

Trial title (number): Real life effectiveness of Oxis Turbuhaler as needed in asthmatic patients during six months (RELIEF).

Development phase:III

First subject recruited: 17 April 2000

Last subject completed: 24 June 2001

Approval date: 14 December 2001

OBJECTIVES

Primary objectives:

Toassess the safety of Oxis® Turbuhaler® 4.5µg/inhalation as needed. The secondary objective was to compare the efficacy of Oxis Turbuhaler 4.5µg/inhalation as needed with salbutamol pMDI 200µg/inhalation as needed (or equivalent dose in dry powder inhaler (DPI)).

METHODS

Study Design:

Multi-national, multi-centre, randomised, open, parallel-group design.

Diagnosis and Main Criteria for Inclusion/Exclusion

This study included subjects with asthma of any severity, aged ≥ 6 years, who used or were candidates for receiving a β_2-agonist as reliever medication. Any ordinary asthma medication, except other reliever medication and any change in prescribed medication, was allowed.

Test Product, Dosage and Mode of Administration

Oxis (formoterol) Turbuhaler 4.5µg/inhalation as needed (delivered dose, corresponding to 6µg/inhalation metered dose).

Comparator Product, Dosage and Mode of Administration

Salbutamol pMDI 200µg/inhalation as needed (or equivalent dose in DPI). Details of inhalation device at country level are available separately.

Duration of Treatment

Six months.

Main Variable(s)

- Safety

The primary safety variables were non-asthma-related and asthma-related serious adverse events (SAEs) and discontinuations due to adverse events (DAEs).

- Efficacy

The primary efficacy variable was time to first asthma exacerbation. An exacerbation was defined by one or more of the following: hospitalisation due to asthma, emergency treatment with nebulized β_2-agonist or glucocorticosteroid (GCS) injection, a course of oral GCS lasting at least five days for a deterioration of asthma, or an increase in maintenance asthma medication due to deterioration in asthma. A severe exacerbation was defined as any of the above except for a change in maintenance medication. Secondary variables were change in concomitant maintenance asthma medication during the study, number of inhalations of study drug, number of days with asthma symptoms, health care resource utilisation and number of days when incapable of conducting normal activities due to asthma.

STATISTICAL METHODS

Treatment differences regarding number of subjects experiencing at least one SAE or DAE in respective subcategory was expressed as odds ratios and tested using aχ2-test. Information regarding adverse events (AEs) in general was analysed by means of descriptive statistics. Time to first asthma exacerbation was analysed using a Cox proportional hazards model adjusting for treatment, asthma medication level at baseline, age class and regional belonging. The distribution of asthma medication level at end of study was compared using a generalised linear model (GLM) (proportional odds) adjusting for treatment and baseline asthma medication level. Use of study drug and days with asthma symptoms was compared between treatments using a linear mixed effects model (LINMEM) adjusting for treatment, period and interaction treatment by period. Number of health care resource utilisation and number of days unable to conduct normal activities due to asthma was compared between treatments using an analysis of variance (ANOVA) model adjusting for treatment, country and time in study. Primarily, the full group was analysed. All treated subjects with data collected during the treatment period were eligible for analysis. Subjects receiving the incorrect study drug (during the complete study) were treated in the analysis as if they had received the correct drug. Data were also analysed stratified for baseline asthma medication level, age class, regional belonging, gender and smoking habits.

RESULTS

SUBJECTS			
	Oxis Turbuhaler	Salbutamol	Total
No. planned	7500	7500	15000
No. randomised	9064	9060	18124
Males/Females	3942/5122	3798/5262	7740/10384
Mean age (range)	39 (5–91)	39 (4–91)	39 (4–91)
No. analysed for efficacy	8924	8938	17862
No. analysed for safety	8924	8938	17862
No. completed	8260	8413	16673

Safety Results

No statistically significant difference in the number of SAEs (including deaths) was detected between the treatments. Overall, AEs, including DAE, do not give rise to any safety concerns. No clinically important treatment-related safety findings were identified. It can be concluded that Oxis Turbuhaler has a safety profile similar to that of salbutamol when used as needed for the relief of asthma symptoms.

Efficay Results

There was a statistically significant difference in time to first asthma exacerbation in favour of the Oxis group for all asthma exacerbations (hazard ratio 0.86, 95% C.I. 0.82-0.91), severe exacerbations and the subcategories emergency treatments, oral GCS courses and increased asthma maintenance medication. There was a statistically significant shift in asthma medication levels towards reduced asthma maintenance treatment in the Oxis group. The use of study drug and the number of days with asthma symptoms were statistically significantly reduced in the Oxis group.

REFERENCES

Pauwels RA, Sears MR, Campbell M, Villasante C, Huang S, Lindh A, Petermann W, Aubier M, Schwabe G, Bengtsson T. Formoterol as relief medication in asthma: a worldwide safety and effectiveness study.Eur Respir J 2003; 22(5): 787-794.

As with any comprehensive clinical trial programme, individual studies may include both approved and non-approved treatment regimens, including doses higher than those approved for clinical use. Before prescribing Oxis® (formoterol), Healthcare Professionals should view their specific country information.