Clinical Study Report Synopsis

Drug Substance	Budesonide/Formoterol
Study Code	D5890L00027
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SYMBICORT MAINTENANCE AND RELIEVER THERAPY, EXPERIENCE IN REAL LIFE SETTING IN MALAYSIA - "SMARTER" STUDY

Study dates:	First subject enrolled: 17 January 2008 Last subject last visit: 21 November 2008
Phase of development:	Therapeutic use (IV)
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This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

Study centre(s)

This study was conducted in 10 government hospitals in Malaysia.

Publications

Roslina AM et al, Satisfaction Levels and Asthma Control in Malaysian Patients on Symbicort Maintenance and Reliever Therapy: Experience in Real-Life Setting (SMARTER study); Respirology (2009) 14, (Suppl.3) PO 010 2009-361

Objectives and criteria for evaluation

Table S1 Primary and secondary objectives and outcome variables

Objectives	Outcome variables	Type
Primary	**Primary**	
To evaluate satisfaction level from a patient's perspective using Symbicort SMART compared with a subject's previous therapy, by assessment of the changes in the Satisfaction in Asthma Treatment Questionnaire Scores (SATQ) in partially controlled and uncontrolled asthmatic subjects.	Change in the SATQ scores from baseline (Visit 2) to the mean of visits 3 and 4.	Efficacy
Secondary	**Secondary**	
To compare Symbicort SMART with a subject's previous therapy, by assessment of the changes in the Asthma Control Questionnaire (ACQ) in uncontrolled asthmatic subjects	Change in ACQ scores from baseline (Visit 2) to the mean of visits 3 and 4. Change in ACQ scores from baseline (Visit 2) to Visit 3.	Efficacy

Study design

This is an open-label single arm local study to evaluate patient satisfaction levels with Symbicort SMART treatment in a real-life setting

Target subject population and sample size

Male or female patients aged > 18 years with confirmed diagnosis of asthma for the past 6 months and on regular treatment with inhaled glucocorticosteroids for the past 3 months. Patient's classified as partially controlled or uncontrolled asthma as defined by the GINA 2006 Guidelines and on a daily dose of 200 – 1000 mcg beclomethasone dipropionate or 100 – 500 mcg fluticasone or 200 – 800 mcg of budesonide or equivalent for at least 4 weeks.

Investigational product and comparator(s): dosage, mode of administration and batch numbers

Budesonide 160 µg/inhalation and formoterol fumarate dihydrate 4.5 µg/inhalation.

Treatment will be initiated with one or two inhalation twice a day of Symbicort® Turbuhaler® (160/4.5 µg /inhalation). In addition they will use Symbicort® Turbuhaler® (160/4.5 µg /inhalation) as required (prn), in response to symptoms. Further instructions on treatment will be in accordance with the approved label for Symbicort SMART.

Batch Numbers: 1H 2029 & KB 2243

Duration of treatment: 6 months

Statistical methods

All hypothesis testing were done using two-sided alternatives. P values less than 5% were considered statistically significant. 95% confidence intervals were calculated.

The difference in SATQ (overall and domain scores) between baseline (visit 2) and the mean of visits 3 and 4 was analysed by a paired t-test. For subjects who discontinued before visit 4, data up to the point of discontinuation was used to estimate response to treatment. No minimal clinically important difference (MCID) has yet been established for the SATQ.

The ACQ was analysed using the same methods as for the SATQ. A change of 0.5 (from baseline to the mean of visits 3 and 4) was deemed to represent the MID for the ACQ. Based on a MID of 0.5 established for the ACQ, subjects were categorised as either improved (change in ACQ $\leq$-0.5), worsened (change in ACQ $\leq$ +0.5) or no change (-0.5 < change in ACQ < +0.5).

As secondary outcome variables, the difference in SATQ (overall) and ACQ between baseline and visit 3 was analysed separately using paired t-test.

SAEs and DAEs were summarized in frequency tables.

Subject population

Number of patients: 201

Number planned: 200

Number analyzed: 195

Summary of efficacy results

The primary efficacy end point indicated by the change of overall SATQ score from baseline of the mean of visits 3 and 4 increased by 0.37 and the result was statistically significant for the ITT population

The secondary efficacy end points indicated by the change in ACQ overall scores from baseline (Visit 2) to the average of Visits 3 and 4 reduced by 0.97 and the result was statistically significant. The ACQ result showed that in 61.5%, 67.7% and 63.6% of patients, asthma condition improved at Visit 3, Visit 4 and average of Visit 3 and 4 respectively. Based on GINA 2006 guidelines, there were 142 patients (72.82%) were partly controlled and 53 patients (27.18%) were uncontrolled during baseline visit. Meanwhile 106 patients (53.36%) and 131 patients (67.18%) were reported to have their asthma at controlled level at visit 3 and visit 4. There were 72 patients (36.92%) and 45 patients (23.08%) reported with partly controlled asthma at visit 3 and 4, while 17 patients (8.72%) and 19 patients (9.74%) were reported with uncontrolled asthma level.

Summary of safety results

There were no deaths reported in this study. There were 30 SAEs reported out of which 10 were reported to be causally related. There were 17 patients reported with serious adverse events (SAEs).